

Pre-operative Duplex and Intra-Operative Venography to Assess the Integrity of the Central Veins in Patients Undergoing Arteriovenous Fistulae

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Introduction: Increasing the prevalence of End stage renal disease (ESRD) patients requiring hemodialysis has resulted in increased dialysis access procedures performed by vascular surgeons. This should be preceded by duplex examination to ensure central venous outflow. Central venous stenosis (CVS) is the most common cause access failure.

Aim of work: Was to study incidence and characteristics of CVS among ESRD patients using preoperative duplex "DUS" and intraoperative venography.

Patients and methods: Prospective study of 100 patients. Patients were excluded in cases of connective tissue disorders, cardiac ejection fraction < 50%, contrast allergy, pregnancy or arterial insufficiency.

Pre-shunt duplex assessment and CVS was diagnosed by direct and indirect signs. Under Regional or Local anesthesia, intraoperative venography as the vein was cannulated and imaged under C-arm fluoroscopy. If there was no CVS, AVF was created, but if there was CVS, operation was aborted for elective management. Characteristics of CVS was registered regarding characteristics (Stenosis or occlusion).

Results: Preoperative duplex and intraoperative venography were done to all patients to detect CVS. The new arteriovenous access was done immediately in cases of free CVS. 24% of the patients had CVS by preoperative duplex and 32% had CVS by duplex and venography and planned for further management. Unfortunately, 8 patients with duplex free of CVS appeared to have CVS by venography.

Conclusion: DUS is a very efficient tool in diagnosis of CVS or occlusion, but has a few fallacies and therefore venography could be required.

Key words: Preoperative duplex, intraoperative venography, arteriovenous fistulae.

Introduction

End stage renal disease (ESRD) is a significant public health problem. Increasing the prevalence of patients requiring hemodialysis has resulted in increased dialysis access procedures which become one of the most common operations performed by vascular surgeons. ESRD patients usually require multiple hemodialysis accesses probably due to the delay in diagnosis and the low rates of renal transplantation leading to multiple insertion of central venous dialysis catheter (CDC) prior to arteriovenous (AV) shunt creation.^{1,2}

There are three types of vascular accesses for hemodialysis; arteriovenous fistula (AVF), arteriovenous graft (AVG) and central dialysis catheter (CDC) which may be either temporary or permanent catheters (Permacath). The arteriovenous accesses could be primary access which is constructed for the first time for Dialysis ,Secondary access which is constructed after a failed fistula or graft and utilizes the conversion of an arterialized outflow vein to a direct or transposed access and the tertiary access which is made after failure of primary and secondary accesses (Arterio-arterial Prosthetic loop).³

An Arteriovenous fistula (AVF) provides a direct connection between the artery and the vein

allowing the vein to dilate and mature. So that it may be accessed repeatedly for hemodialysis. The AVF is generally accepted as the preferred method for long-term dialysis access as it provides excellent blood flow for dialysis and has a complication rate lower than the other access types.⁴ This should be preceded by a duplex ultrasound examination to determine which veins are patent, the diameter of these veins and the quality of the veins in the examined limb. Arterial inflow can be assessed to ensure an adequate flow to both the access and to the hand.⁵

Although discouraged in previous Kidney Disease Outcomes Quality Initiative (K-DOQI) and European best practice guidelines (EBPG), Central venous dialysis catheters (CDC) as access for chronic hemodialysis are being increasingly used in hemodialysis units. The advantage of central venous catheters is that these devices can be quickly and easily inserted and provide immediate access for hemodialysis. These guidelines also discourage the use of catheters unless other options are unavailable. Indeed, some authors recommend a 'catheter-last' approach after having exhausted all avenues.^{4,6}

Central venous cannulation can lead to the development of central venous stenosis (CVS). It is

expected that venous cannulation leads to intimal injury associated with focal endothelial denudation, increased smooth muscle cells and vein wall thickening. The rapid blood flow associated with the hemodialysis catheter can create turbulence that accelerates endothelial proliferation, eventually leading to central venous stenosis. Construction of a peripheral AVF in these patients can cause massive arm swelling and poor dialysis caused by the high incidence of venous stenosis near the catheter insertion site. The high venous pressure and blood flow due to the fistula may overwhelm the collateral venous and lymphatic drainage, resulting in the development of dilated and tortuous collateral veins over the ipsilateral upper arm, neck and upper chest. In severe cases, venous hypertension may eventually lead to disabling arm edema with pain and discomfort. Venous hypertension is a recognized complication of arteriovenous fistula and graft formation. Many of these complications are secondary to a central vein stenosis or the formation of a side to side anastomosis for the AVF. Nowadays, most arteriovenous fistulas are made in an end to side fashion to omit venous hypertension and arm swelling. Moreover, stenosis of the venous outflow may lead to venous hypertension.^{7,8}

Aim of work

The aim of this work was to study the incidence and characteristics of central venous outflow obstruction among ESRD patients who require primary or secondary or tertiary AV access by using preoperative duplex ultrasound "DUS" and intraoperative central venography in Alexandria Main University Hospital during the period from November 2020 to October 2022.

Patients and methods

Patients

This prospective study included 100 ESRD patients requiring AV access, patient was excluded in cases of:-

1. Congenital or acquired connective tissue disorders (e.g.: Systemic lupus, Raynaud's).
2. Cardiac disorders with ejection fraction less than 50%.
3. Absolute contraindication for IV contrast Injection (e.g. Allergy).
4. Absolute contraindication for radiology exposure (e.g. Pregnancy).
5. Peripheral upper limb arterial insufficiency.

Methods

Pre-operative DUS (Pre- shunt assessment):

Central venous stenosis was diagnosed by direct and indirect signs of central venous stenosis:

Direct signs:

- Loss of compressibility of the vein.
- Lack of color Doppler flow within the venous lumen.
- Visualization of thrombus.
- Scarring or an adjacent compressing mass on grey-scale images.

Indirect signs:

- Dampening of waveforms.
- Decreased velocities and loss of transmitted pulsatility and respiratory phasicity.
- Loss of the normal biphasic pattern and development of a non-pulsatile signal.

Intraoperative venography

All patients underwent complete access circuit venography to rule out central venous stenosis (CVS). Under regional or local anesthesia, skin incision, dissection of the vein. The vein was cannulated, then half-strength 10 to 20 mL of radiopaque dye followed by saline was injected. Vein was followed by imaging under C-arm fluoroscopy. If there was no CVS, AVF was created, but if there was CVS, operation was aborted and planned for elective management. Characteristics of central venous disease was registered regarding site, length, pattern (stenosis or occlusion), collateral venous channels, intraluminal filling defect and non-opacification of the veins. An informed consent was taken from all patients after explaining to them the steps, risks and benefits of the procedures.

The data was analyzed using the IBM SPSS version 21.0 (IBM Corp., Armonk, NY, USA). The statistical significance of differences was detected using the Student t-test, chi-square test, and Fisher exact test. All p-values < 0.05 were considered to indicate statistical significance.

Results

The study was conducted on one hundred ESRD patients fulfilling the inclusion criteria. All studied patients were evaluated in this study; 62 patients (62%) were male, 38 patients (38%) were female. The mean age (\pm SD) was 56 ± 13 years. 72% of these patients were hypertensives, 32% smokers, 20% diabetics and 80 % of them had history of CDC insertion. The history of CDC insertion was the highest risk factor predisposing to the development of CVS and venous hypertension. (**Table 1**).

In our study, only twenty patients had no history of

CDC insertion, 50 had history of contralateral CDC insertion, 20 patients had history of bilateral CDC insertion and 10 patients had history of ipsilateral CDC insertion. Significant results were noticed that the largest percentage of patients had history of contralateral CDC insertion in relation to the side of shunt creation as shown in **(Table 2)**.

Regarding the site of insertion of CDC, 20 % had no history of CDC insertion, 50 % had history of jugular CDCs and 30% had history of subclavian CDCs. Thus the tendency of jugular CDC insertion appeared to be higher than subclavian CDC insertion as seen in **(Table 3)**.

According to the AV access, 42% of patients were primary, 46 % were secondary and 12 % were tertiary as shown in **(Table 4)**.

Preoperative duplex and intraoperative venography were done to all patients to detect central venous stenosis (CVS). The new AV access was done immediately after both the duplex and venography were free from CVS. During the study, 76 % of the patients had no CVS by the preoperative duplex, 68 % had no CVS by venography. Thus 24 % of the patients had CVS by preoperative duplex and 32 % had CVS by duplex and venography and were planned for future elective management. Surprisingly, 8 patients with duplex free of CVS appeared to have CVS by venography and procedure was aborted as shown in **(Table 5)**.

All the patients signed consent for the study and contrast injection, no cases had any form of contrast reaction. History of CDC insertion was taken into consideration, 30% of patients with history of CDC insertion had CVS by preoperative duplex, and 40 % of those patients had CVS by venography that confirmed that history of CDC insertion is the most important cause for development of CVS as shown in **(Tables 6,7)**.

The preoperative duplex showed highest level in accuracy in detection of CVS in cases with history of multiple ipsilateral CDC insertion with significance (P value < 0.001) of the frequency and side of CDC insertion in the development of CVS. Furthermore, the results revealed that incidence of CVS detected by duplex in cases of history with subclavian catheter (significant P value < 0.001) was higher than that with jugular catheter (less significant P value 0.008) and this indicated the efficacy of preoperative duplex in diagnosis of CVS. Moreover, absence or single CDC insertion history revealed no risk for development of CVS detected by preoperative duplex.

Incidentally, Most of the cases with history of CDC insertion were with jugular contralateral CDCs as recommended by nephrologists to save the side of

the future AV access in a trial to reduce any risk of venous hypertension. Generally, Most of our findings regarding the accuracy of preoperative duplex taking into consideration history, site, side and frequency of CDC insertion showed very significant results with significant P values.

On the other hand, regarding intraoperative venography, Remarkable results were noticed; putting into consideration the history of CDC insertion including site, side and frequency. Venography appeared to be more significant and more accurate in detection of CVS than preoperative duplex in all aspects with significant P value < 0.05 where 8 cases were missed by duplex and were diagnosed correctly by venography **(Table 7)**.

Among 100 patients, 32 patients were detected by venography to have CVS and they had history of multiple CDC insertion where 24 patients out of them had subclavian CDC history while 8 patients had jugular CDC history. Although out of 80 patients with history of CDC insertion, only 30 patients were with history of subclavian catheters while the rest 50 patients had history of jugular catheters with significant P value (0.002). This showed the higher risk of CVS with subclavian catheter insertion that should be avoided as shown in **(Table 7)**.

Equally, both the preoperative duplex and intraoperative venography showed the same results in exclusion of CVS in patients without history or with history of single of CDC with significant P value < 0.05.

Central vein catheterization was studied also according to the side of the future AV access in relation to detection of CVS by venography where significant P value < 0.05 was observed in both ipsilateral and bilateral CDCs.

Regarding the AV access type in relation to CVS development, preoperative duplex showed CVS with significant P value < 0.001, especially in patients seeking secondary AV access with P value < 0.001, but the results were not significant due to the small number of patients seeking tertiary AV cases only 12 cases and in those seeking primary AV access, only two cases were detected to have CVS by duplex and 6 cases detected by venography out of 42 cases as shown in **(Table 8)**.

The accuracy of preoperative duplex compared to intraoperative venography in detection of CVS was significant about 92% especially showing highest accuracy about 95% in cases seeking secondary AV access with highly significant P value < 0.001. While in cases seeking primary AV access, the results were nearly accurate with borderline significant P value = 0.143.

Table 1: Distribution of the studied cases according to demographic data and risk factors (n = 100)

	No.	%
Age (years)		
Min. – Max.		14.0 – 72.0
Mean ± SD.		52.14 ± 13.58
Median		56.0 (47.0 – 60.0)
Sex		
Male	62	62.0
Female	38	38.0
Risk factors		
Hypertension	72	72.0
Diabetes	20	20.0
Smoking	32	32.0
History of CDC insertion	80	80.0

Table 2: Distribution of the studied cases according to side of CDC insertion related to future AV access side (n = 100)

	No.	%
Side of CDC insertion		
• No	20	20.0
• Contralateral	50	50.0
• Ipsilateral	10	10.0
• Bilateral	20	20.0

Table 3: Distribution of the studied cases according to Site of CDC insertion (n = 100)

	No.	%
Site of CDC insertion		
No	20	20.0
Jugular	25	50.0
Subclavian	30	30.0

Table 4: Distribution of the studied cases according to AV access (n = 100)

AV access	No.	%
Primary	42	42.0
Secondary	46	46.0
Tertiary	12	12.0

Table 5: Distribution of the studied cases according to incidence of CVS detected by preoperative duplex and intraoperative venography (n = 100)

	No.	%
Preoperative duplex		
No CVS	76	76.0
CVS	24	24.0
Venography		
No CVS	68	68.0
CVS	32	32.0

Table 6: Relation between CDC insertion with CVS findings by preoperative duplex (n = 100)

	Preoperative duplex			
	No CVS (n = 76)		CVS (n = 24)	
	No.	%	No.	%
History of CDC insertion				
Negative	20	26.3	0	0.0
Positive	56	73.7	24	100.0
Side of CDC insertion				
No	20	26.3	0	0.0
Contralateral	48	63.2	2	8.3
Ipsilateral	0	0.0	10	41.7
Bilateral	8	10.5	12	50.0
Site of CDC insertion				
No	20	26.3	0	0.0
Jugular	46	60.5	4	16.7
Subclavian	10	13.2	20	83.3
Frequency of CDC insertion				
No	20	26.3	0	0.0
Once	20	26.3	0	0.0
Many	36	47.4	24	100.0

Table 7: Relation between CDC insertion with CVS findings by intraoperative venography (n = 100)

	Venography			
	No CVS (n = 68)		CVS (n = 32)	
	No.	%	No.	%
History of CDC insertion				
Negative	20	29.4	0	0.0
Positive	48	70.6	32	100.0
Side of CDC insertion				
No	20	29.4	0	0.0
Contralateral	44	64.7	6	18.8
Ipsilateral	0	0.0	10	31.3
Bilateral	4	5.9	16	50.0
Site of CDC insertion				
No	20	29.4	0	0.0
Jugular	42	61.8	8	25.0
Subclavian	6	8.8	24	75.0
Frequency of CDC insertion				
No	20	29.4	0	0.0
Once	20	29.4	0	0.0
Many	28	41.2	32	100.0

Table 8: Agreement (sensitivity, specificity and accuracy) for CVS detection by preoperative duplex compared to venography in each AV access

		Venography				Sensitivity	Specificity	PPV	NPV	Accuracy
		No CVS		CVS						
		No.	%	No.	%					
Primary AV access	Preoperative duplex	(n = 36)		(n = 6)						
	No CVS	36	100.0	4	66.7	33.33	100.0	100.0	90.0	90.48
	CVS	0	0.0	2	33.3					
	χ^2 (FEp)	6.300 (0.143)								
Secondary AV access	Preoperative duplex	(n = 30)		(n = 16)						
	No CVS	30	100.0	2	12.5	87.50	100.0	100.0	93.75	95.65
	CVS	0	0.0	14	87.5					
	χ^2 (FEp)	18.867* (<0.001*)								
Tertiary AV access	Preoperative duplex	(n = 2)		(n = 10)						
	No CVS	2	100.0	2	20.0	80.0	100.0	100.0	50.0	83.33
	CVS	0	0.0	8	80.0					
	χ^2 (FEp)	2.400 (0.333)								
Total sample	Preoperative duplex	(n = 68)		(n = 32)						
	No CVS	68	100.0	8	25.0	75.0	100.0	100.0	89.47	92.0
	CVS	0	0.0	24	75.0					
	χ^2 (FEp)	33.553* (<0.001*)								

χ^2 : Chi square test.

FE: Fisher Exact.

P: p value for comparison between different categories.

*: Statistically significant at $p \leq 0.05$.

PPV: Positive predictive value.

NPV: Negative predictive value.

Discussion

Results achieved with ESRD patients who made preoperative duplex compared to intraoperative venography, which central venous stenosis findings by duplex were closely accurate to that detected by intraoperative venography. Furthermore, this study showed that 24 patients out of 100 patients were diagnosed to have CVS by preoperative duplex, and 32 cases were diagnosed accurately by intraoperative venography with significant P value less than 0.001. Unfortunately, only in a few patients (8 patients), the intraoperative venography is still to be more accurate than preoperative duplex in detection of CVS, and this is referred to that the duplex is operator dependent or depends on device quality or due to vessel spasm during duplex examination. Sometimes, due to the presence of many collaterals over the chest wall, the duplex may be misleading and venography should be mandatory for CVS diagnosis as shown in our study. One case of the CVS was missed by the duplex and diagnosed by venography and this was due to the presence of large tortuous venous collateral that compensated the stenosis and the venous hypertension, and this might explain the survival of the fistula for a

while but all ended with failure due to progressing subclavian vein occlusion.^{9,10}

Our study showed statistically significance in incidence of CVS with history of CDC insertion clarifying that the most important risk factor for development of CVS is central venous catheterization. This finding was also found with Georgiadis GS et al,¹¹ that aimed to identify the incidence of CVS in patients with history of CDC insertion and concluded that the key to decrease the incidence and prevalence of CVS is in reducing CDC placement for dialysis before AVF creation.

Yoo DW et al,¹² found that central venous cannulation may initiate central venous stenosis. This was mainly attributed to the insertion of an ipsilateral central venous catheter, but it might also occur without a previous history of contralateral catheter insertion. As regards to this study, central venous stenosis was higher in patients with ipsilateral and bilateral CDCs insertion (26%) than those with contralateral catheter insertion (6%). This explained the tendency of most of the nephrologists not to insert CDCs at the side of the planned AV access to avoid the risk of development of CVS.

It was noted by Ferring M et al,¹³ that turbulence of the blood flow caused by hemodialysis catheter may lead to intimal damage accompanied with localized endothelial baring, development of more smooth muscle cells and venous wall thickening resulting in central venous stenosis. According to the site of CDC placement in relation to development of CVS. Our study showed that patients with subclavian catheters had higher risk than those with jugular catheters. This was mentioned that 25% of patients with CVS by venography had jugular CDC while 75% had subclavian CDC. These results also matched with Galt S et al,¹⁴ stated that creation of a peripheral AV fistula in those patients might cause massive arm swelling and inefficient dialysis when temporary dialysis catheters were inserted in the subclavian veins. Repeated central vein cannulation and CDC insertion is also considered a prime risk factor for development of CVS and this met our results where all the cases without history or with a single history of CDC insertion (40%) had no CVS while those with multiple CDCs insertion (60%) had.

The study of Georgiadis GS et al,¹¹ aimed to determine specific criteria and data for a clinically remarkable central vein outflow disorder with duplex (DUS) in ESRD patients and organized the use of duplex in these cases. Moreover, Bakhshoude B et al,¹⁵ conducted their study from February to October 2015 on ESRD patients undergoing upper limb venography and they saw that the diagnostic value of venography in the detection of subclavian stenosis had 88% sensitivity and 90% specificity especially in the superior vena cava. Fraum TJ et al,¹⁶ concluded that Venography based on its marvelous sensitivity, specificity, and predictive value, should be used as an effective method in the study of central venous stenosis mainly in subclavian veins and superior vena cava.

Al-Jaishi AA et al,¹ suggested that central venous stenosis might be clinically evident in the formation of tortuous and dilated venous collateral circulation over the ipsilateral arm, upper chest and neck predisposing to venous hypertension and severe pain. Fedorova E et al,¹⁷ assumed that vascular access stenosis might cause thrombosis, frequent infections, decreased blood flow and impaired hemodialysis. Many complications could make the arteriovenous access unusable despite of various efforts to save the access by endovascular and/or surgical treatment modalities, leaving no other option except to close the vascular access.

Conclusion

DUS is a very efficient tool in diagnosis of central venous outflow disorder whether stenosis or occlusion prior to arteriovenous fistulae creation, but has fallacies in some cases especially in patients with history of multi access failure or multi central

catheter insertion, so venography should be applied for those patients and not routinely in all patients as a higher tool for imaging of central venous outflow. It is suggested to have a venoplasty set up plan to correct the detected central venous stenosis instead of losing the cannulated vein.

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Conflicts of interest

There are no conflicts of interest.

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