Section A-Research paper

Causes of Early and Late of Native Arterial-Venous Fistula Creation Failure

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Abstract

Background: Chronic kidney disease represents is considered a major public health burden. Hemodialysis is the most common renal replacement therapy and requires a well-functioning vascular access (VA) to provide the 300–500 mL/min of blood considered necessary for an effective and efficient treatment**.** The creation of a native Arteriovenous Fistula (AVF) is currently the gold standard to obtain a safe and reliable VA for Hemodialysis (HD) treatment**.** We planned this study to identify the main causes of native A-V fistula creation failure. This study conducted at 24 patients with ESRD on regular hemodialysis the Vascular Surgery Department, Zagazig University Hospital. Age ranged from 20 to 75 with mean ± SD = 50.62 ± 17.6. Number of male patients in the study population was 10 (41.67%). Number of patients with DM in the study population was 9 (37.50%). Number of patients with maturation before 6 weeks in the study population was 16 (66.67%). Number of patients with maturation after 6 weeks in the study population was 6 (25%). Number of patients with start of dialysis before shunt creation was 19 (79.17%). Number of patients with start of dialysis after shunt creation was 4 (16.67%). Number of patients with hand exercise was 19 (79.17%). The majority of patients had a functioning fistula within 6 weeks of creation. However, a significant proportion of patients experienced complications such as thrombosis, hematoma, and pseudoaneurysm, which can contribute to early or late fistula failure. Also, most patients had a proximal brachiocephalic fistula created for vascular access.

Abbreviations: Renal failure, dialysis, vascular access, arteriovenous fistula.

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Introduction

Chronic kidney disease represents the 19th cause of worldwide mortality and is considered a major public health burden [(1)].

Hemodialysis is the most common renal replacement therapy currently available and requires a well-functioning vascular access (VA) to provide the 300–500 mL/min of blood considered necessary for an effective and efficient treatment [(1, 2)].

The creation of a native Arteriovenous Fistula (AVF), consisting of the surgical shunt of a vein into an artery, is currently the gold standard to obtain a safe and reliable VA for Hemodialysis (HD) treatment [(3)].

The first procedure was performed by Brescia and Cimino in 1966 and the surgical procedure has been optimized in the past few decades [(4)].

A-V fistula creations failure causes can be divided into two main group: early (primary) failure and late (secondary) failure.

- Primary failure refers to those accesses that never adequately mature to support HD treatment due to a lack of vascular remodeling (outward remodeling and/or venous arterialization) after creations.

- Secondary failure refers to those accesses that have been successfully used for treatment but suffer from

post-maturation stenosis due to an uncontrolled neo-intimal hyperplasia (IH) development, albeit not adequately compensated by outward remodeling (inward remodeling) **(5).**

Despite the numerous factors involved in AVF failure, the overall failure mechanism is not clear. The current hypothesis addresses both biological and mechanical (hemodynamically-related) aspects of the A-V Fistula failure **(6)**.

Pre-existent CKD, diabetes, and hypertension are known to affect the vascular biology **(3, 6)** of patients undergoing the creation of an AVF and may enhance the failure risk **(7).**

Mechanical aspects involved in AVF remodeling are mainly related to the pressure drop that occurs at the AVF anastomosis and to the change in wall shear stress (WSS) exerted on the endothelium due to altered hemodynamics caused by AVF creation **(6, 8)**.

The aim of this study to identify the main causes of native A-V fistula creation failure to improve the selection of patients.

2. Patients and Methods

This prospective cohort study was conducted on 24 patients with ESRD on regular hemodialysis or preparing for regular hemodialysis. Patients were recruited from the Vascular Surgery Department, Zagazig University Hospital.

2.1 Inclusion criteria:

Patients of different ages (not younger than 18) and genders with ESRD requiring maintenance hemodialysis, first time to do A-V fistula in upper limb.

2.2 Exclusion criteria:

- Children (age younger than 18).
- Patients with peripheral ischemia in the target limb.
- Patients with current cardiac problem affected by the shunt.

2.3 Methods:

All patients were subjected to the following:

I. Complete history taking:

Including personal, complaint, present, past, and family history

II. Clinical examination:

Full clinical examination either general examination or local A-V fistula examination by inspection, palpation, and auscultation.

III. Ultrasonography:

- Radiological examination of the A-V fistulabefore operation.
- Careful follow up postoperatively by duplex ultrasonography.

2.4 Surgical procedure:

An AV fistula is a connection that's made between an artery and a vein for dialysis access. A surgical procedure, done in the operating room, is required to stitch together two vessels to create an AV fistula. The access point must be durable enough to withstand dialysis treatment several times a week without collapsing.

Statistical methodology

All data were collected, tabulated and statistically analyzed using IBM SPSS Statistics for Windows, Version 23.0. Armonk,NY: IBM Corp.).

Quantitative data were expressed as the mean ± SD &median (range), and qualitative data were expressed as number and percentage.

Mann Whitney u test was used between two groups not normally distributed, variable. Percent of categorical variables were compared using Chi-square test or Fisher exact test when appropriate.

All tests were two sided. p-value< 0.05 was considered statistically significant and p-value ≥ 0.05 was considered statistically insignificant.

3. Results

The study included 51 patients; 26 of them (51%) were females and 25(49%)males. Mean age of all patients was 47.27 years, ranging from 20-75years.

Table (1): Demographic characters in studied group

Variables	**The studied group (51)**	
	n.(51)	**%**
Sex Females Males	 26 25	 51.0% 49.0%
Age(years): mean ± SD (Range)	 47.27±17.72 (20-75)	

Table (2) showed that thrombosis has been found in 8 patients (1%), hematoma in 4 patients (7.8%), pseudo aneurysm in 3 patients (5.9%) and one patient develop steal syndrome.

Table (2): Distribution of post shunt complications among studied group

Complications n.16		**n.**	**%**
Thrombosis	**yes** **No**	8 43	15.7 84.3
Hematoma	**yes** **No**	4 47	7.8 92.2
Pseudo aneurysm	**yes** **No**	3 48	5.9 94.1
steal	**yes** **No**	1 50	1.9 98.1

Table (3) showed that mean duration of shunt functional maturation was 8.41 weeks with range from 4 to 16 weeks. While there were 10 patients (19.6%) failed to develop functional maturation shunt.

Table (3): Mean functional maturation time among studied group

Time of functional maturation (weeks)	**The studied group (51)**	
functional maturation time mean ± SD (Range)	 8.41±4.24 (4-16)	
	n.(51)	**%**
functional maturation mature Failed or non mature	 41 10	 80.4% 19.6%

In table (4), there was not significant relation between smoking, diabetes mellitus, hypertension or ischemic heart disease and maturation time of shunt, p>0.05.

Table (4): Relation between patients with functional maturation time below or equal to 6 weeks and above 6 weeks regarding smoking and medical history

Variables	**Functional maturation time**				χ^2	**p-value**
	dialysis≤ 6 weeks n.19		**Dialysis > 6weeks n.22**			
	No.	**%**	**No.**	**%**		
Smoking						
yes	7	36.8	8	36.4	0.001	0.97
No	12	63.2	14	63.6		
Diabetes mellitus						
Yes	6	31.6	11	50.0	1.42	0.233
No	13	68.4	11	50.0		
Duration of diabetes years					u	
Median(range)	18(7-30)		9(2-23)		0.153	0.126
Hypertension						
Yes	15	78.9	11	50.0	3.68	0.055
No	4	21.1	11	50.0		
Ischemic heart disease						
Yes	5	26.3	6	27.3	0.005	0.95
No	14	73.7	16	72.7		

χ 2 Chi square test, u: Mann Whitnney u test, p>0.05: non-significant

In table (5), there was not significant relation between type of shunt and its functional maturation time , p>0.05.

Table (5): Relation between time of functional maturation and type of shunt

Variables	**Functional maturation time**				χ^2	**p-value**
	dialysis≤ 6 weeks n.19		**Dialysis > 6weeks n.22**			
	No.	**%**	**No.**	**%**		
Type of shunt						
Brachial dependent	11	57.9	15	68.2	0.465	0.475
Radial dependent	8	42.1	7	31.8		

χ 2 Chi square test p>0.05: non-significant

Table (6) defined that there is no significant relation between type of shunt and medical history of studied patients, p>0.05.

Table (6): Relation between type of shunt & medical history

Variables	Type of shunt				χ^2	p-value
	Brachial dependent n.26		Radial dependent n.15			
	No.	%	No.	%		
Age per years Median (range)	55(20-71)		50(26-75)		U 0.32	0.74
Sex						
Males	14	53.8	8	53.3	0.001	0.97
Females	12	46.2	7	46.7		
Smoking						
Yes	7	26.9	8	53.3	2.86	0.091
No	19	73.1	7	46.7		
Diabetes mellitus						
Yes	12	46.2	6	40.0	0.146	0.702
No	14	53.8	9	60.0		
Duration of diabetes per years Median (range)	12(5-22)		15(2-30)		0.15	0.88
Hypertension						
Yes	17	65.4	9	60.0	0.119	0.73
No	9	34.6	6	40.0		
Ischemic heart disease						
Yes	7	26.9	5	33.3	0.198	0.66
No	19	73.1	10	66.7		

χ 2 Chi square test u :Mann Whitney u test p>0.05: non-significant

In table (7), there was not significant relation between age or sex and occurrence of failed shunt, p>0.05.

Table (7): Relation between successful or failed shunt regarding demographic data

Variables	Shunt				Test of sig	p-value
	Success n.41		failed n.10			
	No.	%	No.	%		
Age per years Median(range)	52(20-75)		42(20-63)		u 0.36	0.71
Sex						
Males	22	53.6	3	30.0	F	0.16
Females	19	46.4	7	70.0		

u :Mann Whitney u test f:Fisher exact test p>0.05: non-significant

In table (8), there was no significant relation between medical history of patients and shunt failure, p>0.05.

Table (8): Relation between successful or failed shunt regarding smoking and medical history

Variables	**Shunt**				**Test of sig**	**p-value**
	Success n.41		**failed n.10**			
	No.	**%**	**No.**	**%**		
Smoking						
Yes	15	36.6	1	10.0	F	0.14
No	26	63.4	9	90.0		
Diabetes mellitus						
Yes	17	41.5	5	50.0	F	0.73
No	24	58.5	5	50.0		
Duration of diabetes per years Median(range)	12(2-30)		8.5(3-18)		U 0.12	0.901
Hypertension						
Yes	26	63.4	7	70.0	F	0.99
No	15	36.6	3	30.0		
Ischemic heart disease						
Yes	11	26.8	4	40.0	F	0.45
No	30	73.2	6	60.0		

u :Mann Whitney u test f:Fisher exact test p>0.05: non-significant

In table (9), there was no significant relation between patients previous history of dialysis and shunt failure, p>0.05.

Table (9): Relation between successful or failed shunt regarding previous history of dialysis

Variables	**Shunt**				**fp-value**
	Success n.41		**failed n.10**		
	No.	**%**	**No.**	**%**	
Catheter vascular axis					
Yes	30	73.2	7	70.0	0.99
No	11	26.8	3	30.0	
Site of shunt					
Same site of shunt	18	43.9	4	40.0	0.99
opposite site of shunt	23	56.1	6	60.0	
Shunt					
Brachial dependent	26	63.4	4	40.0	0.28
Radial dependent	15	36.6	6	60.0	
Before shunt					
Yes	33	80.5	6	60.0	0.22
No	8	19.5	4	40.0	

u :Mann Whitney u test f:Fisher exact test p>0.05: non-significant

4. Discussion

autogenous arteriovenous fistulae (AVF) are known to be the preferred vascular access for hemodialysis in patients with end-stage renal disease [9].

An arteriovenous fistula (AVF) is the preferred access type due to its superior patency rates and fewer complications compared with arteriovenous grafts and catheters [10]. However, the patency of this access type is far from optimal with primary patency rates ranging from 44 to 60% [11].

The main cause of AVF primary failure is considered to be the stenosis at the juxta-anastomotic venous segment.8 This is mainly related to intimal hyperplasia,6 which is thought to be triggered by turbulent flow generated at the anastomotic site [12].

The geometrical characteristics of the anastomosis determine the hemodynamic pattern of the AVF [13]**.** In fact, an anastomosis angle between 40° and 50° was associated with lower hemodynamic stress at the level of the vein wall, namely it reduced wall shear stress and turbulent flow [14]**.**

An AVF is deemed mature if after 6 weeks it supports a flow of 600 mL/ min, it is located 6 mm from the surface of the skin and has a diameter greater than 6 mm [15]**.** Inadequate dilation or outward remodelling is a leading cause of maturation failure and is a factor that is often overlooked [16].

Venous stenosis is the other leading cause of failure; it is a form of inward remodelling which is characterized by abnormal intimal hyperplasia which reduces the lumen area [17].

The abnormal hemodynamics arising from fistula creation are believed to provide a stimulus for both facets of remodeling. An important feature of AVF hemodynamics that is often overlooked is the pressure gradient between the artery and vein. The pressure drop across an AVF is tightly linked to instabilities that arise at the anastomosis and is considered a global indicator of the overall hemodynamics of a fistula [18].

The aim of this study was to identify the main causes of native A-V fistula creation failure to improve the selection of patients, to observe outcome of A-V fistula creations in the matter of success and failure and to assess the most important cause of A-V fistula creations failure.

This study conducted at 24 patients with ESRD on regular hemodialysis the vascular surgery department, Zagazig University Hospital during the period of the study.

Age in the study population ranged from 20 to 75 with mean ± SD = 50.62 ± 17.6. Number of male patients in the study population was 10 (41.67%). Number of Smoking patients in the study population was 7 (29.17%).

This was comparable to study done by **Sahasrabudhe et al. (2014)** in which the mean age of population was 54.58 ±14.092). Number of male patients in the study population was 279 (62.98%) Number of female patients in the study population was164 (37.02%).[19]

Other study done by **Meyer et al. (2020)** (12) found that age in the population ranged from 51 to 87.Number of male patients in the study population was 15 (36.6%). Number of female patients in the study population was 26 (63.4%).[20]

Similarly, **Schinstock et al. (2011)** found that 293 patients underwent 317 procedures for AVF creation. The patients' mean age was 65.1 ± 16.8 years (mean ± SD), 191 patients were male (65.2%).[21]

As regard to chronic illness among the study population , number of patients with DM in the study population was 9 (37.50%). Duration of DM in the study population ranged from 7 to 30 with mean ± SD = 18 ± 7.46. Number of patients with HTN in the study population was 19 (79.17%). Number of patients with IHD in the study population was 8 (33.33%).

Other study done by **Bahrami-Ahmadi et al. (2022)** found There was no statistically significant relationship between the history of diabetes and early AVF failure risk inESRD patients. Furthermore, the history of hypertension was significantly lower in the early failure of AVF group, although this effect faded when using regression analysis. [22]

On the contrary, diabetes was associated with a higher risk of AVF failure. In this regard, **Jeong et al. (2019)** reported higher mortality rates and worse AVF patency rates in diabetic patients vs. non-diabetic patients undergoing hemodialysis. [23]

Our results showed that number of patients with Catheter dialysis in the study population was 22 (91.67%). Number of patients with same site of shunt in the study population was 14 (58.33%). Number of patients with opposite site of shunt in the study population was 20 (83.33%).

In study done by **Robbin et al. (2002)** found that fistula adequacy for dialysis doubled if the minimum venous diameter was 0.4 cm or greater (89% [24 of 27]) versus less than 0.4 cm (44% [12 of 27]; $P < .001$). Fistula adequacy for dialysis was nearly doubled if flow volume was 500 mL/min or greater (84% [26 of 31]) versus less than 500 mL/min (43% [nine of 21]; $P = .002$). Combining venous diameter and flow volume increased fistula adequacy predictive value: minimum venous diameter of 0.4 cm or greater and flow volume of 500 mL/min or greater (95% [19 of 20]) versus neither criterion met (33% [five of 15]; $P = .002$). [24]

Our results showed that number of patients with maturation before 6 weeks in the study population was 16 (66.67%). Number of patients with maturation after 6 weeks in the study population was 6 (25%). **Meyer et al. (2020)** found that the maturation rate was 85.4% at 6weeks. [20]

Assessment of maturation is crucial at 4–6 weeks after AVF creation for early diagnosis of immature AVF and prompt referral for radiological or surgical treatments; excellent results are obtained using endovascular treatments to dilate stenotic lesions (the main cause of non-maturating AVF), or open surgical repairs (proximal AVF reanastomosis in anastomotic stenosis, ligature of collaterals, superficializations) [(25)]. This approach could decrease the number of patients who start hemodialysis with central venous catheters [(26)].

Regarding type of shunt among the study population, number of patients with Proximal BCF in the study population was 13 (54.17%). Number of patients with Distal RCF in the study population was 12 (50%). Number of patients with failed shunt in the study population was 5 (20.83%).

Also **Mittal et al. (2016)** found that Out of 37 patients, 8 (21.62%) had distal that was radiocephalic fistula (RCF) and 29 had (78.37%) proximal with 25 (67.56%) BCF. Radial artery and cephalic vein diameter less than 1.6 mm was associated with early fistula failure. [(27)]

Meyer et al. (2020) found that Number of patients with brachiocephalic fistula was 4 (9.8%). Number of patients with Distal RCF in the study population was 9 (22.0%). Six fistulae failed within 6 weeks due to thrombosis. Four of them thrombosis within 24 h after creation and two failed fistulae were identified 5 weeks after creation. [(20)]

Regarding start of Dialysis among the study population, number of patients with start of dialysis before shunt creation in the study population was 19 (79.17%). Number of patients with start of dialysis after shunt creation in the study population was 4 (16.67%).

Similarly **Wilmink et al. (2016)** found that AVF created before patients started dialysis had significantly better survival. The pre-dialysis state at AVF operation resulted in 13% more functional dialysis use.More importantly, the pre-dialysis state at the time of AVF creation is modifiable by better pre-dialysis organization and timely access planning. [(28)] However**, Wilmink et al. (2015)** discrepancy with our results that some 658 (55%)] patients were on dialysis at the time of AVF creation. [(28)]

Also **Wilmink et al. (2017)** found that number of patients with start of dialysis before shunt creation in the study population was 536 (46%). Number of patients with start of dialysis after shunt creation in the study population was 631 (54%).[(29)]

Regarding operative complications incidence among the study population, number of patients with thrombosis in the study population was 7 (29.17%). Number of patients with hematoma in the study population was 3 (12.50%). Number of patients with pseudo aneurysm in the study population was 3 (12.50%). Number of patients with wound infections in the study population was 0 (0%).

On the other hand, **Gupta et al. (2022)** found that the overall complication rate in this study was 22.22%. The most common complications were distal limb edema (10.3%) and thrombosis (8.7%). Other complications included aneurysm formation1 (0.46%), bleeding due to clip slippage, hematoma formation 3(1.39%) and the most common complication in our study thrombosis was 7 (29.17%).[(30)]

Similarly, **Schinstock et al. (2011)** found that complications included bleeding (33.0%, 27 of 82), infection (26.8%, 22 of 82), steal syndrome (18.3%, 15 of 82), aneurysm (8.5%, 7 of 82), thrombosis (4.9%, 4 of 82), seroma (4.9%, 4 of 82), subclavian stenosis (2.4%, 2 of 82), and nerve injury (1.2%, 1 of 82). Among the 78 AVFs with primary failure, 24.4% resulted in at least one complication. [(31)]

Our results agreement with **Dember et al. (2008)** who found that the primary outcome was fistula thrombosis, determined by physical examination at 6 weeks. The secondary outcome was failure of the fistula to become suitable for dialysis. Fistula thrombosis occurred in 53 (12.2%) participants assigned to clopidogrel compared with 84 (19.5%) participants assigned to placebo (relative risk, 0.63; 95% confidence interval, 0.46-0.97; P = .018). [(32)]

Similarly, **Fokou et al. (2012)** found that Aneurysms, failure to mature and thrombosis were the most frequent complications occurring in 26.54%.[(33)]

Our results agreement with **Manjunath et al. (2021)** who found that the other complications encountered in this study were post-operative thrombosis in 15/194 (7%) of the patients until 8 weeks of follow-up. There were 15 cases (7.7%), which had post-operative thrombosis. [(34)]

Our results showed that Hand exercise among the study population. Number of patients with hand exercise in the study population was 19 (79.17%).

The pre-operative isometric hand exercise was an effective way to enhance AVF maturation, improve blood flow in the AVF, and decrease morbidity associated with vascular access [(35)]**.**

Chen, et al. (2022) suggested that recommend arm and hand exercises before and after creating a new AVF to accelerate the maturation or maintenance of the AVF. Several studies have described increased blood flow and acceleration of this process resulting from exercise training programs. [(36)]

The current study showed that there was not significant relation between age or sex and maturation time of shunt, $p>0.05$.

In concordance with the current study **Hakim et al. (2022)** revealed that there was no significant

association between maturation time of shunt with age or sex. [37]

As well, consistent with the current study **Gasparin et al. (2022)** showed that there was no significant association between shunt maturation with age or sex. [38] Similar results were reported by **Abreu (2022).** [39]

Also, in agreement with the current study, **Bashar et al. (2016)** showed that there was no significant association between maturation time of shunt with age. But vin contrast to the current study female gender showed significant association with non-maturation (P = 0.004) and was the only predictor for non-maturation in a logistic regression model (P = 0.011). [40]

Regarding comorbidities, the current study showed that there was no significant relation between smoking, diabetes mellitus, hypertension or ischemic heart disease and maturation time of shunt, p>0.05.

In agreement with the current study, **Bashar et al. (2016)** showed that there was no significant association between functional maturation of shunt with smoking, diabetes mellitus, hypertension, dyslipidaemia, CAD, and ischemic heart disease. [40]

The present study showed that there was not significant relation between type of shunt and its functional maturation time, p>0.05. In agreement with the current study, **Khan et al. (2015)** found no significant association between shunt type and shunt maturation. [41]

Regarding the relation between type of shunt and medical history, it was revealed that there was no significant relation between type of shunt and medical history of studied patients, p>0.05.

To our knowledge this is the first study assessed the relation between type of shunt and medical history.

The present study showed that there was no significant association between shunt failure with age or sex.

In agreement with the current study **Gonzalez et al. (2017)** showed that neither age nor sex were independently associated with shunt failure. [42] As well, **Anderson et al. (2018)** revealed that age and sex were no significantly associated with 30-days shunt failure among HD children and adults. [43]

The current study showed that there was no significant relation between medical history of patients and shunt failure, p>0.05. In agreement with the current study, **Gasparin et al. (2022)** found no association between shunt maturation failure and medical history. [38]

The present study also showed that there was no significant relation between shunt failure and Catheter vascular axis, shunt site, shunt type and previous shunt(p>0.05 all).

In agreement with the current study **Anderson et al. (2018)**[43] revealed that shunt type was non significantly associated with 30-days shunt failure among HD adults. However, **Gonzalez et al. (2017)** showed that the revision groupwas significantly more likely to experience shunt failure compared to the initial-placement group (14vs. 8%, p < 0.0001). [42]

5. Conclusion and Recommendations

Our results showed that the majority of patients in the study population had a functioning fistula within 6 weeks of creation. However, a significant proportion of patients experienced complications such as thrombosis, hematoma, and pseudoaneurysm, which can contribute to early or late fistula failure. The data also indicates that the majority of patients in the study population had a proximal brachiocephalic fistula created for vascular access.

The current study found no association between patients' demographics and medical history with shunt maturation time or shunt failure.

Type of shunt have no significant impact on the time of functional maturation.

Patients' demographics and medical history were not determinants of the selection of the shunt type.

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