

Abdullah AH^{1,2},
*Besari AM^{1,2},
Kamaruddin
MI^{1,2}, Abdullah
NH^{1,2}, Ismail
MZ^{1,2}

Outcomes of Temporary Vascular Access and Factors Influencing Delayed Arteriovenous Fistula Creation

¹Department of Internal Medicine, School of Medical Sciences, Universiti Sains Malaysia, 16150 Kubang Kerian, Kelantan, Malaysia.

²Hospital Universiti Sains Malaysia, 16150, Kubang Kerian, Kelantan, Malaysia.

*Corresponding author
Dr Alwi Bin Muhd Besari
dralwi@usm.my

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Abstract – Introduction: Haemodialysis is Malaysia's main modality of kidney replacement therapy (KRT) for end-stage kidney disease patients. However, most of the patients needed for long-term KRT are initiated with intermittent haemodialysis via a central venous catheter before placement of an arteriovenous fistula (AVF) or arteriovenous graft (AVG). **Objectives:** This study aimed to identify types of vascular access among incident end-stage kidney disease patients on intermittent haemodialysis and to determine the proportion of vascular access-related complications. We also aimed to study the factors that contributed to the delay in AVF creation at our institution. **Methods:** This is a single-centre, retrospective study of CKD stage 5 patients who were initiated on intermittent haemodialysis between 1st January 2021 and 31st December 2021. Data were collected from the medical record unit of Hospital Universiti Sains Malaysia, Kubang Kerian, Kelantan. Demographic data, comorbidities, catheter-related complications, factors associated with mortality, and delayed AVF creation were analyzed using SPSS version 27. The association between types of a catheter with complication were analyzed by chi-square test. A P-value of less than 0.05 was considered statistically significant. **Results:** A total of 74 patients started on intermittent haemodialysis were identified. Of these, males were 52.7 %, and females were 47.3 %. Most patients were of Malay ethnicity, with a mean age of 55 years old. Most of them have comorbidities of hypertension 95.9%, diabetes 79.7% and ischemic heart diseases 23%. Majority of them were initiated on haemodialysis with an uncuffed femoral catheter, 93.2% and later, changed to the uncuffed internal jugular catheter, 71.6%. The highest complication seen was central line-associated bloodstream infections (CLABSI) (17.6%), followed by hematoma (8.5%). There was no significant association between the types of haemodialysis catheters used with their complications. The delay in AVF creation was due to patient's fear (36.2%) and small venous access (34%). A total of 18 patients died during this study period of which 6 were due to catheter-related complications. **Conclusion:** This study highlights complications associated with intermittent haemodialysis via CVC, mostly with bleeding and infections. The leading cause of mortality in this study is CLABSI. Practical concerns and fear contribute to delays in AVF creation. Early creation of arteriovenous fistula in pre-dialysis patients is vital in improving the outcomes of the patients.

Keywords – Intermittent haemodialysis, HD, central venous catheter, CVC, AVF, AVG, catheter-related complications

1 INTRODUCTION

End-stage kidney disease (ESKD) is a permanent chronic kidney disease. In ESKD, the kidney function has declined and can no longer function independently. For survival, a patient with ESKD must receive KRT by kidney transplantation or dialysis. Two main long-term dialysis options are haemodialysis (HD) or peritoneal dialysis (PD).

In Malaysia, it was reported 51299 ESKD patients received KRT in the year 2020 [1]. HD is the most popular therapy (86%), followed by peritoneal dialysis (10%). It was reported that only 4% of patients lived with a functioning kidney transplant at the end of 2020. The number of new kidney transplant patients was not increased over the last ten years, and the total number remained around 1800 patients only [1]. The dialysis acceptance rate in Kelantan is still low (197 per million population), which was among the lowest

with other states (Perlis and Sabah) [2]. Our centre always encounters ESKD patients who refused dialysis for various reasons. Consequently, they require emergency HD via a central venous catheter (CVC).

Intermittent HD is often performed using a CVC as a temporary measure while awaiting the establishment of definitive vascular access or when waiting for permanent vascular access maturation, as they can be easily placed and provide quick access in urgent situations. According to the National Kidney Foundation, the preferred and definitive choice for vascular access is through an arteriovenous fistula (AVF) or arteriovenous graft (AVG) [3]. AVF or AVG is recommended over CVC usage in HD patients due to the lower risk of infection [3]. Infection serves as a common indication for CVC removal in HD patients.

Besides infection, HD patients using CVC are also exposed to other short and long-term complications. The immediate complications include pneumothorax, hemothorax, arterial puncture, bleeding, and arrhythmias. The long-term complications include central vein stenosis and catheter malfunction secondary to thrombus formation, catheter kinks or malposition [4].

The delayed creation of AVF leads to the need for alternative access methods in HD. Several factors contribute to these delays, with patient-related factors being of initial importance. According to Al Farhan et al., these factors include denial of kidney disease, reluctance to accept AVF as a necessary option, fears associated with dialysis, practical concerns, and patient refusal. Insufficient pre-dialysis education and late referral to a nephrologist are additional causes of AVF creation delays [5].

This study aims to identify the different types of catheters used among incident ESKD patients initiated on intermittent HD and their complications (infections, central vein stenosis, thrombosis, and bleeding). We also want to explore the factors contributing to delayed AVF creation. The study emphasizes the importance of early vascular access for HD. The findings can guide pre-KRT counseling and provide valuable information to physicians and hospitals, benefiting the management of HD patients.

2 MATERIALS & METHODS

2.1 Data Collection

This retrospective cohort study was conducted at Hospital Universiti Sains Malaysia, Kubang

Kerian, Kelantan, Malaysia, over one year in 2021. Ethical approval was obtained from the Human Research Ethics Committee of Universiti Sains Malaysia (JEPeM Code: USM/JEPeM/22120774).

All patients who were admitted to the adult medical ward from 1st January 2021 to 31st December 2021 were screened and identified. The data was collected from the patient's medical notes obtained from the Medical Unit Record of Hospital Universiti Sains Malaysia. The data collected included age, gender, race, comorbidity, type of catheter used, duration of catheter used, complications, and any reason for delayed arteriovenous fistula creation. Delayed AVF creation is defined as initiating intermittent HD without an AVF or with an AVF created less than six months prior. Any mortality that occurs during the study period is evaluated and included in the data analysis.

The study included patients who met the following inclusion criteria: aged 18 years or older, newly diagnosed ESKD and dependent on dialysis for more than four weeks (based on RIFLE criteria), underwent intermittent HD using a central venous catheter from 1st January 2021 to 31st December 2021, and opted for HD as their long-term kidney replacement therapy and has no AVF created. On the other hand, the exclusion criteria consisted of patients receiving temporary dialysis for acute kidney injury lasting less than four weeks, patients already on long-term HD with a permanent catheter, and patients using HD catheters for conservative or palliative treatment of kidney replacement therapy. These criteria were used to select the appropriate study participants and ensure the findings' relevance and accuracy.

2.2 Statistical Analysis

All data were analyzed using Statistical Product and Service Solutions (Version 27, SPSS Inc., Chicago, IL, USA). Descriptive statistics were used to summarize the socio-demographic data of the patients. Categorical data were presented as frequency (n) and percentage (%). The association between categorical variables was analyzed by the Chi-squared test. The P-value of <0.05 was considered statistically significant.

3 RESULTS

3.1 Demographic Data of Intermittent Haemodialysis Patients

Between January and December 2021, a total of 74 patients initiated on intermittent HD were

identified at Hospital Universiti Sains Malaysia. Among these patients, 52.7% were male and 47.3% were female. The majority of the study population (75.7%) were over 50 years old, ranging from 18 to 77 years. Regarding comorbidities, the most prevalent conditions were hypertension (95.9%), followed by diabetes mellitus (79.7%) and ischemic heart disease (23.0%). A few patients were also presented with other comorbidities, such as cerebral-vascular accidents, gouty arthritis and glomerulonephritis. Demographic details of the patient population are provided in **Table 1**.

3.2 The Types of Catheters Used for Intermittent Haemodialysis

The catheters used in our study were classified into two groups: initial catheters and subsequent catheters. The initial catheter refers to the first type of catheter used by patients, while subsequent catheters indicate a change to other catheter types. The majority of patients (93.2%) initially started intermittent HD with an uncuffed femoral catheter. Subsequently, 71.6% of patients transitioned to an uncuffed internal jugular catheter. The proportion and duration of catheter use are presented in **Table 2 and Table 3**.

We observed that the majority of patients who initiated intermittent HD with uncuffed femoral catheters used them for less than four weeks (81.1%) with a mean duration of 2.7 weeks. Upon transitioning to uncuffed internal jugular catheters, a significant number of patients (39.6%) used the catheter for 5-12 weeks, and (49.1%) used it for more than 12 weeks.

3.3 The Proportion of Catheter-related Complications

The most prevalent catheter-related complication observed in our study was central line-associated bloodstream infections (CLABSI) (17.6%), followed by hematoma (8.5%). **Table 4** presents additional complications such as vascular abscess, deep vein thrombosis, and central vein stenosis.

3.4 The Association of Types of Catheters with Their Related Complications

Our analysis revealed no statistically significant association between the catheter types and their related complications, including infection, bleeding, deep vein thrombosis, and central vein

stenosis, as presented in **Table 5**. However, bleeding was prominently observed with uncuffed femoral catheters compared to other catheter types (11.6%). We also noted a higher incidence of infections with uncuffed internal jugular catheters (30.2%). Deep vein thrombosis occurred in only two patients using uncuffed femoral catheters (2.9%). Central vein stenosis was observed in only one patient using uncuffed internal jugular catheter (1.9%).

3.5 The Clinical Outcome of Intermittent Haemodialysis Patients and Factor-delayed the AVF Creation

Among the 74 patients in our study, (63.5%) had an AVF created, while (27%) underwent long-term CAPD, and the remaining patients died due to multifactorial reasons. We also examined the factors contributing to delayed AVF creation, summarized in **Table 6**.

Throughout the study period, a total of 18 patients succumbed to various causes. The initial causes of death were as follows: CLABSI (27.7%), sepsis unrelated to catheter insertion (27.7%), acute coronary syndrome (16.7%), Covid-19 infections (16.7%), refractory hyperkalemia (5.6%), and cerebral-vascular accident (5.6%).

4 DISCUSSION

Intermittent HD using a central venous catheter (CVC) serves as a temporary solution while awaiting the placement and maturation of permanent access, such as a fistula or graft. This approach enables patients to commence dialysis treatment in an emergent situation. The CVC is inserted into a central vein, typically through the femoral or internal jugular site and in rare cases, the subclavian site.

The use of CVC is a commonly employed method to initiate HD. Upon starting long-term HD, it is estimated that over 70% of patients in the United States choose CVC as their initial access device [6]. In a separate study, the utilization of CVC for HD is reported at 23% among prevalent patients and 58-73% among incident patients [7]. This significant reliance on CVC can be attributed to several factors, including delayed diagnosis of kidney disease, late referral to a nephrologist, deferred planning for permanent vascular access, and financial or logistical constraints [8].

In our study, we found 74 patients with incident ESKD on intermittent HD. Most of them were male patients and beyond 50 years old.

Table 1. Demography of newly diagnosed CKD stage 5 patients with intermittent haemodialysis in 2021, (n=74 patients)

Age distribution	Years
Mean	55.26
Range	18-77
	Proportion n (%)
≤29	4 (5.4)
30-39	7 (9.5)
40-49	7 (9.5)
≥50	56 (75.7)
Gender	Proportion n (%)
Male	39 (52.7)
Female	35 (47.3)
Races	Proportion n (%)
Malays	73 (97.9)
Chinese	1(2.1)
Pre-existing Co-morbid	Proportion n (%)
Hypertension	71 (95.9)
Diabetes mellitus	59 (79.7)
Ischemic heart diseases	17 (23.0)
Cerebral-vascular accident	7 (9.5)
Gouty arthritis	5 (6.8)
Glomerulonephritis	3 (4.1)
Lupus nephritis	1 (1.4)

Table 2. Types of initial catheters used for intermittent haemodialysis among CKD stage 5D patients and their total duration of usage

Types catheter	Proportion n (%)	Duration		
		≤ 4 weeks	5-12 weeks	>12 weeks
Cuffed Internal Jugular	1 (1.4)	-	-	1 (100)
Cuffed Femoral	2 (2.7)	1 (50)	-	1 (50)
Uncuffed Internal Jugular	2 (2.7)	1 (50)	-	1 (50)
Uncuffed Femoral	69 (93.2)	60 (81.1)	9 (12.2)	-
Total: 74 (100)				

Table 3. Types of subsequent catheters used for intermittent haemodialysis and total duration

Types catheter	Proportion n (%)	Duration		
		≤ 4 weeks	5-12 weeks	>12 weeks
Cuffed Internal Jugular	1 (1.4)	-	1 (100)	-
Cuffed Femoral	2 (2.7)	-	-	2 (100)
Uncuffed Internal Jugular	53 (71.6)	6 (11.3)	21 (39.6)	26 (49.1)
Not on catheter due to death, or AVF was created or on long-term peritoneal dialysis	18 (24.3)	-	-	-
Total: 74 (100)				

Table 4. The proportion of catheter-related complications among intermittent haemodialysis patients

	The initial catheter used n = 74	The subsequent catheter used n = 56	Total proportion n = 130
Central line-associated bloodstream infection (CLABSI)	7 (9.5)	16 (28.6)	23 (17.6)
Hematoma	8 (10.8)	3 (5.4)	11(8.5)
Vascular Abscess	2 (2.7)	-	2 (1.5)
Deep vein thrombosis (DVT)	2 (2.7)	-	2 (1.5)
Central vein stenosis	-	1 (1.8)	1 (0.8)

Table 6. Factors contributing to delay in AVF creation, (n=47 patients)

Factor	Proportion n (%)
Dialysis fear and practical concern	17 (36.2)
Small venous access	16 (34.0)
Denial of kidney diseases or needs of AVF	8 (17.0)
Changing the mode of KRT	4 (8.5)
Late referral to the nephrologist	2 (4.3)

Table 5. The association of types of catheters used for intermittent haemodialysis with catheter-related complications

Complication	Types of catheters								
	Initial catheter used n = 74 (n,%)				P-value	Subsequent catheter used n = 56(n,%)			P-value
	Cuffed Internal Jugular n = 1	Cuffed Femoral n = 2	Uncuffed Internal Jugular n = 2	Uncuffed Femoral n = 69		Cuffed Internal Jugular n = 1	Cuffed Femoral n = 2	Uncuffed Internal Jugular n = 53	
Infection	0	1 (50)	1 (50)	7 (10.1)	0.124 ^a	0	0	16 (30.2)	0.670 ^a
Non-infection	1 (100)	1 (50)	1 (50)	62 (89.9)		1 (100)	1 (50)	37 (69.8)	
Bleeding	0	0	0	8 (11.6)	0.885 ^a	0	0	3 (5.7)	0.914 ^a
Non-bleeding	1 (100)	2 (100)	2 (100)	61(88.4)		1 (100)	2 (100)	50 (94.3)	
Venous thrombosis	0	0	0	2 (2.9)	0.985 ^a	-	-	-	
Non-venous thrombosis	1 (100)	2 (100)	2 (100)	69 (97.1)		-	-	-	
Stenosis	-	-	-	-		0	0	1 (1.9)	0.972 ^a
Non-stenosis	-	-	-	-		1 (100)	2 (100)	52 (98.1)	

^a Chi-Square Test

In Malaysia, the treatment gap between males and females accepted for dialysis has remained consistent over the years, with the proportion of male and female dialysis patients being about 52% to 48%, respectively [2]. We also found that our study population has existing co-morbidities with chronic diseases such as hypertension (95.9%), diabetes mellitus (79.7%), and ischemic heart disease (23.0%). In China, the authors found the three most common reasons for ESKD were diabetic kidney disease (27.3%), initial nephropathy (16.5%) and hypertensive nephropathy (11.1%) [9]. A recent report by Wang et al. also discovered a significant association between diabetes mellitus, hypertension, hypercholesterolemia, and ischemic heart diseases with chronic kidney diseases [6].

4.1 Catheter-related Complications among Intermittent Haemodialysis Patients

CVC is associated with a range of complications, both immediate and delayed. Immediate complications involve issues related to catheter insertion and direct access, while longer-term complications can also occur. Immediate complications may include arterial puncture, arrhythmia, air embolism, thoracic duct injury, catheter malposition, pneumothorax, and haemothorax. Delayed complications commonly observed include infection, venous stasis, venous thrombosis, and catheter malfunction. These complications highlight the potential risks and challenges associated with the use of CVC [10]. The most common catheter-related complications observed in our centre were CLABSI and hematomas. Infections were the most common complications observed across all types of catheters. Upon initiating intermittent HD, a majority of our patients utilized uncuffed femoral catheters, with 10.1% of them experiencing infections. The use of the femoral vein as vascular access is fraught with complications due to its proximity to the groin area. These include catheter-related bacteraemia and issues such as reduced dialysis blood flow and potential loss of vascular patency [11].

While waiting for permanent haemodialysis placement, the patient required multiple admissions to our centre for intermittent haemodialysis. Due to operational preferences as well as a high bleeding risk at presentation, the uncuffed femoral site was chosen for the initial catheter. Before discharge, they switch from an uncuffed femoral catheter to an uncuffed internal

jugular catheter. The change in catheter types was made to reduce the number of procedures. A higher incidence of infection was observed with uncuffed internal jugular catheters (30%), which we attribute to their more prolonged usage. A study in India discovered that 19.2% of patients had catheter-related infections, and 27.7% had bacteremia when using uncuffed internal jugular vein catheters [12].

An epidemiological study conducted in Henan province of China, involving 865 HD patients, reported a prevalence of catheter infections in 38.61% of all patients [9]. Furthermore, a recent study conducted in Italy revealed that the use of CVC was associated with an increased risk of infection, longer hospital stays, and a higher likelihood of death compared to using AVF for dialysis patients [13].

Hematoma complications with uncuffed femoral catheters were observed in our study. This is due to azotaemia with platelet dysfunction that contributes to the bleeding. However, the risk of hematoma was found to be equivocal between femoral and IJV catheter [14]. The initial cause of hematomas from transfemoral catheterization is an arterial puncture, which can be mitigated by proper needle insertion within the femoral triangle [10].

In our study, other catheter-related complications, such as venous thrombosis and stenosis were relatively low. Only two patients experienced deep vein thrombosis, and one developed central venous stenosis. The exact underlying mechanism of catheter-associated thrombosis remains unclear. However, several contributing factors have been proposed, including recurrent vascular puncture, platelets and endothelium dysfunction, inflammation, and clotting abnormalities [6]. The development of central venous stenosis is a complex process likely related to catheter placement. This placement is often complicated by increased inflammation, heightened oxidative stress, activation of leukocytes, myeloperoxidase release, and coagulation cascade activation [6].

We observed two cases (2.9%) of deep venous thrombosis associated with uncuffed femoral catheters. Compared to other studies, the reported incidence of symptomatic catheter-related thrombosis ranges from 0.3% to 28.3%, while venography reveals an incidence of thrombosis between 27% and 66% [15]. A systematic review comparing central venous access sites indicates that subclavian sites are preferable to femoral venous access for short-term catheterization due

to lower risks of thrombotic complications [16]. However, the study observed no significant differences in thrombotic complications between the femoral and internal jugular routes (17).

The development of central venous stenosis is a recognized risk associated with the use of CVC. In a single-centre experience in Sudan, central venous stenosis was found in 28.3% of 106 patients ([17]. Another study reported a prevalence of 41% of central vein stenosis on venography in HD patients with access dysfunction [18]. Our study observed a small number of central vein stenosis in patients undergoing intermittent HD. It is important to note that central vein stenosis secondary to CVCs is often asymptomatic [15], leading to the true incidence remaining unknown.

Other factors may also influence the likelihood of patients experiencing complications. For instance, a study in China revealed that factors such as older age, diabetes, lower educational level, rural residence, lack of pre-dialysis nephrologist visits, lower serum albumin levels, and higher ferritin levels were independently associated with catheter infections [9]. Additionally, carrying methicillin-resistant *Staphylococcus aureus* (MRSA) or having a history of bacteremia or bacteriuria three months before catheter implantation were identified as significant risk factors for catheter-related infections [19]. Although our study did not investigate these factors, they could be included in future research to gain further insights.

4.2 Factor Associated with Delayed Arterio-venous Fistula Creations

The AVF is recognized as the gold standard vascular access modality for HD. It offers prolonged patency, enhanced durability, and a reduced risk of infection once matured. AVF or AVG is recommended over a CVC for HD patients, primarily due to the lower infection risk [20].

We found 63.5% of patients had AVF created for their definitive kidney replacement therapy. Of these, only 13.5% had a chance for AVF creation in less than four weeks after the first initiation of dialysis, while 23% of patients had AVF created between 5-12 weeks, and another 27% had AVF created beyond 12 weeks. According to Malaysia KRT guidelines, it was recommended to place a fistula at least six months before the anticipated start of HD [21]. In another study, the authors conclude that AVF referral within about 12 months of the estimated time to dialysis performed best

among time frame strategies and referral of eGFR < 15-20 mL/min/1.73 m² would be the best among threshold strategies [22]. We did not explore the AVF creation site in relation to prior IJV catheter sites.

Kevin E. Chan et al. proposed a guideline known as the 30-20-10 rule, which is based on the estimated glomerular filtration rate (eGFR). According to this rule, referral to a nephrologist should be made when the eGFR reaches or falls below 30 mL/min. When the eGFR falls below 20 mL/min, and the patient chooses HD as their long-term KRT option, referral for the creation of an arteriovenous fistula (AVF) should be initiated. If eGFR falls below 10 mL/min (or 15 mL/min, in patients with diabetes), the patient should have a matured access in place and be ready for the initiation of long-term KRT [23]. However, it is essential to consider the individual CKD progression rate when determining the referral timing. For elderly patients with CKD, a delayed referral may be appropriate to minimize the risk of creating an AVF that may not be utilized [24].

We explore the possible cause of delay in AVF creation among CKD patients in our centre. We found dialysis fear and practical concern are among the major factors contributing to AVF creation delay. In addition, small veins also led to the delay. Al Farhan et al. found the three most important factors are denial of kidney disease or the need for AVF, dialysis fears and patients refusing to undergo AVF surgery [5]. We also found a late referral to a nephrologist contributing to the delay. More frequent nephrology clinic visits for patients with a recent hospitalization may improve rates of placement of AV access [25].

4.3 Clinical Outcomes of Intermittent Haemodialysis Patients

During the study period, 18 patients unfortunately passed away. The leading causes of death were CLABSI (27.7%) and sepsis unrelated to the catheter (27.7%). CLABSI has been identified as a significant risk factor for increased mortality. A systematic review and meta-analysis reported an odds ratio of 2.75 for in-hospital death associated with CLABSI, and a subgroup analysis of ten matched studies yielded an odds ratio of 1.51 [26]. Although we did not investigate the specific causative organisms for CLABSI in our study, previous research has highlighted several common pathogens associated with this complication. Gram-positive organisms were frequently identified, including coagulase-negative

staphylococci, enterococci, and Staphylococcus aureus. Gram-negative organisms such as Klebsiella, Enterobacter, Pseudomonas, Escherichia coli, Acinetobacter, and Candida species were also implicated [27,28].

5 CONCLUSION

In conclusion, our study highlights the potential complications associated with intermittent HD via CVC, including bleeding, infections, and mortality. Furthermore, we identified practical concerns and fear as major contributing factors leading to delays in AVF creation. To address these challenges, we emphasize the importance of enhancing pre-dialysis counselling and education for patients. By providing comprehensive information and addressing patients' worries and fears, we can potentially improve the timely creation of AVFs and promote better patient outcomes.

Notably, a native arteriovenous fistula remains the preferred vascular access for ensuring adequate dialysis and optimizing patient outcomes. Efforts should be directed towards promoting AVF as the initial choice for long-term vascular access, considering its associated benefits and reduced risk of complications. Future research and interventions should focus on developing strategies to address patient concerns, improve education and awareness, and enhance the utilization of AVF to further enhance the quality of care in HD patients.

Author's Contributions

Initial concept & Research design: AMB, AHA, MIK. Collection data and interpretation: AHA, NHA, MZI. Drafting manuscript: AHA, AMB. Approval of the final version of the article: AMB, AHA, MIK, NHA, MZI. All authors read and approved the final manuscript.

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Competing Interests

The Authors declare no conflict of interest upon submission of this article.

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