

# Lesion Type Analysis of Hemodialysis Patients Who Underwent Endovascular Management for Symptomatic Central Venous Disease

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**Purpose:** Central venous lesions (CVLs) can adversely affect hemodialysis access maturation and maintenance, which in turn worsen patient morbidity and access circuit patency. In this study, we assessed several clinical variables, patient characteristics, and clinical consequences of symptomatic central vein stenosis and obstruction in patients who underwent renal replacement therapy in the form of hemodialysis.

**Patients and Methods:** The medical records of all hemodialysis patients with clinically symptomatic CVLs who underwent digital subtraction angiography treatment at King Abdullah University Hospital between January 2017 and December 2019 were retrieved. Patient characteristics and the clinical and anatomical features of CVLs were analyzed retrospectively. Pearson's chi-square tests of association were used to identify and assess relationships between patient characteristics and CVLs.

**Results:** The study cohort comprised 66 patients with end-stage renal disease who developed symptomatic central vein stenosis. Of the 66 patients, 56.1% were men, and their mean age was approximately 52 years. Most (62.1%) of the patients were determined to have a history of central catheter insertion into the jugular vein. Hypertension was the most common comorbidity (78.8%,  $p < 0.001$ ), followed by type 2 diabetes mellitus (47.0%,  $p < 0.01$ ). The incidence of stenosis was found to be significantly higher in the brachiocephalic vein than in other central veins (43.9%,  $p < 0.001$ ). A repeated central catheter insertion in a patient was predictive of central venous occlusion ( $p < 0.05$ ). Stenotic lesions were found to be associated with a significantly higher success rate than occlusive lesions (91.2%,  $p < 0.01$ ).

**Conclusion:** Multiple central venous catheters (CVCs) are found to be associated with occlusive CVLs and unfavorable recanalization outcomes. Multiple CVC should be avoided by creating a permanent vascular access in a timely fashion for patients with chronic kidney disease and by avoiding the ipsilateral insertion of CVC and AVF.

**Keywords:** central venous lesions, brachiocephalic vein, central line catheterization, percutaneous transluminal angioplasty, fistula, hemodialysis

## Introduction

Central venous lesions (CVLs) are somewhat clinically overlooked, and their true incidence is likely underestimated<sup>1-3</sup> In developing countries such as Jordan, a lack of access monitoring protocols and surveillance of access-related issues serves as a challenge to access circuit patency. Consequently, diagnosis is limited to symptomatic patients with intractable complications that are mostly related to upper limb edema and inadequate dialysis. The clinical manifestations of CVLs can be subtle

and covert, but they may become clinically cumbersome when a clinically silent CVL is uncovered during vascular access creation.<sup>1,4,5</sup> The symptoms observed may include arm swelling, ipsilateral breast and neck swelling, visible venous collaterals, and loss of access circuit patency.<sup>1,5,6</sup> The severity of symptoms remains to be unpredictable and poorly understood.<sup>2</sup> Studies on various patient-, intervention-, and access-related features such as previous central catheterizations, venous collaterals, lesion-related characteristics (eg, lesion location including stenotic and obstructive lesions), access flow, and type and site of vascular access have been published.<sup>2,4,7–10</sup> Furthermore, the etio-pathogenesis of CVLs was determined to be multifactorial and controversial. Proposed mechanisms of CVL development include endothelial trauma due to repeat catheterizations, uremic milieu, flow dynamics with increased shear stress, platelet dysfunction, and intimal hyperplasia with fibrotic response, and these mechanisms may act synergistically.<sup>1,11</sup>

Access circuit complications (mostly due to sepsis and stenosis of access outflow) account for 20–30% of dialysis patient hospitalizations.<sup>12</sup> Pre-emptive treatment of clinically silent CVLs is not recommended, and there is a paradigm shift toward treatment using current modalities of only symptomatic lesions that result from rapid progression of stenotic segments following intervention and from disappointing long-term intervention-free period.<sup>13,14</sup>

The aim of this study was to retrospectively assess hemodialysis patients with symptomatic CVLs. A digital subtraction angiography was used to assess and treat symptomatic CVLs. Cohort demographics, lesion type, catheter- and non-catheter-related lesions, and procedural outcomes were analyzed to identify correlations between CVLs and these variables.

## Materials and Methods

### Patients

We retrospectively assessed the demographic characteristics of 66 hemodialysis patients who underwent endovascular treatment for CVLs between January 2017 and December 2019. The following data are extracted from our university hospital electronic medical records: demographics, type and site of vascular access, location and nature of CVL, history of central venous catheterization, indications for central venous interventions, and the outcomes of each intervention. Patient consent was waived as data was used in aggregate with no personal identifiers.

## Lesion Characteristics

According to the Society of Interventional Radiology classification, central veins include intrathoracic segments of internal jugular veins (IJVs), subclavian veins (SCVs), brachiocephalic veins (BCVs), and superior vena cava (SVC).<sup>15</sup> CVL diagnosis was made based on clinical and radiological data. Patients with debilitating symptoms of edema in the affiliated limb, breast, and face and with inadequate dialysis were included in our analysis. CVLs were then diagnosed using digital subtraction angiography. Radiologically, all selected CVLs were referenced to the adjacent upstream normal vein to assess the degree of stenosis. A stenosis of greater than 50% in a central intrathoracic vein was considered an indication for treatment. In this study, patients with thrombosed access or <50% stenosis were excluded, and compression by extrinsic structures was not examined. Additionally, patients with pacemaker interventions were excluded to avoid the confounding effect of the pacemaker.

## Procedural Success

Percutaneous endovascular management was initiated by placing a vascular sheath under ultrasound guidance into the main draining vein of the fistula or via the venous side of the graft in the symptomatic arm. Right common femoral vein approaches were used in cases of complete central venous occlusion that cannot be crossed using the venous outflow approach. Our standard approach to central vein stenosis in hemodialysis patients was high-pressure plain balloon angioplasty (PBA) as first-line therapy, with reference to adjacent normal-looking veins in order to accurately assess balloon size. Additionally, the balloon was carefully inflated with concern to the patient's pain complaint during dilatation. Intravenous heparin was administered at a range of 3000–5000 IU with most patients received 3000 IU. Certain patients received 5000 IU of heparin as those were patients with AVG or obese patients with high body mass index. Angioplasty of the CVL was initially performed using high-pressure non-compliant 10–16 mm angioplasty balloons (Atlas or Conquest; Bard Peripheral Vascular Inc., Tempe, Arizona, USA). These balloons had a burst pressure of 1600–2000 kPa. Repeat balloon dilatation was performed for 3 minutes if the initial dilatation did not render stent placement unnecessary. Stents were inserted if the CVL was due to refractory angioplasty with immediate flow-limiting elastic recoil, residual stenosis >30% with

persistent and significant collaterals, or early recurrent symptomatic stenosis within 4 weeks after PBA. Self-expanding nitinol bare-metal stents (Sinus-Venous stent, OptiMed GmbH, Ettlingen, Germany) 12–18 mm in diameter and 40–80 mm in length were used. To ensure adequate stent–vessel contact, the stents were dilated using balloons of appropriate size following deployment.

Successful treatment was administered in accordance with radiological and clinical criteria. In radiological terms, success was considered as anatomical luminal gain with <30% residual stenosis and resolution of most collateral vessels. Clinical success was determined using symptom resolution and adequate dialysis. We did not use SCV dialysis catheters as per hospital policy.

## Statistical Analysis

The factors that were investigated in relation to CVLs were described using frequency distribution for categorical variables and mean  $\pm$  standard deviation for continuous variables. Pearson's chi-square ( $\chi^2$ ) tests were used to analyze the associations between categorical variables, and Student's t-tests were used for continuous variables. In addition, logistic regression analysis was used to determine the main predictors of CVL in the study model, and  $P < 0.05$  was considered statistically significant. If a substantial association was found between categorical variables, a post-hoc residual analysis was then conducted to determine the exact significance in the contingency table.

## Results

The study cohort consisted of 66 hemodialysis patients with CVLs (stenotic or occlusive). All patient characteristics and clinical presentations are summarized in Table 1. The mean age of patients was  $51.9 \pm 14.9$  years, almost 50% of the patients were 41–60 years old, and approximately 56% of the patients were men. Sixty patients (90.9%) were determined to have arteriovenous fistula (AVF), but six of these patients switched to arteriovenous graft (AVG) after failed AVF. Another six patients had AVG from the beginning without AVF creation. With regard to comorbidities, there was a significantly high prevalence of hypertension (78.8%,  $P < 0.001$ ) and type 2 diabetes mellitus (47.0%,  $P < 0.01$ ). Interestingly, 41 of the 66 patients (62.1%) had a history of central venous catheterization. The duration from initiation of hemodialysis until symptomatic CVL was widely ranged among the patients from 1 to 36 months, with a median duration of

6 months. The most commonly affected solitary vein was the BCV (43.9%,  $P < 0.001$ ), and more than a third of the cases (36.4%) involved a combination of more than one central vein. Nineteen out of 24 combined cases (28.8% of total patients) had contiguous CVLs that spanning two or more veins as follows: 9 cases involved contiguous stenosis for both SCV and BCV, 9 cases BCV and SVC, and 1 case involved the three veins IJV, SCV, and BCV at their junction. The anatomical distribution of the CVLs is described in Figure 1.

## Factors Affecting Lesion Type

There was no significant difference in the number between patients with partial stenosis (39/66, 59.1%) and patients with total occlusion (27/66, 40.9%) (Table 1). Further, no significant differences were determined in terms of sex, age, comorbidities, and affected central vein between these two patient groups (Table 2). However, patients with two central vein dialysis catheters were more likely to have an occlusive lesion than a stenotic lesion ( $P < 0.05$ ). The technical outcomes after the intervention were documented for 56 of the 66 patients. The rate of successful recanalization was significantly ( $P < 0.01$ ) higher in patients with stenosis (31/34, 91.2%) than in patients with occlusion (12/22, 54.5%). The results of the comparison between patients with central venous stenosis and patients with central venous occlusion are summarized in Table 2.

In addition, a binary logistic regression model that included all the variables in Table 2 was also performed. The regression analysis revealed that patients with central venous occlusion had a significantly (6.35 times) higher risk of recanalization failure than patients with central venous stenosis did ( $P < 0.05$ ).

## Factors That Determine the Side of CVLs

A summary of the factors that determine the side of a CVL is provided in Table 3. No significant associations were determined in terms of sex, age, or affected vein with relation to the lesion side. However, we found a significant correlation between the number of CVLs and the anatomical distribution of these lesions, ie, if a patient is suffering from three synchronous lesions both ipsilateral and contralateral central veins will be affected compared to patients having two lesions where synchronous lesions tend to lateralize to one body side ( $P < 0.05$ ). Furthermore, there were significant associations between the side of the lesion and the sides of the catheter and

**Table 1** Characteristics and Clinical Presentations of Hemodialysis Patients with Central Vein Disease

Associated Variables	Number	Percent (%)
	Mean ± SD	
<b>Sex</b>		
Male	37	56.1
Female	29	43.9
<b>Age (y)</b>	51.9 ± 14.9	
<b>Age category</b>		
Young adults (21–40 y)	15	22.7
Old adults (41–60 y)	31	47.0
Seniors (61–80 y)	20	30.3
<b>Comorbidities</b>		
Diabetes mellitus	31	47.0 <sup>a1††</sup>
Hypertension	52	78.8 <sup>a1†††</sup>
Dyslipidemia	15	22.7
Stroke	4	6.1
Myocardial infarction	13	19.7
Peripheral vascular disease	6	9.1
<b>Duration of hemodialysis (y)</b>	6.8 ± 4.1	
<b>Type of central vein lesion</b>		
Stenosis	39	59.1
Occlusion	27	40.9
<b>Number of lesions/patient</b>		
1	42	63.6
2	20	30.3
3	4	6.1
<b>Side of the lesion</b>		
Right	29	43.9
Left	35	53.0
Both	2	3.0
<b>Affected vein</b>		
Subclavian	10	15.2
Internal jugular	1	1.5
Brachiocephalic	29	43.9 <sup>b1†††</sup>
Superior vena cava	2	3.0
Combined (more than one vein)	24	36.4
<b>Patients with previous central line catheterization</b>	41	62.1
<b>Number of central line catheters per patient</b>		
0	25	37.9
1	30	45.4
2	10	15.2
More than 2	1	1.5

(Continued)

**Table 1** (Continued).

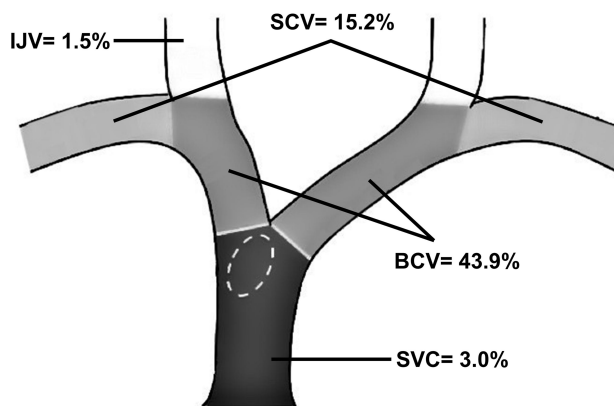
Associated Variables	Number	Percent (%)
	Mean ± SD	
<b>Side of central line catheterization</b>		
Right	19	46.3
Left	14	34.2
Both	8	19.5
<b>Presence of AVF</b>	60	90.9
<b>Side of the AVF</b>		
Right	20	33.3
Left	31	51.7
Both	9	15.0
<b>Presence of AVG</b>	6	9.1

**Notes:** <sup>a1††</sup>Significantly higher than expected frequency of comorbidity ( $P < 0.01$ ,  $\chi^2$ ; AR = 3.2). <sup>a1†††</sup>Significantly higher than expected frequency of comorbidity ( $P < 0.001$ ,  $\chi^2$ ; AR = 9.3). <sup>b1†††</sup>Significantly higher than expected frequency for this vein ( $P < 0.001$ ,  $\chi^2$ ; AR = 5.4).

**Abbreviations:** AVF, arteriovenous fistula; AVG, arteriovenous graft; SD, standard deviation; y, years.

fistula as CVLs tend to develop on the ipsilateral side of the catheter and fistula ( $P < 0.01$ ).

In addition, a multinomial logistic regression model that included all the variables in Table 3 was used. The regression analysis revealed that the side of the AVF was the only significant predictor of the side of the lesion ( $P < 0.05$ ). For example, patients with left-sided fistulae were found to have a 16.67 times higher risk of developing



**Figure 1** The anatomical distribution of solitary central vein lesions in hemodialysis patients. Combined lesions (not illustrated) contributed to 24 (36.4%) of the patients as follow: 9 (13.6%) cases involved SCV + BCV, 9 (13.6%) cases BCV + SVC, 2 (3.0%) cases SCV+BCV+SVC, 1 (1.5%) case IJV + SVC, 1 (1.5%) case IJV + BCV, 1 (1.5%) case IJV + BCV + SVC, and 1 (1.5%) case SCV + IJV + BCV.

**Abbreviations:** IJV, internal jugular vein; SCV, subclavian vein; BCV, brachiocephalic vein; SVC, superior vena cava.

**Table 2** Factors Associated with the Type of Central Vein Lesion (Stenosis Vs Occlusion) in Hemodialysis Patients

Lesion Type	Stenosis N (% from Stenosis)	Occlusion N (% from Occlusion)	P-value
<b>Sex</b>			
Male	21 (53.8)	16 (59.3)	NS
Female	18 (46.2)	11 (40.7)	
<b>Age (y), mean ± SD</b>	52.0 ± 14.8	51.7 ± 15.4	NS
<b>Age category</b>			
Young adults (21–40 y)	9 (23.1)	6 (22.2)	NS
Old adults (41–60 y)	19 (48.7)	12 (44.4)	
Seniors (61–80 y)	11 (28.2)	9 (33.3)	
<b>Comorbidities</b>			
Diabetes mellitus	18 (46.2)	13 (48.1)	NS
Hypertension	29 (74.4)	23 (85.2)	NS
Dyslipidemia	9 (23.1)	6 (22.2)	NS
Stroke	3 (7.7)	1 (3.7)	NS
Myocardial infarction	7 (17.9)	6 (22.2)	NS
Peripheral vascular disease	4 (10.3)	2 (7.4)	NS
<b>Number of lesions per patient</b>			
1	26 (66.7)	16 (59.3)	NS
2	10 (25.6)	10 (37.0)	
3	3 (7.7)	1 (3.7)	
<b>Affected vein</b>			
Subclavian	8 (20.5)	2 (7.4)	NS
Internal jugular	0 (0.0)	1 (3.7)	
Brachiocephalic	16 (41.0)	13 (48.1)	
Superior vena cava	2 (5.1)	0 (0.0)	
Combined (more than one vein)	13 (33.3)	11 (40.7)	
<b>Previous central line catheterization</b>	24 (61.5)	17 (63.0)	NS
<b>Number of central line catheters per patient</b>			
0	15 (38.5)	10 (37.0)	NS
1	20 (51.3)	10 (37.0)	NS
2	3 (7.7)	7 (25.9) <sup>†</sup>	0.04
More than 2	1 (2.6)	0 (0.0)	NS
<b>Presence of AVF</b>	35 (89.7)	25 (92.6)	NS
<b>Technical outcome (recanalization)</b>			
Success	31 (91.2) <sup>††</sup>	12 (54.5)	< 0.01
Fail	3 (8.8)	10 (45.5) <sup>††</sup>	

**Notes:** <sup>†</sup>( $P<0.05$ ), <sup>††</sup>( $P<0.01$ ): significantly higher than expected frequency,  $\chi^2$ .

**Abbreviations:** AVF, arteriovenous fistula; N, number; NS, not significant; P, probability; SD, standard deviation; y, years.

**Table 3** Factors Associated with the Side of the Central Vein Lesion in Hemodialysis Patients

Lesion Side	Right N (%)	Left N (%)	Both N (%)	P-value
<b>Sex</b>				
Male	18 (62.1)	19 (54.3)	0 (0.0)	NS
Female	11 (37.9)	16 (45.7)	2 (100.0)	
<b>Age (y)</b>				
Mean ± SD	48.6 ± 13.8	54.6 ± 15.8	50.5 ± 12.0	NS
<b>Age category</b>				
Young adults (21–40 y)	8 (27.6)	7 (20.0)	0 (0.0)	NS
Old adults (41–60 y)	16 (55.2)	13 (37.1)	2 (100.0)	
Seniors (61–80 y)	5 (17.2)	15 (42.9)	0 (0.0)	
<b>Number of lesions per patient</b>				
1	17 (58.6)	25 (71.4)	0 (0.0)	0.043
2	11 (37.9)	8 (22.9)	1 (50.0)	
3	1 (3.4)	2 (5.7)	1 (50.0) <sup>†</sup>	
<b>Affected vein</b>				
Subclavian	3 (10.3)	7 (20.0)	0 (0.0)	NS
Internal jugular	1 (3.4)	0 (0.0)	0 (0.0)	
Brachiocephalic	11 (37.9)	18 (51.4)	0 (0.0)	
Superior vena cava	2 (6.9)	0 (0.0)	0 (0.0)	
Combined (more than one vein)	12 (41.4)	10 (28.6)	2 (100.0)	
<b>Catheterization side</b>				
Right	14 (73.7) <sup>††</sup>	5 (23.8)	0 (0.0)	0.003
Left	2 (10.5)	12 (57.1) <sup>††</sup>	0 (0.0)	
Both	3 (15.8)	4 (19.0)	1 (100.0) <sup>†</sup>	
<b>Side of AVF</b>				
Right	17 (63.0) <sup>††</sup>	3 (9.7)	0 (0.0)	<0.001
Left	6 (22.2)	24 (77.4) <sup>††</sup>	1 (50.0)	
Both	4 (14.8)	4 (12.9)	1 (50.0)	

**Notes:** <sup>†</sup>( $P<0.05$ ), <sup>††</sup>( $P<0.01$ ): significantly higher than expected frequency,  $\chi^2$ .

**Abbreviations:** AVF, arteriovenous fistula; N, number; NS, not significant; P, probability; SD, standard deviation; y, years.

a CVL on the left-hand side of the body than on the right-hand side of the body.

## Central Catheter-Related Factors

No significant association was found between CVC placement and sex or affected vein. However, a significant association was found between catheter installation and age category ( $P<0.05$ ). The number of young adult patients aged 21–40 who needed a CVC was less than



**Table 4** Factors Associated with Installation of a Central Venous Catheter in Hemodialysis Patients with Central Vein Disease

Central Venous Catheter	Yes N (%)	No N (%)	P-value
<b>Sex</b>			
Male	23 (56.1)	14 (56.0)	NS
Female	18 (43.9)	11 (44.0)	
<b>Age (y)</b>			
Mean $\pm$ SD	52.3 $\pm$ 13.4	51.2 $\pm$ 17.5	NS
<b>Age category</b>			
Young adults (21–40 y)	6 (14.6) <sup>†</sup>	9 (36.0)	0.04
Old adults (41–60 y)	22 (53.7)	9 (36.0)	NS
Seniors (61–80 y)	13 (31.7)	7 (28.0)	NS
<b>Comorbidities</b>			
Diabetes mellitus	21 (51.2)	10 (40.0)	NS
Hypertension	33 (80.5)	19 (76.0)	NS
Dyslipidemia	13 (31.7) <sup>†</sup>	2 (8.0)	0.03
Stroke	3 (7.3)	1 (4.0)	NS
Myocardial infarction	9 (22.0)	4 (16.0)	NS
Peripheral vascular disease	3 (7.3)	3 (12.0)	NS
<b>Affected vein</b>			
Subclavian	5 (12.2)	5 (20.0)	NS
Internal jugular	1 (2.4)	0 (0.0)	
Brachiocephalic	19 (46.3)	10 (40.0)	
Superior vena cava	1 (2.4)	1 (4.0)	
Combined (more than one vein)	15 (36.6)	9 (36.0)	
<b>Presence of AVF</b>			
Yes	41 (100.0) <sup>††</sup>	19 (76.0)	< 0.001
No	0 (0.0)	6 (24.0)	
<b>Technical outcome</b>			
Success	26 (74.3)	17 (81.0)	NS
Fail	9 (25.7)	4 (19.0)	

**Notes:** <sup>†</sup>( $P < 0.05$ ), <sup>††</sup>( $P < 0.01$ ): significantly higher than expected frequency,  $\chi^2$ .  
<sup>‡</sup>( $P < 0.05$ ): significantly less than expected frequency,  $\chi^2$ .

**Abbreviations:** AVF, arteriovenous fistula; N, number; NS, not significant; P, probability; SD, standard deviation; y, years.

expected (Table 4). Patients with dyslipidemia were found to have a significantly higher association with CVC placement than patients without dyslipidemia ( $P < 0.05$ ). Finally, all patients with a CVC ( $n = 41$ ) also had an AVF ( $P < 0.01$ ). A summary of the variables affecting central vein catheterization is presented in Table 4.

## Discussion

To the best of our knowledge, this is the most comprehensive study of its kind in the Middle East and North Africa region that analyzed the contemporary management of CVLs. The

association between patient demographics and the onset of central vein disease has not been well substantiated in literature, and sex, age, and comorbidities are possible prognostic variables that may predict disease progression.<sup>16</sup> Sex distribution was comparable in our study, whereas other earlier studies reported that women were more susceptible to CVL development than men.<sup>16–18</sup> Further, age at hemodialysis initiation was reported to provide a more comprehensive picture of the distribution of lesion onset.<sup>2</sup> The mean age of patients at hemodialysis initiation in our study was  $51.9 \pm 14.9$  years, which was found consistent with the age ranges reported in other studies.<sup>10,12,19</sup> Renaud et al<sup>13</sup> concluded that older populations (age:  $75 \pm 10$  years) are more likely to have symptomatic CVLs than younger populations. Older patients usually have more comorbidities and longer catheter dwell times than younger patients, and these factors increase the duration of injury to vessel walls. In our study, more central lines were inserted into older patients than into younger patients. Our data showed that, compared to older patients (patients more than 40 years old), the number of central lines inserted into younger patients (patients less than 40 years old) was far less than expected ( $p = 0.04$ ).

Hemodialysis patients with CVL are more likely to have multiple comorbidities.<sup>20</sup> Although the results of the study by MacRae et al<sup>21</sup> suggest that there are null associations between diabetes and central venous stenosis, in a later study by Wang et al<sup>22</sup> it was reported that the risk of central venous stenosis is determined to be higher in patients with diabetes than in patients with no primary disease. However, we reckon that there is no correlation between these two comorbidities and CVL, and we suppose that the association is a coincidence as the two conditions are the most common comorbidities in the Jordanian population.

Data on the most common sites of CVLs are inconsistent.<sup>7</sup> Although several studies reported that the SCV is the most frequent site of CVLs,<sup>16</sup> others identified the BCV as the most common site of CVLs.<sup>6</sup> In a recent study, it was reported that most CVLs occurred in the BCV, and stenotic lesions were four times more common than occlusive lesions.<sup>17</sup> Oguzkurt et al<sup>8</sup> have identified important correlations between previous central vein catheterizations and SCV stenosis and between concomitant extrinsic compression and BCV lesions. We reckon that CVLs are more likely to occur in the BCV in patients who had IJV instrumentation, while SCV is the most common site of CVLs in patients who had SCV catheterization. Moreover, CVLs associated with previous central

vein catheterization usually develop faster than CVLs not associated with previous central vein catheterization.<sup>23</sup>

In this study, we compared the types of CVLs (stenotic versus obstructive). Increased frequency of central vein catheterization using >2 catheters were found to be significantly associated with occlusive lesions. Our results are in concordance with the reports in the literature. Adwaney et al<sup>19</sup> identified patients with multiple CVCs and reported an increased risk of CVL with an increased number of previous catheter exposures in these patients. Endothelial injury, hemodynamic turbulence with stasis, and prothrombotic status are fundamental components of vascular occlusion identified by Rudolf Virchow over a century ago.<sup>1</sup> Multiple central vein catheterizations were performed due to catheter malfunction, infection, or access dysfunction. The aforementioned indications are associated with exaggerated uremic environment, provoked inflammatory response, and access circuit complications in addition to direct endothelial injury from multiple instrumentations. Hernandez et al<sup>24</sup> reported a threefold increase in the incidence of CVLs in patients with documented catheter infections, which may predispose patients to stagnation and infection. Furthermore, peri-catheter sleeve and thrombus formation are suggestive of a prothrombotic environment in such patients.<sup>1</sup> Regardless of the inciting factor, a challenging CVL remains the ultimate result. Individual data on the indications for multiple central vein catheterizations in our cohort remain to be lacking; however, they are likely related to catheter dysfunction or infection. To avoid multiple CVC insertions, it is important to adopt reliable measures that maintain CVCs until a permanent vascular access is created in a timely fashion.

In renal replacement therapy, hemodialysis catheters play a vital role as a bridging solution or occasionally as a permanent resort.<sup>22,23</sup> The inclusion of right IJV catheterization in our analysis is in accordance with our hospital policy. Published literature identified the right IJV as the best access site for CVCs as it presents the shortest traversed vessel pathway with the least vessel–catheter interaction. A CVC advanced via the left IJV passes across the mediastinum for it to reach the SVC with greater vessel–catheter interaction and extra turbulence due to complex angulated paths, thereby increasing the risk of catheter-related complications. Furthermore, the left IJV usually has a smaller cross-sectional area than the right IJV, and intimate endothelial contact is inevitable.<sup>16</sup> Laterality of insertion has consistently been reported to be a predictor

of CVLs.<sup>2,25</sup> In our study, 26 of the 41 patients (about two-thirds) who underwent central vein catheterization developed an ipsilateral CVL.

However, there is a disparity in published literature regarding the effect of previous central vein catheterizations on the development of CVLs. Some authors consider previous central vein catheterization as the main cause of CVLs, while others suppose that the majority of CVLs occur in the absence of previous central vein catheterizations.<sup>7</sup> Thus, our understanding of the etiopathogenesis of CVLs continues to evolve, and a lot remains unknown. Despite being associated with approximately 50% of non-catheter-related CVLs, compression by extrinsic thoracic structures (ie, innominate vein compression syndrome) and access flow rates were not examined in this study.<sup>7,8,10</sup> The influence of non-catheter-related factors may explain the 15.2% incidence of SCV lesions in our study despite a lack of direct-vein instrumentation at this site. Additionally, from 31 patients who received AVF on the left side there were 9 patients with initial ipsilateral CVCs and 4 patients with repeated bilateral catheterization. In these 13 patients, it is challenging to predict whether the stenosis occurred due to the catheter and tended to uncover later by the flow from the fistula or it was actually initiated by the increased flow rate from the fistula itself.

Despite the adoption of fistula-first policy for renal replacement therapy in clinical practice guidelines,<sup>26</sup> our analysis revealed that dialysis was initiated in 62.1% of patients via central vein catheterization, and this is a considerably higher percentage than that in developed countries.<sup>27</sup> It is noteworthy that young age at dialysis is protective against catheterization. Younger patients are more likely to accept fistula-first policy than elderly patients who are medically depleted and therefore more likely to refuse fistula creation. Further, surgeons are more likely to turn down or defer operations on elderly patients. However, central vein catheterization was found not to be predictive of treatment outcomes of CVLs as the technical success rate of recanalization does not differ significantly between patients with previous central vein catheterization and patients without previous central vein catheterization.

The limitations of our study are mainly reflected in the data limitations encountered during retrospective analysis. One limitation of this study is that this was a single-center study. As such, the patient population in this tertiary center may be more complex and have advanced comorbidities; therefore, this is not representative of the

broader population. Another limitation of this study is its lacking data on the confounding variables (access flow rates and extrinsic compression) that were not assessed but can predict CVLs in patients with non-catheter-related CVLs. Additionally, the diagnosis of CVLs was confined to digital subtraction angiography without using CT-scan. It is agreed that the vein diameter can be better studied with CT-scan. Lastly, the technical success rate was reported to 56 patients as there were ten patients without post-interventional outcome documentation. These were elderly patients with multiple comorbidities, and living in far rural areas. It was very difficult to communicate with them as they did not attend their assigned follow-up visits and did not respond to our phone calls.

## Conclusion

The BCV was the most affected vein in our study cohort. Multiple central vein catheterizations were associated with occlusive-type CVLs, which result in unfavorable recanalization outcomes. Therefore, multiple CVC should be avoided by creating a permanent vascular access in a timely fashion for patients with chronic kidney disease and by avoiding the ipsilateral insertion of CVC and AVF. In addition, the side of AVF was found to be the main predictor of lesion side as CVLs were observed to develop more often on the ipsilateral side of the fistula. Lastly, young age was found to be protective against the initial use of CVCs. However, central vein catheterization did not affect recanalization outcomes.

## Abbreviations

CVL, central venous lesion; CVC, central venous catheter; SVC, superior vena cava; SCV, subclavian vein; BCV, brachiocephalic vein; IJV, internal jugular vein; AVF, arteriovenous fistula; AVG, arteriovenous graft.

## Consent for Publication

Not applicable. Data was used in aggregate with no personal identifiers.

## Ethics Approval and Consent to Participate

This is a retrospective cohort study in which we utilized existing data from electronic medical records. Institutional Review Board approval was obtained from Jordan University of Science and Technology. For this type of

study, formal and informed consent were waived since data was used in aggregate with no personal identifiers. The study was conducted with assurance of patient data confidentiality and in accordance to the Declaration of Helsinki and its later amendments for ethical research performance.

## Disclosure

The authors declare that they have no competing interests.

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