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LIEGEDAUER UND BEEINFLUSSENDE FAKTOREN VON DIALYSEKATHETERN IN EINER "REAL-WORLD" – POPULATION – EINE SINGLE CENTER ERFAHRUNG

Inaugural-Dissertation zur Erlangung der Doktorwürde der Medizinischen Fakultät der Universität zu Köln

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Dedications

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Abbreviations

- **ADC: Acute dialysis catheter**
- **AV: Arteriovenous**
- **AVF: Arteriovenous fistula**
- **AVG: Arteriovenous graft**
- **CDC: Chronic dialysis catheter**
- **CKD: Chronic kidney disease**
- **ESKD: End-stage kidney disease**
- **ESRD: End-stage renal disease**
- **HD: Hemodialysis**
- **IQR: Interquartile range**
- **NKF-KDOQI: National Kidney Foundation-Kidney Disease Outcomes Quality Initiative**
- **OR: Odds ratio**
- **RRT: Renal replacement therapy**

1. ZUSAMMENFASSUNG

1.1. Ziel

Das Ziel der vorliegenden Studie ist die Auswertung des Behandlungsergebnisses von Patienten, die mit einem getunnelten Katheter in einem "High Volume Centerr" versorgt wurden. Unseren primären Endpunkt haben wir definiert, als die Feststellung der Liegedauer des Hämodialysekatheters, während der sekundäre Endpunkt die Identifizierung von Faktoren umfasst, die die Liegedauer des Katheters negativ beeinflussen.

Zu vermerken ist, dass eine prolongierte Liegedauer der Katheter, über den geplanten Zeitraum hinaus, und infolgedessen entstandene, katheterbezogene Komplikationen als negativer Einfluss definiert wurden. Die Identifizierung solcher Faktoren kann zur Entwicklung von Verbesserungsstrategien anregen, um die Zeit, in der Patienten mit einem Katheter dialysiert werden, bis zum Einsatz des definitiven Verfahrens (z.B. bis zur nativen Shuntanlage) möglichst komplikationsarm zu überbrücken. Patienten, bei denen ein getunneltes Katheterverfahren als endgültige Shunt-Methode geplant ist, können durch die entsprechende Identifikation dieser Faktoren besonders überwacht werden und Komplikationen vorgebeugt werden.

1.2. Methoden

Diese retrospektive Studie basiert auf einer Patientenkohorte, in der alle Patientinnen und Patienten im Zeitraum von Januar 2014 bis Dezember 2019 in einem "High Volume Center" mittels eines Hämodialysekatheters behandelt wurden. Die erhobenen Daten wurden hinsichtlich der Baseline-Parameter, prozeduralen Ereignisse und des klinischen Follow-ups analysiert.

1.3. Ergebnisse

Während der Studiendauer wurden 393 Patienten (56,5 % männlich) identifiziert, die den definierten Einschlusskriterien unserer retrospektiven Studie entsprachen. Das Durchschnittsalter betrug 64 Jahre (IQR 13–88), wobei die Mehrheit der Patienten, bei denen eine Kathetereinlage indiziert war, zum Zeitpunkt der Prozedur das fünfzigste Lebensjahr bereits überschritten hatte. Die am häufigsten vorkommenden, ursächliche Faktoren einer terminalen Nierenerkrankung, die wesentlich zur Indikationsstellung einer Hämodialyse beigetragen haben, waren: Erkrankungen prärenaler Genese, Diabetes mellitus, Hypertonie, Glomerulonephritis. Bei 162 Patienten wurde der Katheter bei einer erfolgreich maturierten Shuntvene explantiert. Bei 24 Patienten erfolgte die Katheterexplantation aufgrund eines Wechsels auf einen anderen Zugangstyp, und bei 81 weiteren Patienten wurde der Katheter aufgrund einer Infektion entfernt. Die mediane Liegedauer betrug 95 Tage (0-2974).

Die meisten der eingebrachten Katheter (351/393) wurden rechtsseitig implantiert. Es zeigte sich statistisch signifikant, dass die Liegedauer bei rechtsseitiger Implantation länger war als bei linksseitiger Implantation (p=0,006). Bei Patienten, die unter Antikoagulationsbehandlung standen (n=78), wurde ebenfalls eine längere Verweildauer der implantierten Dialysekatheter festgestellt (p=0,034).

1.4. Schlussfolgerung

Unsere Ergebnisse zeigten statistische Signifikanz bei bestimmten chirurgischen (anatomischen und technischen) sowie medizinischen (Vorerkrankungen, Antikoagulation) und patientenbezogenen Faktoren (Alter und Einfluss des AV-Shunts über getunnelten Katheter), die die Liegedauer beeinflussen. Eine optimale Bestimmung aller möglichen Faktoren, die die Katheterverweildauer beeinflussen, könnte tatsächlich positive Veränderungen in der Praxis mit sich bringen und den Patienten eine "gesündere" Dialyse ermöglichen.

2. INTRODUCTION

2.1. Chronic Kidney Disease and Hemodialysis

The number of diseases or disabilities that are untreatable or require lifelong therapies is dwindling. A new era in the treatment of chronic kidney disease was ushered in by the development of extracorporeal blood circulation, i.e., hemodialysis. It took nearly two hundred years of research and biotechnological development to establish hemodialysis as a routine, which today over two million patients deeply appreciate¹. The history of renal replacement therapy can be briefly divided into three distinct epochs. The pioneering work of Thomas Graham and Heinrich Fick (on the transport of molecules by diffusion), as well as the work of John J. Abel, Georg Hass, and Heinrich Necheles (on the first dialysis machines), heralded the beginning of the experimental dialysis therapy era. In the second innovative phase, Willem Kolff, Niels Alwall, Frederic Kiil, and Richard Stewart established the framework conditions and performance characteristics of tube, flat, and capillary membranes, as well as dialyzers¹. Niels Alwall deserves special mention for his description of controlled ultrafiltration¹. Currently, we are in the third phase, in which dialysis has become a standard method for renal replacement therapy $^{\rm 1}.$

2.2. Epidemiology of End-Stage Renal Disease

Anomalies pertaining to kidney structure or function that have persisted for three months or more and have an impact on health are referred to as chronic kidney disease (CKD) 2 . Chronic kidney disease (CKD) is categorized into stages depending on the etiology, glomerular filtration rate (GFR) category (G1–G5), and albuminuria category (A1–A3), abbreviated as CGA². The three components of the categorization system help in cardiovascular risk assessment, illness severity determination, and therapeutic planning². The number of people suffering from CKD is rising steadily around the world. Between 1990 and 2017, the worldwide prevalence of CKD grew by 29.3%. Roughly 10% to 15% of the population in Europe, the United States, and Australia has kidney disease at some stage 3 . In 2017, there were 697.5 million cases (with a global prevalence of 9.1%); in 2021, 850 million cases of all-stage CKD worldwide were recorded, surpassing the number of people with diabetes (422 million) and the prevalence of cancer worldwide (42 million) or people living with AIDS/HIV (36.7 million) ². There are considerable differences in the incidence of CKD among the world's different regions, but the overall number of individuals with CKD is rising. CKD claimed the lives of about 1.2 million people worldwide in 2017, mostly due to cardiovascular events, the leading cause of mortality among patients

with advanced CKD³. Diabetic nephropathy accounted for over a third of the 35.8 million disability adjusted life years(DALYs) caused by chronic kidney disease (CKD) in 2017³. The number of patients receiving renal replacement therapy (RRT) globally exceeds 2.5 million, and that figure is expected to double by $2030^{3,4}$. In many countries, access to renal replacement therapy is limited; an estimated 2.3–7.1 million adults have died prematurely due to a paucity of RRT^{3,4}. Three primary factors are propelling the growth of CKD patients requiring dialysis: patient selection, competitive risks, and an actual rise in the prevalence of CKD. Patient selection: In the early years of RRT, patients with significant comorbidities and/or those who were very old were not allowed access to dialysis. There has been a sharp increase in the number of patients gaining access to RRT⁵. Competitive risks: Even in the early stages of CKD, patients have a substantial risk of mortality, and many patients in CKD Stages 3 and 4 die before receiving RRT⁵. Having a glomerular filtration rate that is lower than the normal range is recognized as one of the most significant risk factors for coronary heart disease². There have been significant advancements in the treatment of heart disease and survival in recent decades, allowing many people with advanced CKD to survive and require RRT. Rise in the prevalence of CKD: The higher incidence of end-stage renal disease (ESRD) may also be due to an increase in the prevalence of CKD. According to the Framingham Heart Study, the incidence of type 2 diabetes doubled from the 1970s to the 1990s 6 . In 2021, there were 529 million (95% UI 500–564) people of all ages, worldwide, living with diabetes, yielding a global agestandardized prevalence of 6.1%⁴. There has also been an increase in the use of potentially nephrotoxic medications, such as non-steroidal anti-inflammatory drugs, antibiotics, and chemotherapeutic treatments². Finally, a decline in cardiovascular and cancer-related deaths may be linked to an increase in the number of individuals who develop ESRD. Kidney transplantation is the best modality of renal replacement therapy for those with ESRD⁵. However, the latency for a kidney transplant might last for several years; thus, the patient could be on hemodialysis for a prolonged period. As the need for kidney transplantation rises, the number of organs available has not kept pace. Over 90,000 patients in Germany were on other modalities of RRT (e.g., hemodialysis or peritoneal dialysis) in 2019⁷. According to the annual report of organ donation and transplantation for Germany, 1,909 kidneys were transplanted in 2020, while the number of transplantable patients on the active waiting list for a kidney in 2020 was 7,3387 . Patients may have to switch from one RRT modality to another over time because all of these modalities have the potential to fail.

2.3. Vascular Access for Hemodialysis

The quality of dialysis is strongly related to the dependability and integrity of the patient's vascular system, which in turn affects the patient's longevity on dialysis 8 . The NKF-KDOQI Clinical Practice Guidelines for Vascular Access which published in 1997 as part of an attempt to promote the creation of autogenous arteriovenous (AV) access and extend the usage of newly created access by detecting malfunction prior to thrombosis 9 .

The initial recommendations stated that at least 50% of all new hemodialysis patients and eventually 40% of existing hemodialysis patients should have autogenous AV accesses established⁹.

In 2003, the Centers for Medicare and Medicaid Services (CMS) proposed the introduction of a National Vascular Access Improvement Initiative (NVAII); in 2005, this was expanded to the Fistula First Breakthrough Initiative (FFBI)¹⁰. FFBI identified clinical and organizational changes to enhance the creation and utilization of autogenous AV access. The FFBI outlined clinical and organizational modifications that could be adapted and applied locally by nephrologists, dialysis staff, access surgeons, and patients¹⁰. By August 2005, the nationwide (USA) rate of autogenous access had reached 40 percent prevalence, followed by a steady rise until 2011, when it leveled out to around 60 percent¹¹. Between 2013 and 2021, the percentage of individuals initiating hemodialysis (HD) with an AV fistula declined from 17.0% to 12.2%, while the percentage starting with a catheter and a maturing fistula decreased from 18.0% to 10.2%12. The proportion of patients starting hemodialysis (HD) solely with a catheter, which hit a low point of 60.3% in 2013, steadily rose to 74.0% by 2021. This marks a 13.7% increase in absolute terms and a 22.7% increase in relative terms.¹²

The DOPPS (Dialysis Outcomes and Practice Patterns Study) has indicated a wide range of vascular access practices¹³. Patients who dialyzed with a catheter had higher mortality risks, whereas the risk for patients dialyzed with a useable AVF was the lowest¹⁴. The DOPPS has tracked international trends in vascular access procedures since 1996¹³ .In Japan, Italy, Germany, France, Spain, the UK, Australia, and New Zealand, between 2005 and 2007, 67-91% of patients utilized a native AVF, while 50-59% used a native AVF in Belgium, Sweden, and Canada $13,15,16$.

Even among non-diabetic patients aged between 18 and 70 years old, catheter usage increased 1.5-3 times in various countries from 1996 to 2007 despite inferior results for CDCs⁵. Furthermore, in five countries, 58-73% of incident patients used a CDC for dialysis commencement, despite 60-79% of patients having been examined by a nephrologist more than four months before being dialysis-dependent⁵. Italy, Japan, and Germany all had median times of around 5 to 6 days for referral for vascular access creation whereas the United Kingdom and

Canada had median times of 40-43 days⁵. Patient preference for CDCs also varied widely from 1% in Japan and 18% in the United States to 42% in Belgium and Canada¹⁶.

Age, female sex, and previous or current catheter usage were all related to a preference for a CDC16. The wide variety in patient preferences for vascular access shows that socio-cultural variables may impact patient choice and hence be modifiable 5 .

2.3.1. The Role of Vascular Access Surgeon

Patients with end-stage renal disease rely on vascular surgeons in the majority of nations to provide and maintain vascular access for renal replacement therapy. Together with nephrologists, dialysis staff, and interventional radiologists, they contribute to a multidisciplinary access service. The access surgeon must deliver a product that can be rapidly utilized for dialysis. In the event of an acute change in RRT modality, the surgeon must be prepared to take action when necessary to maintain access function. The skills and experience of the vascular access surgeon are critical in generating predominantly AVFs and also have a considerable influence on surgical outcomes¹⁷⁻¹⁹.

2.3.2. Choice of Vascular Access

The 2019 KDOQI clinical practice quideline for vascular access¹¹ takes a look at how patients with vascular access are treated. A more patient-centered approach is emphasized in these guidelines, which call for the creation of an ESKD Life-Plan¹¹ that takes into account each patient's preferences and needs when deciding on access and planning for potential complications and solutions for the current access, as well as a strategy for moving on to the next access. Surgeons are strongly encouraged to consider not only the initial choice of access but also alternative accesses that could serve as backups in the event of failure of the primary access. The ESKD Life-Plan encourages a detailed evaluation of the patient's lifetime with ESKD and kidney replacement therapy alternatives. This approach has several advantages, including the preservation of vessels essential for future AV access development and utilization, and the avoidance of unnecessary interventions and complications. Briefly stated, KDOQI has shifted its attention to an individual "P.L.A.N" (Patient Life-Plan first, followed by their corresponding Access Needs) for the patient. Priority is given to the patient's long-term goals and then to the patient's access requirements¹¹. When compared to an AVG or CDC, prior recommendations largely supported the idea that the AVF was linked with better results (superior patency, fewer problems, and the lowest cost) 20.

2.3.3. Indications for a Permanent Catheter for Vascular Access

The guidelines from American and European societies provide recommendations regarding the utilization of tunneled chronic dialysis catheters (CDCs) in the management of chronic kidney disease (CKD) patients undergoing renal replacement therapy. Guideline 2.2 by the Kidney Disease Outcomes Quality Initiative (KDOQI) vascular access quidelines¹¹ recommends the judicious use of tunneled CDCs in both short-term and long-term clinical scenarios, contingent upon specific clinical contexts¹¹. Short-term utilization of CDCs is deemed appropriate in circumstances such as transitional phases where arteriovenous fistula (AVF) or arteriovenous graft (AVG) creation is incomplete but immediate dialysis initiation is necessitated, as well as instances of acute transplant rejection or other acute complications requiring dialytic intervention¹¹. Additionally, temporary deployment of tunneled CDCs is recommended for peritoneal dialysis (PD) patients experiencing complications necessitating temporary cessation of peritoneal function or resolution of complications, such as pleural leaks¹¹. Similarly, patients with imminent living donor renal transplants but requiring interim dialysis support, or those encountering AVF or AVG complications prompting temporary non-use, are deemed suitable candidates for short-term tunneled CDC deployment¹¹. Long-term or indefinite utilization of tunneled CDCs is warranted in scenarios such as recurrent failures of AV access options, patient-directed preferences against AV access based on quality-of-life considerations or life expectancy, or inherent anatomical limitations precluding traditional AV access establishment¹¹. Notably, these circumstances may include but are not limited to, complex arterial or venous pathology precluding AV access creation, limited life expectancy, or specific medical exigencies¹¹. Complementing this, European Society for Vascular Surgery (ESVS) Vascular Access: 2018 Clinical Practice Guidelines Recommendation 7 advises considering tunneled cuffed chronic dialysis catheter s as a durable hemodialysis modality when conventional AV access establishment is unfeasible or in patients with restricted life expectancies, thus reaffirming their role as a viable therapeutic option in select CKD populations 5 .

2.3.4. Preoperative Evaluation

2.3.4.1. Medical History and Physical Examination

Medical history should include details such as prior long-term central line placement, previous AVF creation or AVG implantation, prior hemodialysis catheter infections, coagulation disorders, and the existence of a pacemaker .

Performing a thorough examination of the chest, neck, and arms is essential. Evidence of past tunneled catheters, scars from previous permanent accesses, upper extremity, or facial swelling, and visible collateral veins should alert the physician to the risk of central veno-occlusive disease²¹. Both tunneled catheter and permanent access creation are restricted by a lack of accessible access sites. In this way, a holistic strategy that incorporates the evaluation of all available hemodialysis access sites allows us to select the access site that is most beneficial to the patient. With regards to maintaining consistent care, it is advantageous if the tunneled hemodialysis catheter and/or the permanent access for hemodialysis are placed by the same surgeon.

2.3.4.2. Central Venous Imaging

2.3.4.2.1.Color-Flow Venous Duplex Imaging

Color-flow duplex imaging is the preferred preoperative imaging technique to assess the feasibility of the vein for the tunneled hemodialysis catheter. The patency of a vein can be determined by applying pressure to the jugular or axillary veins with the transducer and demonstrating the compressibility or non-compressibility of the vein **(Figure 1)**. However, when imaging progresses toward the central chest, air-tissue interaction and ribs make central vein imaging unfeasible 22 .

Figure 1: Transverse Gray-Scale Image of the Left Internal Jugular Vein Demonstrating Intraluminal Echoes and Noncompressibility Consistent with Venous Thrombosis

2.3.4.2.2.Magnetic Resonance Venography

When compared directly to digital subtraction angiography, three-dimensional gadolinium-enhanced magnetic resonance venography (MRV) has been proven to be very sensitive in detecting central venous occlusions and stenoses higher than 50% 23. Gadolinium-based contrast agents used in magnetic resonance imaging have previously been associated with the development of nephrogenic systemic fibrosis (NSF) prior to 2010, with elucidated underlying mechanisms 24 . It is noteworthy that the incidence of this condition has not been reported beyond 2012, prompting inquiries into the actual risk of nephrogenic systemic fibrosis²⁵. Individuals at the highest risk for nephrogenic systemic fibrosis include patients with acute kidney injury, those undergoing renal replacement therapy, and individuals with chronic kidney disease stages G4 and G5²⁶. Consequently, the American College of Radiology Manual on Contrast Media(ACR Committee on Drugs and Contrast Media 2023) recommends the utilization of newer linear and macrocyclic gadolinium-based contrast agents, such as gadobenate dimeglumine, gadobutrol, gadoteridol, gadoterate meglumine, and gadoxetate disodium, in the aforementioned patient cohorts^{25,26}. The most recent KDIGO 2024 quideline on chronic kidney disease, published in April 2024², recommends for patients with glomerular filtration rate < 30 ml/min per 1.73 m² (CKD G4–G5) who require gadolinium-containing contrast media, preferentially offering the American College of Radiology group II and III gadolinium-based contrast agents.

2.3.4.2.3.Computed Tomographic Venography

Computed tomographic venography (CTV) is comparable to magnetic resonance venography (MRV) in that it is capable of imaging several vessels in the chest in a single setting **(Figure 2)**. CTV, on the other hand, has the advantages of being commonly available in the majority of medical settings, having rapid acquisition times, and posing fewer adverse contrast agent problems. A study comparing CTV with digital subtraction venography for the diagnosis of benign thoracic central venous occlusion in 18 patients indicated that CTV results were well correlated with those of digital subtraction venography²⁷.

The significant precautions and recommendations for the utilization of contrast media for CT scans in patients with chronic kidney disease are elucidated in the KDOQI 2024 guidelines for chronic kidney disease 2 .

Figure 2: Computed Tomographic Venography of the Upper Central Venous System (Courtesy of Mike Winkler, MD, University of Kentucky ©2015)

2.3.4.2.4.Catheter-Based Contrast Venography

Catheter-based contrast venography is still the "gold standard" for detecting central venous stenosis (CVS) or occlusion¹¹ Contrast venography offers the unique benefit of enabling the surgeon to commence endovascular therapy if severe stenosis is found during venography. Additionally, catheter-based venography may frequently be performed with a significantly lower volume of contrast than CTV, minimizing nephrotoxicity risk.

The greatest risk for acute kidney injury (AKI) is linked to interventional rather than diagnostic coronary angiography, particularly in cases of acute myocardial infarction. This heightened risk may be due to the larger contrast volumes utilized in interventional procedures and the hemodynamic instability often present in such clinical contexts^{28,29}.

Catheter-based salvage techniques for failing arteriovenous fistulas can be carried out using ultrasonography, offering additional mitigation against contrast-associated renal injurv³⁰.

2.3.5. Chronic Dialysis Catheter (CDC) Types and Materials

In most cases, tunneled dialysis catheters have two lumens and a polyester cuff positioned one to two centimeters proximal to the skin exit site. Silicone and other polymers, such as thin polyurethane, are utilized in catheters because they are less thrombogenic than the materials used in non-tunneled catheters³¹. In comparison to nontunneled catheters, these have a blunter and softer tip. Additionally, reducing the phenomenon of recirculation as much as possible is crucial to ensure efficient dialysis. The "arterial lumen" of the catheter refers to the blood flow from the patient to the dialysis machine, while the "venous lumen" refers to the blood flow from the dialysis machine back to the patient. In access recirculation, dialyzed blood is reintroduced into the arterial lumen directly from the venous lumen³².

The first cuffed catheters were rigid and straight. A wide variety of hemodialysis catheters are now available, and early catheter designs have been mostly replaced by pre-curved flexible catheters with a variety of tip designs due to technological advancements. In comparison to nontunneled catheters, tunneled catheters are available in larger sizes (15.5 or 16 Fr , F for French-size³³), allowing for higher blood flow rates (>300 mL/min) (largest 13.5 Fr). Coaxial, shotgun, step tip, Double D, symmetric, and split-tip catheters are just some of the options available **(see Figure 3)**. It is asserted that the various designs will improve blood flow, reduce the likelihood of recirculation, and prevent obstruction at the catheter tip. Even though some isolated favorable properties of a specific catheter have been proven, no universal major benefit has been demonstrated by one catheter over the others $32,34-39$. There was no significant difference found between the risks of thrombosis, infection, or overall catheter survival between symmetric-tip catheters and step-tip catheters in one of the few randomized trials conducted 37 .

Several different surface coatings, such as heparin, silver, chlorhexidine, rifampin, and minocycline, have been utilized to reduce the risk of hemodialysis catheter-related thrombosis as well as hemodialysis catheter-related infection⁴⁰.

In preliminary research, it was found that antimicrobial- and anti-thrombogenic-coated hemodialysis catheters helped avoid intravascular catheter infections in the setting of dialysis⁴¹⁻⁵⁰. In a systematic review that assessed 29 studies with a total of 2886 patients and 3005 hemodialysis catheters, antimicrobial-coated hemodialysis catheters were reported to have a similar incidence of catheter-related bacteremia and exit-site infections as noncoated catheters⁴⁸.

Catheter-related thrombosis can also be reduced with the help of heparin-coated catheters. The rates of catheter failure and overall survival were comparable in observational studies⁵¹. While the incidence of catheter-related bacteremia was significantly less frequent for heparincoated catheters compared with non-coated catheters (34 versus 60 percent), infection-free catheter survival was not different⁵⁰. One recent study showed symmetrical and split tip catheters had a lower risk of catheter dysfunction requiring removal than step tip catheters⁵².

Figure 3: Double-lumen Catheter tip designs A, B, C, and D, with arterial and venous lumens indicated. (Courtesy of De Oliveira DC et al. Plos One 2021). Catheter A and B represent step-tip catheters, while Catheter C features a split tip, and Catheter D exhibits a symmetric tip configuration, devoid of side holes.

2.3.6. Chronic Dialysis Catheter (CDC) Locations

The most common CDC placement location is the internal jugular vein. Catheters should preferably be placed in the right internal jugular vein because it has better patency, reduced kinking, and avoids thoracic duct injury when compared to left-sided insertion. Tunneled hemodialysis catheters were studied in a cohort of 812 catheters in 492 patients in a prospective study ,a tunneled hemodialysis catheter inserted into the right internal jugular vein had considerably better survival than one inserted into the left internal jugular vein³⁴. The worst long-term survival was observed with femoral tunneled hemodialysis catheters^{34,53,54}. Avoiding the subclavian vein, if possible, would help to prevent catheter-induced subclavian stenosis, which would have a detrimental impact on the insertion of ipsilateral permanent access³⁴.

When all other options for vascular access have been exhausted, patients may need tunneled hemodialysis catheters inserted transhepatically or translumbally. It is common practice to introduce translumbar catheters with the patient in the prone position by performing a percutaneous puncture of the inferior vena cava slightly above the right iliac crest. The catheter is tunneled into the body and exits via the right lateral abdominal wall. For transhepatic catheters, percutaneous access to the right or middle hepatic vein is gained under fluoroscopic guidance through the eighth intercostal gap in the midaxillary line. The catheter is subsequently tunneled to an exit site in the lateral anterior chest wall⁵⁵⁻⁵⁸.

Two of the most comprehensive published series showed that over 60% of patients required at least one catheter replacement. The most often reported reasons for catheter exchange are migration, thrombosis, and infection. Translumbar catheter exchanges may be more challenging than transhepatic catheter exchanges due to the development of retroperitoneal fibrosis along the route $55-58$.

2.3.7. Evidence-Based Best Practice Recommendations for Chronic Dialysis Catheter Insertion Techniques

The most recent NKF KDOQI Clinical Practice Guideline for vascular access¹¹, which was published in 2019, concurs with the previous KDOQI quideline for vascular access²⁰, which was published in 2006 recommends the CDC insertion be performed under ultrasound and fluoroscopy guidance. Furthermore, sonographic guidance is even stronger advocated 11,59.

To reduce the risk of complications during insertion, such as accidental arterial cannulation, all tunneled, cuffed chronic dialysis catheters (CDCs) should be placed under ultrasound guidance⁵⁹. One single-center randomized controlled trial with 110 participants compared the success rates of ultrasound-guided insertion to those of conventional insertion. The success rate was considerably greater with ultrasound (98% vs. 80%; $P = 0.002$)⁶⁰. In comparison to the anatomic landmark group, the ultrasound group had a much lower incidence of sequelae such as hematoma and arterial puncture⁶⁰.

One observational study ($n = 202$) compared the placement of a chronic dialysis catheter (CDC) using fluoroscopy quidance ($n = 136$) to the placement of a CDC without imaging 61 . The majority of the CDCs were inserted into the right internal jugular vein. There was a considerably greater success rate (defined as CDC installation and usage with sufficient blood flow) using fluoroscopy (98 percent versus 92 percent; $P = 0.03$). Due to the necessity for adequate asepsis, the likelihood of further endovenous procedures (such as venography and venoplasty), and the requirement for fluoroscopic guidance, bedside implantation is not recommended¹¹.

During all wire manipulations, fluoroscopic imaging should be employed to verify the wire's location^{62,63}. Due to the size and stiffness of most tunneled hemodialysis catheters, a substantial degree of forward push may be required during implantation. To prevent unintended cannulation and injury to the heart chambers the guidewire should be placed in a course from the superior vena cava to the inferior vena cava $62,63$.

2.3.8. Timing of Chronic Dialysis Catheter (CDC) Removal

In comparison to acute dialysis catheters (ADCs), cuffed, tunneled CDCs are less prone to infections^{64,65}. ADCs should thus only be used sparingly. One study found that after just one week of usage, the infection rate increased exponentially, with an analysis of 272 catheters (37 CDC versus 235 ADC) demonstrating a significant difference in infection rates by the second week 64 . In the same study, the infection rates per 1,000 days at risk for ADCs were more than 5 times higher compared to internal jugular CDCs and approximately 7 times higher with femoral ADCs⁶⁴. Prospective studies have not addressed the debate of transition from an ADC to a tunneled CDC in patients who do not recover from AKI. However, one study found that dialysis was frequently required for more than three weeks in patients with acute kidney injury (AKI) ⁶⁶. If the CDC is left in place for an extended length of time, there may be concerns about the CDC's longevity and the possibility that it could scar the venous wall. Complications arising from these concerns have been recorded, such as broken and migrated CDC components and resulting embolization and sepsis, etc. ⁶⁷. Adherent CDCs, also known as stuck catheters, may necessitate open-heart surgery if endovascular treatments fail to remove them⁶⁸.

2.3.9 Aim of the study

The present study aimed to investigate the dwell time of tunneled dialysis catheters and to identify the factors that influence dwell time. Our primary endpoint was to identify the median dwell time of the hemodialysis catheter in our patient cohort, while our secondary endpoint was to identify potential factors which negatively influence the dwell time and hemodialysis to develop improvement strategies. Negative influence was defined as patients exhibiting a longer dwell time than planned and subsequently experiencing catheter-related complications. By identifying these factors, improvement strategies can be developed to minimize complications during the duration in which patients are dialyzed with a catheter until creation of definitive access succeeds (e.g., native shunt placement).

3. MATERIALS AND METHODS

3.1. Study design

A retrospective review of all records of patients receiving a CDC between 2014 and 2019 was conducted. A multidisciplinary team comprised of vascular/access surgeons and nephrologists participated in the process of indicating the catheter placement/explantation, whereas a standardized team performed the implantations and explantations of CDCs. All of the operations were conducted by two surgeons.

The primary endpoint was the catheter dwell time, defined as the time interval between the first documented catheter placement and the first documented catheter explantation or replacement. The secondary endpoint was to identify factors (e.g., gender, age, comorbidities, presence of AV-Fistula) or implantation-related technical factors (e.g., method of implantation, type of CDC, side of implantation, reason for explantation) that may have an impact on the catheter dwell time. Regarding age, patients were divided into 4 age groups: Group I; 11-20 years, Group II; 21-50 years, Group III; 51-70 years, and Group IV; 71-88 years. Ethics Committee approval was waived due to the study's retrospective design.

3.2. Data Collection

The data collection process involved filtering our in-hospital patient database using the ICD code "5-399.5 Implantation or Replacement of Venous Catheter Systems." Additionally, we conducted a comprehensive review of operations performed between the years 2014 and 2019 to include patients who may have had incomplete documentation (i.e., patients present in the system but lacking complete protocol or operation reports). From this scanned database, we identified patients who underwent procedures within our department. Subsequently, the protocols and reports of these operations were scrutinized to ascertain the dates of catheter implantation and explantation. Patients with missing implantation or explantation dates, rendering calculation of dwelling time impossible, were excluded from the analysis. Patients were included only if data regarding the implantation or explantation of catheters were available.

Following the identification of patients with definitive implantation and explantation dates, demographic data as well as comorbidities, including causes of renal failure, were extracted from the electronic database. However, a challenge emerged regarding patients who presented with multiple potential causes of their renal disease, such as concurrent diabetes and hypertension.

3.3. Techniques of CDC Implantation Employed in the Study

3.3.1. Standard Chronic Dialysis Catheter (CDC) Implantation

In our study, all catheter implantations were performed exclusively by two surgeons, employing standardized techniques for each method in our Clinic (new puncture, Seldinger-exchange, and Inside-Out).

In the procedure for inserting a hemodialysis catheter that we utilize, precise positioning is crucial. The site of venous puncture is typically 2-3 centimeter cephalad to the clavicle, ensuring placement between the two heads of the sternocleidomastoid muscle. Ultrasound guidance is employed to enhance accuracy during puncture. Following successful cannulation, the guidewire is carefully inserted under fluoroscopic control, guiding a 1-centimeter incision made at the skin surrounding the wire entry point.

The catheter's pathway is further facilitated by the introduction of a peel-away sheath, monitored closely under fluoroscopy. With meticulous care, the catheter is then passed through the sheath after the withdrawal of the introducer and wire. The sheath is removed upon complete implantation of the tunneled hemodialysis catheter. In our institution, the catheter is inserted retrogradely under fluoroscopic guidance to ensure precise placement of the catheter tip. The absence of connected ports on tunneled hemodialysis catheters which we utilised makes it possible to insert them in a "reverse-tunneled" or "retrograde" fashion, a method usually applied due to its advantages for precise catheter tip position.

Figure 4: the sequential steps of the catheter insertion procedure for the Internal Jugular Vein (IJV). A: Initial identification of anatomical landmarks and sonographic evaluation of the IJV. B: Ultrasoundguided puncture of the internal jugular vein (IJV) after local anesthetic administration, followed by the insertion of a J-Tip guidewire using the Seldinger technique. C: Advancement of a Peel-Away sheath over the guidewire. D: Insertion of the catheter after retrieval of the sheath dilator. E: Creation of a subcutaneous tunnel approximately 10-15 centimeter away from the vein insertion site. F: Emergence of the catheter from underneath the skin and fixation in place.

Following the initial insertion into the vein, a tunnel is created from the neck incision to the chest exit site. The catheter is then attached to a tunneling device and passed subcutaneously to its final chest location. Ports are connected, and the catheter is blocked using a heparinized saline solution to prevent thrombosis.

In cases requiring catheter exchange, a careful approach is taken. Under fluoroscopic guidance, a stiff wire is utilized to cannulate the catheter to be replaced, facilitating the removal of the old catheter. The new catheter is then introduced via the Seldinger-technique⁶⁹, ensuring a smooth transition and maintaining the integrity of the procedure⁶⁹ (**Figures 4, 5)**

Figure 5: Placement of Tunneled Hemodialysis Catheters. Tunneled hemodialysis catheters are ideally positioned under radiographic guidance. The optimal location for the catheter tip is at the cavoatrial junction.

3.3.2. Implantation of Catheter Using Surfacer® System

For patients with central venous obstructions, the Surfacer® System from Merit Medical® was used to insert CDCs through the inside-out technique. The device consists of a lengthy 8F(F for French) sheath that has a dilator, two radiopaque exit targets, and a 16F peel-away sheath that is 20 centimeter long.

The device has a handle that incorporates a pumping system and is coupled to a steel shaft that is 95 centimeter long. The tip of the steel shaft has a needle guide built into it, and it also has a needle wire that is 180 centimeter long and is already inserted **(Figure 6)**.

Figure 6: Components of the Surfacer® Inside-Out® Catheter Access System: A) Workstation (Sheath and Dilator), B) Surfacer Device, and C) Surfacer Device Handle. (Courtesy of Bluegrass Vascular Technologies)

An ultrasound is used to guide the placement of a short sheath with a diameter of 10 French in the right common femoral vein. This is principally the conduit for all devices utilized during the procedure. This is followed by the catheterization of the superior vena cava (SVC) through the inferior vena cava (IVC). The exit target is then marked on the skin just above the sternal edge of the clavicle. After obtaining the anteroposterior venography, the sheath is guided to the area of venous obstruction using a stiff wire.

The Surfacer® device is then inserted into the sheath and gradually advanced until the tip of the device is just above the clavicle in the anterior-posterior projection. Fluoroscopy is adjusted until the tip of the device is visible within the exit target. The device is rotated until the target window appears. The needle guide is advanced out of the tip. The venous occlusion acts as a stabilizer, like a purse-string suture, as the needle wire pierces the skin at the exit point establishing a through-and-through configuration of the wire. Over this wire, a sheath is introduced for a CDC placement. The Surfacer will be removed, and the insertion of CDC is accomplished traditionally. **(Figure 7)**

Figure 7: Procedure Steps of the Surfacer® Inside-Out® Catheter Access System: A) Advancement of the Surfacer Workstation Sheath to the point of occlusion. B) Progression of the Surfacer Device tip towards alignment with the upper margin of the clavicle, with the device rotated to demonstrate the maximum opening of the needle tip. C) Externalization of the Surfacer Needle Wire. D) Advancement of the Peelable Introducer over the Needle Wire.

3.4. Statistical analysis

Descriptive statistics were applied to describe the population's characteristics. Continuous data are documented as median (range) after assessing the normality of distribution using the Shapiro-Wilk and Kolmogorov-Smirnov tests⁷⁰. Categorical variables were described as numbers/proportions. Comparisons among groups were performed by applying the non-parametric Kruskal-Wallis test⁷⁰ (one-way analysis of variance, ANOVA on ranks), as the distribution of the investigated variable (catheter dwell duration) was not normal. Yates's correction for continuity was applied if indicated (sample size ≤ 5)⁷⁰. The level of statistical significance was set at .050. All statistical analyses were conducted using SPSS Statistics, version 28 for Windows.

4. RESULTS

During the study period, a total of 393 patients (56.5% males) who received a CDC were identified. The median age of the participants was 64 years (IQR 13-88). Two hundred and seventynine (279) patients who required catheter implantation were above the age of 50.Diabetes mellitus, hypertension, glomerulonephritis, and prerenal causes were the four most common causes of end-stage renal disease requiring hemodialysis. Diabetes mellitus was diagnosed in 117 patients, accounting for 29.8% of the total. Seventy-eight patients (19.9%) were under anticoagulation therapy (Vit-K antagonists or NOAK) at the time of implantation.

The most common implantation side was the right internal jugular vein (in 351 patients). Primary puncture with retrograde insertion was the implantation technique most commonly utilized (in 336 patients); 33 patients underwent an "inside-out" procedure, whereas a modified Seldinger technique was practiced to replace catheters in 24 patients who already had a catheter in place. The catheters used were Achim Schulz-Lauterbach® single- and double-lumen catheters with a length of 20-25 centimeter for single lumen (length from the cuff) and 23-28 centimeter for double-lumen (length from the cuff). A single-lumen catheter was implanted in 92.4% of the patients, and in the majority of cases (64.6%), it was inserted concomitantly with the AVF formation. **(Table 1)**

| Baseline characteristics | N of patients (%) |
|--|-------------------|
| Age Groups | |
| $1(0-20 \text{ years})$ | 21 (5.3%) |
| II (21-50 years) | 93 (23.7%) |
| III (51-70 years) | 132 (33.6%) |
| IV (\geq 71 years) | 147 (37.4%) |
| | |
| Gender | |
| Male | 222 (56.5%) |
| Female | 171 (43.5%) |
| | |
| Cause of ESKD | |
| Diabetic Nephropathy | 139 (35.36%) |
| Glomerulonephritis | 59 (14.99%) |
| Prerenal cause | 40 (10.18%) |
| Hypertensive Nephropathy | 39 (9.92%) |
| Vasculitis | 15 (3.82%) |
| Polycystic Kidney Disease | 12 (3.05%) |
| Renal artery stenosis | 12 (3.05%) |
| Drug-induced Nephrotoxicity | 10 (2.54%) |
| Postoperative renal failure | 9(2.29%) |
| HIV associated nephropathy | 9(2.29%) |
| Cast Nephropathy (Multiple Myeloma) | 6(1.52%) |
| CKD after Nephrectomy | 6(1.52%) |

Table 1: Baseline characteristics of the recruited patients

ESKD = End-stage kidney disease $$ IJV = internal jugular vein *AVF = arteriovenous fistula *DOAK= direct oral anticoagulant *Vit-K = Vitamin – K *CDC = tunneled dialysis catheter

The CDC was explanted after AVF maturation in 162 patients (41.2%). CDC dysfunction or a CDC-associated infection was the indication for explantation in 87 (22.1%) and 81 (20.6%) patients, respectively. In 63 (16.1%) further patients, the CDC was explanted due to other reasons (including no further need for HD, change to peritoneal dialysis, etc.). Among the 81 patients who experienced a CDC-associated infection, the most commonly isolated microorganisms were Staphylococcus spp. (MSSA, MRSA, hemolyticus, epidermidis), Streptococcus spp., Candida spp. (albicans, metapsilosis), or other pathogens (E. coli, P. aeruginosa, E.

faecium, E. cloacae, Morganella morganii). The median CDC dwell time in the whole cohort was 95 days (range 0-2974).

*male = male patients *female = female patients

Figure 8: Independent-Samples Kruskal-Wallis Test for dwell time of CDCs corresponding to biological gender.

Among female patients, a CDC had a median dwell time of 111 days, which was not statistically longer when compared with male patients (87.5 days, p = 0.119) **(Figure 8)**. Moreover, the youngest patients had a shorter CDC dwell time (median 56 days) compared to older patients. However, the difference failed to reach statistical significance among age groups ($p = 0.234$) **(Figure 9).**

*11-20 = Patients with ages between 11-20 (Group I) *21-50= Patients with ages between 21-50 (Group II) *51-70 = Patients with ages between 51-70 (Group III) *71-88= Patients with ages between 71-88 (Group IV)

Figure 9: Independent-Samples Kruskal-Wallis Test for dwell time of CDCs corresponding age groups.

Figure 10: Dwell time of CDCs according to etiology of renal disease.

The median CDC dwell time for patients diagnosed with renal artery stenosis was the longest (median 1002 days) **(Figure 10).**

*no = non-diabetic patients *yes = diabetic patients

Figure 11: Independent-Samples Kruskal-Wallis Test for Dwell time of CDCs with diabetic and nondiabetic Patients

The presence of diabetes did not have a statistically significant impact on the CDC dwell time (111 vs. 94 days, p = 0.327) **(Figure 11)**, while anticoagulation therapy was associated with longer CDC dwell times (median 126 days for patients receiving Vit-K Antagonists, median 151 days for patients receiving NOAKs) compared to patients without anticoagulation therapy (median 91 days, p = 0.034) **(Figure 12)**.

*Marcumar = patients taking marcumar/Vit-K Antagonists *NOAK = Non-vitamin K antagonist oral anticoagulants *no = not anticoagulated

Figure 12: Independent-Samples Kruskal-Wallis Test for dwell time of CDCs corresponding to anticoagulation

right = right internal jugular vein $$ left = left internal jugular vein

Figure 13: Independent-Samples Kruskal-Wallis Test for dwell time of CDCs corresponding to side of implantation.

A statistically significant shorter CDC dwell time was observed in patients, who received a CDC in the left internal jugular vein (102 vs 62.5 days, p.006), as well as among patients who underwent a seldinger exchange when compared to those with primary implantation (p.042)

*Inside-out = implantation of CDC with Surfacer® Inside-Out® Catheter Access System *puncture= implantation of CDC with fresh puncture and implantation *seldinger= wire exchange of a catheter with new catheter

Figure 14: Independent-Samples Kruskal-Wallis Test for dwell time of CDCs corresponding method of implantation.

*Single lumen= Single lumen CDC *Double lumen= Double lumen CDC

Figure 15: Independent-Samples Kruskal-Wallis Test for dwell time of CDCs corresponding to catheter design

No statistically significant difference was found regarding the design of the implanted catheter (single lumen, median 95 days; double lumen, median 93.5 days, p = 0.884) **(Figure 15)**.

Furthermore, CDCs implanted before AVF creation had a shorter dwell time when compared to those implanted after or concomitantly to AVF creation; however, this difference was not statistically significant (73 vs. 114 vs. 94 days, p = 0.257) **(Figure 16)**. CDCs that were explanted due to infection or dysfunction had a shorter dwell time compared to those explanted after AVF maturation (94 vs. 63 vs. 116.5 days, p = 0.003) **(Figure 17).**

*Shunt + Demers together= Patient beginning dialysis with the creation of an AV fistula and receiving a CDC. *Shunt first= Patient anticipated to commence dialysis in the future but not currently, undergoing preemptive AV fistula creation.

*CDC First= Patient commences dialysis with a CDC due to urgency, without waiting for AV fistula maturation.

Figure 16: Independent-Samples Kruskal-Wallis Test for dwell time of CDCs corresponding to AVF creation

*Infection=Explantation of CDC due to infectious complications.

*Shunt maturation = Explantation of CDC due to AV fistula maturation.

*Dysfunktion= Explantation of CDC due to thrombosis or other mechanical issues.

*Others= Explantation due to various reasons other than infectious or mechanical complications, such as patient preference.

Figure 17: Independent-Samples Kruskal-Wallis Test for dwell time of CDCs corresponding reason of explantation.

5. DISCUSSION

Numerous factors may influence catheter dwell time, e.g., AV access patency, age, sex, diabetes mellitus (DM), peripheral vascular disease (PVD), smoking, obesity, hyperparathyroidism (hPTH), anemia, and medications. In this chapter, catheter dwell time will be discussed in relation to biological gender, age, diabetes mellitus, anticoagulation, catheter design, implantation side, and the influence of a concomitantly existing AV fistula and difference of dwell time according to the reason for explantation of the catheter. Renal artery stenosis, an indicator of an advanced stage of generalized advanced atherosclerosis —an independent predictor of catheter dependence⁷¹— had the longest catheter dwell time which can be explained by accelerated arterial calcification, resulting in reduced patency of arteriovenous (AV) fistulas and consequently, dependence on catheters.

5.1. Influence of Diabetes Mellitus and Generalized Atherosclerosis on Catheter Dwell Time

Our analysis showed no statistically significant difference regarding catheter dwell time between diabetic and non-diabetic patients.

It is anticipated that diabetes mellitus may have a detrimental impact on the catheter dwell time. The prothrombotic state caused by diabetes mellitus might potentially lead to earlier occlusion of the catheter. Furthermore, since diabetes increases a patient's risk of infection, the catheter may need to be removed earlier than expected or require frequent catheter changes. Elevated levels of PAI-1(Plasminogen activator inhibitor-1) lead to a decrease in fibrinolytic activity and an increase in tissue factor, together with an increase in coagulation factors VII and $XIII^{72}$. Additionally, there is a decrease in antithrombin III, as well as protein C, von Willebrand's factor and factor VIII are both elevated, leading to a hypercoagulable state^{$72,73$}. Both the intracellular killing of bacteria and the chemotaxis of leukocytes are negatively affected by hyperglycemia^{72,74}. In the presence of chronic renal failure, immune function will be further impaired.

Diabetes-associated atherosclerosis affects not only arterial but also venous fistula segments (venous atherosclerosis), and it does not vary from conventional atherosclerosis in any way75,76.

Dialysis outcomes and practice patterns study (DOPPS) data show that patients who are female, older, have higher BMIs, diabetes, or peripheral vascular disease are less likely to use an AVF than other kinds of vascular access¹³. One study investigating the lock solutions for

CDCs in diabetic patients showed 109 CDCs placed among 96 diabetic ESRD patients recorded 28 episodes of catheter thrombosis (25.7%), 107 episodes of catheter related blood mstream infections in 39785 catheter days (2.68/1000 catheter days), amounting to a mean percent catheter survival at 365 days of 56.9% (62/109) and a catheter related blood stream infection related mortality of 16.7% (16/96) during the study period⁷⁷. Another study investigating catheter removal versus guidewire exchange to treat catheter-related bloodstream infection found no statistically significant difference in catheter infection-free survival time for guidewire exchange and catheter removal groups ($P = .69$), which was not affected by age, sex, presence of diabetes mellitus, or type of causative organism 78 .

To summarize, the atherosclerotic and calcific changes may lead to early AV fistula failure, resulting in longer catheter dependency and therefore longer dwell time, but also the aforementioned theoretical effects of diabetes might cause frequent catheter changes due to infection and thrombosis. Based on our observation of a significantly shorter dwell time for CDCs explanted due to infection or dysfunction, compared to those explanted following AVF maturation, it can be considered that diabetes mellitus-induced hypercoagulability and immunodeficiency may theoretically result in frequent catheter occlusions and infections, thereby causing a shorter catheter dwell time , at the same time diabetes-induced atherosclerosis negatively influences AVF maturation, which might lead to catheter dependency. This might explain and might cause the lack of a notable difference regarding catheter dwell time between diabetic and non-diabetic patients.

5.2. Influence of Biological Gender on Catheter Dwell Time

In our study, we observed a statistically insignificant difference in catheter dwell time between genders. Male patients had a slightly shorter catheter dwell time compared to female patients. Female gender is linked to a lower prevalence of pre-emptive AVFs, higher utilization of cath-

eters as a bridge to AVFs, and lower patency rates compared to males, as indicated by a retrospective analysis of all patients in the United States Renal Data System who underwent AVF or AVG placement for HD access between January 2007 and December 2014⁷⁹. Even though in our study, we couldn't reach statistical significance due to our small cohort, we believe that there is a difference between genders. This difference may be attributed to the fact that female patients generally have smaller vessel calibers compared to male patients, potentially resulting in delayed fistula maturation. This delay could indirectly increase catheter utilization and, consequently, dwell time. However, in terms of access maturation, one study couldn't show a disparity between male and female patients, although female patients exhibited

better survival rates⁷⁹. However, a recent systematic review revealed that female patients exhibit lower rates of maturation, reduced rates of primary, primary-assisted, and secondary patency, necessitate a higher number of procedures per capita to attain maturation and sustain fistula patency, are more inclined to undergo dialysis using an arteriovenous graft or chronic dialysis catheter , and necessitate a prolonged duration and potentially more invasive interventions to achieve fistula maturity leading to increased cathteter dependency⁸⁰.

5.3. Influence of Age on Catheter Dwell Time

In our study, patients were categorized into four age groups: Group I (11-20), Group II (21-50), Group III (51-70), and Group IV (71-88). Group I exhibited a median catheter dwell time of 56 days, Group II showed a median of 109 days, and Group III had a median of 101 days ($p =$ 0.234). These results were not statistically significant. However, the youngest patients (Group I) tended to have slightly shorter CDC dwell times compared to older patients.

Globally, the renal replacement therapy (RRT) population comprises a substantial and growing percentage of elderly individuals, accounting for 25-30 percent of the total^{81,82}. Between 1996 and 2003, there was a 57% increase in the number of dialysis patients over 65 in the United States, representing an annual growth rate of over 10%⁸¹. Researchers speculate that the increase in end-stage renal disease (ESRD) cases may be linked to the greater acceptance of elderly individuals (>80 years old) into dialysis programs^{83,84}. The higher prevalence of comorbidities (such as peripheral vascular disease, diabetes, etc.) in older age groups may elevate their risk.

We believe that the lack of significant difference between Groups II and Groups III and IV may be attributed to the choice of AVF employed. In our institution, we tend to favor Gracz fistulas more frequently with elderly or aging patients, as they provide maturation for more than one outflow access vein. Consequently, the likelihood of a patient experiencing a mature, dialysiscapable vein is higher with Gracz fistulas, leading to statistically insignificant reduced catheter dwell times in Group III and Group IV compared to Group II.

Recent data from a meta-analysis of 13 cohort studies (11 of which were retrospective) indicated that wrist radiocephalic AVFs (RC-AVFs) had a higher risk of primary failure and lower patency rates in older patients across all periods⁸⁵. This meta-analysis revealed that elderly patients faced a significantly higher risk of RC-AVF failure at 12 months compared to nonelderly individuals (OR, 1.525)⁸⁵. The elevated incidence of steal syndrome following proximal access procedures, particularly in elderly patients, is also a concern may lead to catheter utilization ⁸⁶. Catheter utilization cannot be analyzed separately from shunts, as the goal is to bridge the periods when the shunts are not functional, maturing, or in the planning phase.

Although not reaching statistical significance in our cohort, the literature findings support our thesis of a trend towards reduced catheter dependency in Group II compared to older patients (Group III and Group IV).

5.4. Influence of AV-Access on Catheter Dwell Time

The difference in catheter dwell time between patients who received a catheter together with fistula creation and those who had their AV fistula created first, compared to individuals who received the catheter first, couldn't reach statistical significance.

By lacking statistical significance, It could be observed that patients with the longest catheter dwell times belonged to the group who started dialysis with a shunt, while patients whose hemodialysis was initiated with a CDC had less catheter dwell time.

Significant disparities in vascular access exist between Europe, Canada, and the United States, even after adjusting for patient characteristics⁷¹. Vascular access care shares similar challenges across regions but with varying degrees. Obesity, type 2 diabetes, and peripheral vascular disease—all independent predictors of catheter use—are growing concerns globally, potentially leading to more challenges in native AV fistula creation and survival⁷¹.

Nevertheless, in the USA, following the establishment of the Fistula First Initiative, AV fistula use among prevalent HD patients steadily increased from 34.1% in December 2003 to 60.6% in April 2012¹⁰. For incident patients, vascular access statistics at the initiation of chronic HD in 2009 were as follows: AVF in use 14.3%; AVG in use 3.2%; CDC in use 81.8%; AVF maturing 15.8%; and AVG maturing $1.9\%^{8,12}$.

Timely patient referral for vascular access creation is crucial for favorable vascular access outcomes. Early referral results in more well-functioning autogenous AV fistulas, while late referral increases the likelihood of AV fistula non-maturation and the need for a CDC for HD⁸⁷⁻ 90 . Moreover, HD initiation with a CDC and a prolonged AVF maturation time result in poorer long-term AVF patency rates^{90,91}.

According to one study, patients with a history of temporary vascular catheter access had an 81% increased risk of AVF failure⁹². Mechanical injury caused by catheter implantation and movement within the vessel can lead to endothelial damage, inflammation, and intimal hyperplasia^{93,94}. It has been suggested that central venous stenosis resulting from a catheter can impair maturation, reduce function, and decrease the survival of newly created AV fistulas⁹⁵.

Long-term AV fistula survival is poorer in patients with a history of ipsilateral CDC, as per some retrospective investigations⁹⁶. However, the exact impact of the presence and location of a preexisting CDC on the development and early function of a newly created AV fistula is not fully understood. Notably, AV fistulas that mature slowly or require assisted maturation are associated with poorer long-term survival.

There was a correlation between the presence of an ipsilateral CDC and a lower rate of successful AV fistula use at 6 months 97 .

This leads us to the conclusion that our data, while not reaching statistical significance, aligns with existing literature, indicating that patients initiating dialysis with a catheter tend to develop catheter dependence. This tendency may be attributed to the detrimental effects of catheterization on central veins, potentially impeding the maturation of arteriovenous fistulas as well as central venous stenosis and thereby causing blood flow stagnation. Hence, it underscores the critical importance of promptly referring patients to an AV-access specialist for assessment regarding the preemptive creation of autologous AVFs.

5.5. Influence of Implantation Side and Method on Catheter Dwell Time

The right internal jugular vein was the preferred site for catheter implantation in 351 patients, as it drains directly into the superior vena cava and the right atrium, thereby being associated with better patency and fewer complications. Conversely, the left internal jugular vein was chosen in 42 individuals.

The right internal jugular vein is recommended for tunneled hemodialysis catheter insertion due to its higher patency, possibly attributed to reduced kinking. A prospective study involving 812 catheters in 492 patients³⁴ aimed to determine the parameters impacting the durability of tunneled hemodialysis catheters, revealing considerably greater durability for those implanted into the right internal jugular vein compared to the left internal jugular vein.

In an observational study comparing right- versus left-sided catheter placement (409 participants and 532 catheters)⁹⁸, left-sided approaches resulted in significantly more catheter-related infections requiring removal (0.33 vs. 0.24 per 100 catheter-days; P = 0.012). Additionally, reduced blood flow necessitating CDC exchange (i.e., CDC malfunction) was also shown to be non-significantly greater with left-sided approaches (0.13 vs. 0.08 per 100 catheter-days; $P = 0.08$). However, these results were influenced by the CDC tip's location. For CDC tips implanted in the superior vena cava or peri-cavoatrial junction, left-sided approaches resulted in more CDC malfunction and infection than right-sided approaches. Conversely, with CDC tips implanted in the mid-to deep right atrium, left-sided versus right-sided approaches yielded identical CDC malfunction and infection rates. This underscores the importance of correct CDC implantation and confirmation imaging.

Our study revealed a significant difference, with a right-sided (internal jugular vein) approach exhibiting statistically longer dwell times compared to a left-sided approach. Additionally, patients who already had a preexisting catheter and received a catheter exchange through wire had shorter dwell times compared to patients who underwent primary puncture for catheter placement. Moreover, there was no statistically significant difference among the various implantation methodologies.

Nevertheless, drawing definitive conclusions regarding the dwell time disparity between the Inside-Out technique and alternative approaches is unwarranted based on our findings. This is because patients receiving catheters via the Inside-Out technique represent cases where all other possibilities for AV-access have been exhausted. Consequently, catheters implanted using the Inside-Out technique are anticipated to remain in place for an extended period, unlike standard implantation methods intended for subsequent removal upon the establishment of a more secure AV-access.

Furthermore, the utilization of the wire-exchange method in specialized clinical scenarios, where primary puncture and implantation present formidable challenges, serves to preserve the catheter track.

5.6. Influence of Anticoagulation on Catheter Dwell Time

In our study, we were able to demonstrate a statistically significant difference in catheter dwell time between systematically anticoagulated and non-anticoagulated patients.

A study from 2005 showed that adequate anticoagulation with a target INR of 1.5–2.0 may prevent CDC malfunction and improve catheter outcomes⁹⁹.

A systematic review of randomized clinical trials assessing the relative effects of different strategies for the prevention of catheter malfunction in adults with ESKD identified 27 relatively small studies, with an average of 75 participants and 6 months of follow-up. Newer approaches, including alternative anticoagulant locking solutions, systemic agents, and low or no-dose heparin, did not affect rates of catheter malfunction compared with usual care¹⁰⁰.

Currently, it is not possible to make an evidence-based recommendation for anticoagulating patients with CDCs, but it can be considered for patients who have experienced repeating catheter thromboses, present with high grades of stenotic lesions on their central veins, or have complicated backgrounds with AV-access problems.

5.7. Influence of Catheter Design on Catheter Dwell Time

No statistically significant disparity was observed concerning the configuration of the implanted catheter. The luminal structure of catheters has undergone development, transitioning from twin single-lumen catheters to the prevalent dual-lumen catheters featuring a double-D design, known for their minimal hydraulic resistance¹⁰¹. In our cohort predominantly utilized catheter system was single-lumen catheters. Presently, the majority of chronic dialysis catheters are dual-lumen, employing the double-D configuration for the internal lumen due to its advantageous attributes of reduced hydraulic resistance and compact overall diameter¹⁰².

5.8. Limitations of the study

The limitations of our study are rooted in its single-center and retrospective nature, with a limited number of patients. Patient selection at our center was non-standardized, resulting in heterogeneous groups of patients included in the study. The results of the investigation once again highlighted the challenging nature of follow-up care for dialysis patients. It must be noted that during data collection, each patient was assigned a single renal diagnosis leading to renal disease and dialysis. The data were collected from electronic discharge documents, which sometimes provided more than one possible cause of renal disease. Patients were categorized based on the most probable diagnosis chosen as the cause of renal disease, introducing a certain degree of bias. The vascular access center at our institution performs over 600 vascular access procedures annually with a standardized team and technique, which eliminates the potential impact of a learning curve.

5.9. Conclusions

Based on our study, the optimal approach for catheter insertion is to select a new puncture site in the right internal jugular vein. The Seldinger exchange method should only be considered in rare instances, such as when the central venous status prohibits or significantly complicates performing a new puncture. Furthermore, patients who already have autologous AV access created and receive a tunneled dialysis catheter due to AV access dysfunction seem to have the least catheter dependency. Anticoagulation may offer a slight protective effect against thrombotic catheter occlusion.

However, several known factors already described in the literature did not demonstrate statistical significance in our study; therefore, larger studies are required to clarify the role of those factors on the CDC dwell time. An optimal determination of factors influencing the CDC dwell time could lead to more efficient treatment of patients with end-stage renal failure.

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