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Comparative Clinical Performances of Tunneled Central Venous Catheter versus Arterio-Venous Accesses in Patients Receiving High Volume Hemodiafiltration: The Case for High-Flow DualCath, a Tunneled Two Single Lumen Silicone Catheter

Bernard Canaud [1,2,*], H Leray-Moragues [3], Leila Chenine [4], Marion Morena [5], Miller George [6], Ludovic Canaud [7] and Jean Paul Cristol [3,5]

1 Montpellier University, School of Medicine, Montpellier-France
2 MTX Consulting International, Montpellier-France
3 AIDER-Santé, Ch. Mion Foundation, Montpellier, France
4 Nephrology, Intensive Care, Dialysis & Transplantation, Lapeyronie University Hospital, Montpellier, France
5 PhyMedExp, University of Montpellier, INSERM, CNRS, Department of Biochemistry and Hormonology, University Hospital Center of Montpellier, 34000 Montpellier, France
6 Medical Components, Inc., Clinical Affairs, Harleysville, Pennsylvania, USA
7 Chest and Vascular Surgery Department, CHU Montpellier, 34000 Montpellier, France
* Correspondence: canaudbernard@gmail.com; Tel.: +0033 (6) 77 73 55 68

Abstract: Tunneled central venous catheters (CVC) are mainly considered as rescue vascular access option in dialysis but still used in about one quarter of prevalent patients worldwide as being associated with poor performances and higher risks. Study design. In this retrospective single-center study, we aimed to report on clinical performances achieved with high-flow tunneled CVC (DualCath, DCath) and compared it with arteriovenous accesses (AVAs; AV fistula, AV graft, Thomas Shunt) in a hospital-based dialysis unit. Methods. Sixty-eight stage 5 chronic kidney disease dialysis dependent patients (CKD5D) receiving high volume hemodiafiltration were followed-up for 30 months. The study consisted of two phases: baseline cross-sectional and longitudinal follow-up of key performance indicators. Clinical performances consisting of effective blood flow and blood volume, recirculation, urea and ionic Kt/V and total Kt, ultrafiltration volume and percent reduction of ß2-M were measured monthly as part of quality control in our unit.Results. At baseline, effective blood flow with DCath was close to 400 ml/min, similar to AVAs. Recirculation with DCath (7%, 6-13%) was higher than AVAs. Diffusive dialysis dose delivered with DCath (spKt and eKt/V) and convective dialysis dose achieved with DCath were slightly lower than AVAs, but still much higher than recommended by guidelines. Percent reduction of ß2-M achieved with DCath was also 4 to 10% lower than AVAs. On longitudinal follow-up, main clinical performance indicators of DCath (total Kt and total ultrafiltration volume, L/session) were maintained very stable over time and close to those achieved with AVAs. Conclusions. As shown in this study, high-flow DualCath tunneled two single lumen silicone catheters may be used to deliver high volume hemodiafiltration in a reliable and consistent manner without compromising clinical performances. These results rely from the specific design of the two silicone cannulas and the strict adherence to best catheter practices.

Keywords: vascular access; tunneled central venous catheter; dialysis clinical performances; diffusive dialysis dose; convective dialysis dose; effective blood flow; recirculation

Introduction

Tunneled central venous catheters (CVC) are considered as rescue vascular access option in dialysis patients by almost all clinical practice guidelines, as being associated with higher morbidity, lower performances, and greater cost[1-4]. However, prevalent use of CVC in dialysis remains high,

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ranging almost from zero up to 50% with a median value of 25% of dialysis patients worldwide[5-8]. These facts tend to support the notion that CVC are still needed in the vascular access care offering [9-11] of kidney disease management since they provide an interesting option to ensure care continuity in CKD patients facing recurring vascular access problems well recognized in their last KDOQI issue[2].

Intrinsic limitations of CVC are acknowledged and analyzed in various reports[12,13]. They belong either to the geometry of the cannulas (internal lumen diameter, length, polymer characteristics), or the catheter design (single or dual lumen, central and side holes) or to the catheter tip's location within the venous central system (superior vena cava, right atrium)[14,15]. In addition, tunneled CVC bear higher risk (dysfunction, infection, thrombosis) that can be mitigated by better handling and locking solution[16-19]. These facts have raised several controversies in the scientific literature with pros and cons[11,20-22]. It is not our intent to enter this polemic, but rather to assess clinical performances delivered by means of tunneled CVC compared to arterio-venous accesses (AVA) in stage 5 chronic kidney disease (CKD5D) patients receiving high volume hemodiafiltration as mainstream treatment.

In this study, we aimed to report on clinical performances achieved with high-flow tunneled CVC (DualCath, DCath) and compared it with various AVA used at the same time in our hospital-based dialysis unit.

Material and Methods

1. Study design

This is a retrospective single-center study performed in a teaching hospital-based dialysis unit (Lapeyronie Hospital, Montpellier, France) using data extracted from patient electronic dialysis medical records. Data collection extended from October 1, 2009, to May 31, 2012 (30 months of follow-up). All data collected were part of clinical dialysis performances and quality control assessment precisely protocolized and performed monthly (first week of the month, midweek session).

The study consisted of two parts: firstly, a baseline assessment of clinical performances corresponding to a cross-sectional analysis using data of three consecutive months while patients being clustered by vascular access type (tunneled CVC, AVA); secondly, a longitudinal follow-up of clinical performances up to 30 months while patients were clustered by vascular access type.

Clinical dialysis performance indicators consisted of effective blood flow, access recirculation, urea $_{sp}$Kt/V and $_{dp}$Kt/V (Daugirdas), ionic dialysance measurement (Online Clearance Measurement, OCM) from dialysis machine ($_{OCM}$Kt/V), total clearance delivered per session (Kt), total ultrafiltration volume (V_{UF}) and substitution volume (V_{SUB}) per session, albumin, Hemoglobin.

2. Patients

This study enrolled 68 stage 5 chronic kidney disease dialysis dependent patients (CKD5D) receiving high volume hemodiafiltration. Ten were incident patients (< 3 months treatment) and 58 were prevalent patients (≥3 months treatment). Some incident patients were converted during the study to arteriovenous fistula or graft access.

3. Ethics statement

The study was conducted according to the principles of the Declaration of Helsinki and in compliance with International Conference on Harmonization/Good Clinical Practice regulations. According to the French Law, the study has been registered at "Ministère de la Santé et des Solidarités" after approval by the Montpellier University Hospital's ethics committee (Comité de Protection des Personnes Sud Méditerranée IV) with the following number DC-2008-417. All patients gave their written informed consent.

4. Vascular accesses

DualCath (DCath) is manufactured by MedComp in USA and distributed in Europe [23-26]. DCath consists of two independent single lumen silicon catheters and their tubing extension adaptor are presented separately, with all material required for insertion (2 single lumen silicone cannula with their semi-rigid plastic stylets, straight tunneler, syringes, needle, sutures, large bore needles, two

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wire guides 50 cm, two external adaptors, two introducer-dilator catheters), packaged in a sterile tray protected by a double transparent plastic film.

DCath consists of two single lumen silicone cannulas with separate tubing extension adaptors that are docked together at the time of insertion. They present circular mark every 5 cm to precisely know length of the catheter. The intravascular cannula is made of radiopaque silicone polymer tubing (length 40 cm, inner/outer diameters 2.0/3.2 mm). The length of cannulas is adjusted at the time of insertion to patient anthropometry. As such, DCath may differ according to patient height and side of insertion: 25–27 cm and 30–32 cm for the right and left sides respectively. Six holes are disposed spirally along their distal tip. The extension or adaptor is made of 6-7 cm silicone polymer of larger diameter ending in a nylon luer-lock connection device with colored marks (blue, venous; red, artery).

4.1. DualCath Insertion

DCath insertion relies on a percutaneous method performed under local anesthesia by trained nephrologist in a clean room or theater with support of a nurse and appropriate environment and material (bed, resuscitation, light, medication, gas). Most of DCath insertions were performed under local anesthesia, sometimes with support of nitrogen dioxide gas under mask, rarely DCath insertion required general anesthesia (complex case, anxiety). Patient preparation consisted of skin washing, nonabrasive shaving and iodine disinfection (betadine) 1 hour before DCath insertion.

Choice of the central vein location depends on the anatomical condition of the patient. Vast majority of patients had DCath inserted in the right internal jugular vein, few had insertion in the left internal jugular or femoral vein as alternative options. For practical reason, vein cannulation was mainly based on landmark technique rather than guided by US mapping. Vein US mapping was mostly applied in complex cases. During the preparation of catheter insertion, landmarking of skin area and vein location was performed and drawn on skin with surgical skin marker.

Vein cannulation was performed using strictly aseptic surgical conditions, including mask, hat, sterile gown and gloves for the operator and sterile drapes covering most of patient body and leaving access to the region of interest.

DCath insertion consists usually in five main steps. In the case of right internal jugular vein cannulation, a brief description of the different steps is given here:

1. The first step consists of local anesthesia in the prethoracic area and at the base of the neck region at the top of the Sedillot triangle.
2. The second step consists in locating the right internal jugular vein and inserting the two silastic cannulas into the right internal jugular vein based on a percutaneous-based method using a desilet technique relying on an introducer and a vein dilator.
3. The third step consists of tunnelling each cannula with a metallic tunneler advanced in the subcutaneous tissue through the cervical hole downward following the anesthetized track and exiting in the prethoracic area. Cannula is firmly attached to the tunneler with a tressed nylon suture which is then passed through tunnel with cannula. The second cannula is tunneled with the same method in a parallel subcutaneous track.
4. The fourth step consists in shortening the cannulas to fit chest patient size with use of space band marks, putting on a silicone rubber collar, and then docking the external extension piece ending by luer-lock connector to the cannula. Cannula and tubing extension assembly are then rigidified by plastic stylet and pushed back with a twisting movement through the enlarged skin exit. Cannulas are then rinsed with saline and clamped with a vascular atraumatic clamp. Anchoring the two cannulas together is then performed with a subcutaneous nylon suture through the jugular neck hole. The two threads emerging from the cervical cutaneous orifice are recovered, isolated, and firmly tied together to create a bridge suture between the two cannulas (stays).
5. The fifth step consists in closing skin cutaneous orifice with intradermal sutures, rinsing, locking cannulas with antithrombotic solution and capping them with Luer-lock caps.

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4.2. DualCath Looking and Imaging (Figure 1)

Figure 1 presents a cartoon of the DCath inserted in the right internal jugular vein with a picture of the skin exit looking. Chest X-Ray is performed before catheter use to secure catheter position and check the lack of abnormalities or complications.

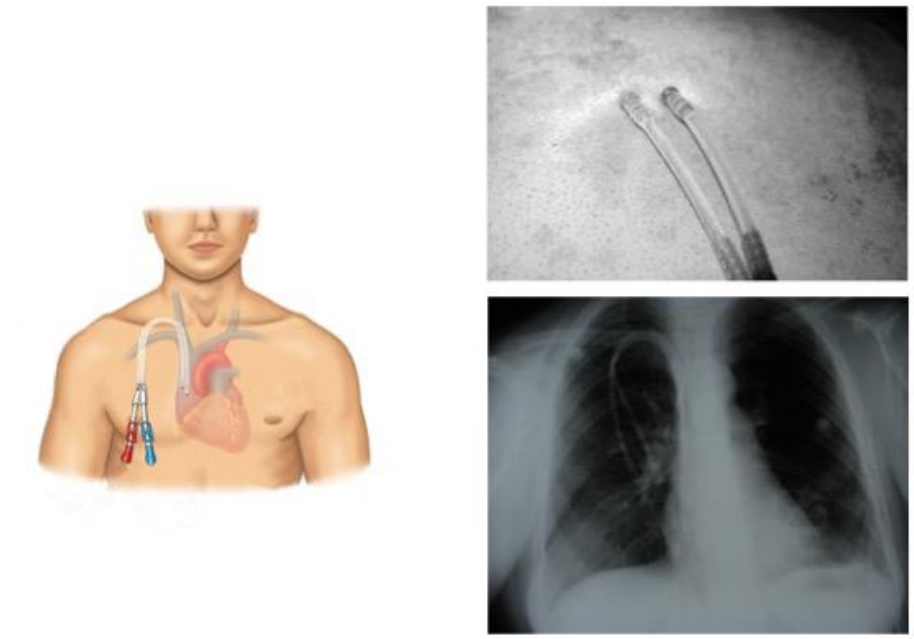

Figure 1

Figure 1. Cartoon of the DCath inserted in the right internal jugular vein with a picture of the skin exit looking. Chest X-Ray is performed before catheter use to secure catheter position and check the lack of abnormalities or complications.

4.3. DualCath Management and Handling

DCath are used exclusively for hemodialysis purpose and any other use (i.e., IV perfusion, blood sampling) is strictly prohibited. DCath are handled by trained nurses (i.e., bearing sterile gown, mask, hat, gloves) in strictly surgical aseptic conditions (ie, sterile drape protection at time of connecting and disconnecting extracorporeal blood circuit). At the time of connection, remaining blood material and antithrombotic solution within each line of DCath is withdrawn with a 10-ml syringe and discarded. Isotonic saline (5 to 10 ml) is then flushed vigorously in each line of DCath to clean and probe resistance of DCath. Extracorporeal blood circuit is then initiated by connecting each DCath line to the corresponding blood line and blood pump is launched and brought progressively to its prescribed speed. At the time of disconnection, blood pump is stopped, and blood is flushed back and returns to patient (about 200-300 ml of saline) by means of online rinsing option alternatively on the arterial and venous side. Blood lines are disconnected, and each line of DCath is filled and locked with a mixture of saline and 0.3% citric acid solution (2.5 to 2.8 ml per catheter line).

Luer-lock cap is then screwed. DCath are wrapped in a split sterile gauze and a transparent sterile adhesive waterproof air-permeable dressing is applied and kept until next dialysis session.

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4.4. Arteriovenous access management

Arteriovenous fistula or grafts are handled with particular care and strictly hygienic conditions relying on betadine as skin disinfectant, using sterile material, drape and gloves as well as mask, gown and cap for the operator at the time of access handling. Needling is performed by trained nurse with fistula needle of 15 gauges in majority of patients using laden rope method.

5. Clinical performances assessed

Baseline clinical performances consisted in six key performance indicators that included the effective blood flow (ml/min), venous pressure (mmHg), vascular access recirculation (VA.REC) (%), single pool Kt/V, double pool Kt/V and convection volume (l/session).

These indicators were measured in the six following vascular accesses: native arteriovenous fistula (AVF), arteriovenous graft (PTFE)(AVG), right femoral DCath (RFDC), right internal jugular DCath (RIJDC), left internal jugular DCath (LIJDC) and Thomas Shunt.

In addition, cumulative clinical performances comparing DCath and grouped AVA over a 30-month follow-up period were performed.

5.1. Blood flow (QB, ml/min)

Blood flow measurement was performed by means of bubble transit time on 1 meter of a calibrated segment of the arterial line[27]. This method is currently used in our unit and fits perfectly with Transonic data. Calculation of effective blood flow relies on the following formula:

5.2. Total blood volume processed (TBVP, L/session)

Total blood volume processed was calculated from dialysis machine as the product of the effective blood flow (QB) times treatment time (tHD) as TBVP = QB x tHD

5.3. Vascular access recirculation (VA.REC, %)

Total recirculation (T.REC) was calculated by using urea dosing issued from three blood samplings (artery (ART) and venous (VEN) sampling, then followed by a second artery sampling after 2 minutes stop of blood pump (ART_{+2})) as follows[27,28]:

$$T.\ REC = (ART_{+2} - ART)/(ART_{+2} - VEN) \times 100$$

This method has been validated in our unit and used as standard of care for years. Results fit perfectly with recirculation obtained with Blood Thermal Monitoring device which also assesses total recirculation. When compared to Transonic data, it has been shown that 10% was coming from the cardiopulmonary bypass created by the arteriovenous bypass[16,29]. A 10% value of cardiopulmonary bypass was then subtracted from arteriovenous access measurements but not from tunneled central venous accesses as follows:

$$VA.\ REC = T.REC - 10 \text{ (for arteriovenous accesses only)}$$

Dialysis dose delivery

Dialysis dose delivery was assessed with three key indicators: firstly, the urea clearance expressed as fractional urea clearance (i.e., $_{urea}Kt/V$), or its surrogate using ionic clearance (online clearance measurement, $_{OCM}Kt/V$)[30,31] and as total urea clearance (Kt) delivered per session (i.e., liters per session) to quantify small molecules clearances[30,32,33]; secondly, the total ultrafiltration volume (liter per session) or convective dialytic dose used as surrogate marker of middle and large molecule clearances[34]; thirdly, percent reduction of ß2M (%) per session.

5.4. Urea Kt/V

Urea Kt/V was calculated from pre and postdialysis blood sampling using the single-pool[35] (sp) and equilibrated (e) double-pool Kt/V formula from Daugirdas[36] as follows. Of note, postdialysis blood sampling was performed after reducing blood pump down to 50 ml/min for two minutes.

$$_{sp}Kt/V = -\ Ln\ (Urea_{post}/Urea_{pre} - 0{,}008 \times t_{HD}) + (4 - 3{,}5 \times Urea_{post}/Urea_{pre}) \times WL/BW_{post}$$

$$_{e}Kt/V = {}_{sp}Kt/V - (0{,}6 \times {}_{sp}Kt/V/t_{HD}) + 0{,}03$$

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where WL is the weight loss during the session, BW the body weight and t_{HD} the effective treatment time

5.5. Ionic dialysance and $_{ocm}$ Kt/V

Ionic dialysance Kt/V and $_{ocm}$Kt/V was measured and calculated from dialysis monitor using integrated ionic dialysance (K_{ocm}) performed across dialysis session, effective HD machine treatment time (t_{HD}) and total body water (V) derived from Watson formula by default.

5.6. Total Kt (TKt, L/session)

Total Kt was calculated as the product of ionic clearance (K_{ocm}) and effective treatment time (t_{HD}) of dialysis session as $TKt = K_{ocm} \times t_{HD}$

5.7. Total ultrafiltration volume (VUF, L/session)

The total ultrafiltration volume (VUF) is the sum of online substitution volume infused during the HDF session (VSUB) plus intradialytic weight loss (WL) to correct fluid overload. This indicator is used as surrogate of convective dialytic dose delivered per session[34].

5.8. Percent reduction of β2-Microglobulin (PRβ2M)

Percent reduction of β2M was used as a marker of HDF efficiency as patients were receiving HDF treatment[34]. Postdialysis β2M was corrected for hemoconcentration using Bergstrom formula[37]

$$_{cor}\ \beta2M = _{post}\ \beta2M\ (1 + \Delta BW/0.2BW_{post})$$

where ΔBW is the difference between pre and post-treatment BW.

PRβ2M was calculated as follows:

$$PR\beta2M = 1 - (_{cor}\beta2M_{post}/\beta2M_{pre}) \times 100$$

5.9. Normalized protein catabolic rate (nPCR)

nPCR (g/kg/24h) was calculated from urea kinetic modeling using the three points method[38] (pre/post and pre next dialysis session)

Blood samples were analyzed on the same day in the central laboratory of our hospital using validated autoanalyzer methods.

6. Statistics

Statistical analyses were performed using JASP Software 0.17.1 (University of AMSTERDAM). Normality and variance equality tests were made for all data, and statistical significance level was set to $p < 0.05$ for all analyses. Continuous variables were reported as means (SD) or as medians [25-75%] depending on whether the data were normally distributed or not. Categorical variables were reported as percentages with number in parentheses. Unpaired normally distributed continuous variables were tested for difference using unpaired t-test. Unpaired non-normally distributed continuous data were analyzed using Mann-Whitney test. Pearson's or Spearman's test were used for correlation analyses depending on whether data were normally distributed or not, respectively.

3. Results

3.1. Patient characteristics

The cohort consisted of 27 females (age 72 [66.5-75.5] yo.) and 41 males (age 68.5 [60.0-75.0] yo.) with a dialysis vintage of 9 [2.5-30] months. Primary kidney diseases were as follows: hypertension and/or ischemic nephropathy 28 (41.2%); Diabetic kidney disease 11 (16.2%); Chronic glomerulonephritis 8 (11.8%); Toxic kidney disease 6 (8.8%); Autosomic polycystic kidney disease 4 (5.9%); Alport 1 (1.5%); Interstitial chronic nephritis uropathy 1 (1.5%); unknown 9 (13.2%). Six patients with toxic kidney disease had received an organ transplant (heart 1, liver 2, kidney 3). Main patient characteristics are given in Table 1.

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Table 1. Patient characteristics at baseline.

Parameter	Age	BWpre	Bwpost	VUap	Alb	Pre-Alb	H	TPPre	TPpost	nPCR
n: 68	(yo)	(Kg)	(Kg)	(L)	(g/l)	(mg/l)	(%)	(g/l)	(g/l)	(mg/kg/24h)
Median	72,0	65,6	64,0	35,2	35,8	300,0	36,6	69,0	76,0	0,955
[25-75%]	[65,0-78,0]	[57,0-74,5]	[55,3-72,5]	[30,5-40,9]	[32,8-38,4]	[230,0-360,0]	[34,3-38,9]	65,0-73,0	[71,0-81,0]	[0,75-1,24]

(BW, body weight; Vupost; Alb, albumin; Pre-alb, pre-albumin; Ht, hematocrit; TP, total protein; nPCR, normalized protein catabolic rate).

3.2. Renal replacement treatment schedule

All patients received online postdilution hemodiafiltration. Treatment schedule consisted of three sessions weekly, 4 hours in 90% of patients and 3 or 3.5 hours in the remaining 10%. Single-used hemodiafilters were made of high-flux polysulfone or polyethersulfone (FX1000, 34.4%; FX800, 59.4%; Arylane H9, 2%). Anticoagulation consisted of a single bolus injection of Fraxiparin (Nadroparin 2000-6000 IU), a low molecular weight heparin, on the venous needle or within catheter line before initiating the extracorporeal circuit. Main features of renal replacement therapy are given in Table 2.

Table 2. Renal replacement therapy treatment schedule.

Parameter	Modality	tHD (min)	REC-VA	QB-eff	TBVP	Vinf	Vuf
n: 68	post HDF	(min)	(%)	(ml/min)	(L/ses)	(l/ses)	(l/ses)
Median		220,0	3,430	400,3	84,0	22,8	24,8
[25-75%]		[195,0-240,0]	[1,76-6,46]	[400-403]	[73,0--96,0]	[19,5-24,4]	[21,2-27,1]

(t_{HD}, dialysis duration; REC.VA, vascular access recirculation; Qb eff, effective blood flow; TBVP, total blood volume processed; V_{inf}, total infusion volume; V_{uf}, total ultrafiltration volume).

3.3. Baseline clinical performances (3 months)

Baseline clinical performances are presented in Table 3. N stands for Number of patients given (first row) and number of measures given (second row). Median and interquartile values are given for each key performance indicator for each access type (Table 3). As shown, the effective blood flow achieved was virtually similar (400 mL/min) in each vascular access including DCath. Recirculation was significantly higher with DualCath in average 7% (6 to 13%) but higher with LIJDC. Dialysis dose delivered (Kt/V) was virtually equivalent across all vascular accesses if we account for differences in patients' body weight and total body water. In all cases, including DCath, median value of Kt/V was superior to 1.70 (spKt/V) or 1.5 (eKt/V). Of note, we also explored the correlations between $_{OCM}$Kt/V and eKt/V values to confirm the validity of such routine parameters as observed in Figure 2. Convective volumes tend to be lower with DCath compared to arteriovenous accesses (AVF, AVG and TS) but still higher than 23 liters per session as recommended. Percent reduction ß2M with DCath was 4 to 10 % lower than AVF, AVG or Thomas shunt still achieving 72.6 and 75.4 percent per session.

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Table 3. Baseline clinical performances (over the first 3 months).

	AVF	AVG	RFDC	RIJDC	LIJDC	THOMAS S
N patients	36	3	1	25	1	2
n measures	99	4	3	57	3	6
QB (ml/min)						
Median [25-75%]	399 [395-403]	400 [395-403]	400 [395-403]	396 [390-403]	395 [390-403]	400 [400-400]
Venous Presssure (mmHg)						
Median [25-75%]	190 [175-215]	205 [194-218]	265 [244-282]	215 [200-230}	225 [200-230]	130 [120-135]
Recirc VA (%)						
Median [25-75%]	2,64 [1,37-4,80]	2,87 [2,1-3,83]	6,42 [6,18-7,91]	7,01 [4,3-8,62]	3,53 [10,63-15,85	2,78 [2-3,79]
spTV						
Median [25-75%]	1,76 [1,54-1,98]	1,98 [1,94-2,55]	[1,89-2,00]	1,70 [1,64-1,90]	2,02 [1,98-2,04]	2,18 [2,11-2,24]
eKt/V daugirdas						
Median [25-75%]	1,53 [1,31-1,69]	1,72 [1,68-2,14]	1,71 [1,65-1,72]	1,47 [1,30-1,59]	1,71 [1,67-1,74]	1,89 [1,84-1,94]
PR B2M (%)						
Median [25-75%]	76,7 [73,2-79,9]	85,8 [83,5-88,1]	72,6 [70,5-76,5]	NA	75,4 [75,4-75,4]	83,3 [82,8-83,8]
Vsub (l/ses)						
Median [25-75%]	23, 3 [20,8-23,3]	24,0 [22,5-24,0]	33,0 [28,7-33]	21,5 [18,0-21,5]	31,5 [25,7-31,5]	29,5 [25,2-29,5]
Vuf (l/ses)						
Median [25-75%]	25,240 [22,0-25,2]	25,7 [24,1-25,7]	35,3 [21,3-35,3]	22,9 [20,5-22,9]	32,1 26,2-32,1]	31,67 [26,6-31,7]

(AVF, native arteriovenous fistula; AVG, arteriovenous graft PTFE; RFDC, right femoral DualCath; RIJDC, right internal jugular DualCath; LIJDC, left internal jugular DualCath; Qb, blood flow; REC.VA, vascular access recirculation;PR, Percentage of reduction; V_{sub}, substitution volume; V_{uf}, ultrafiltration volume).

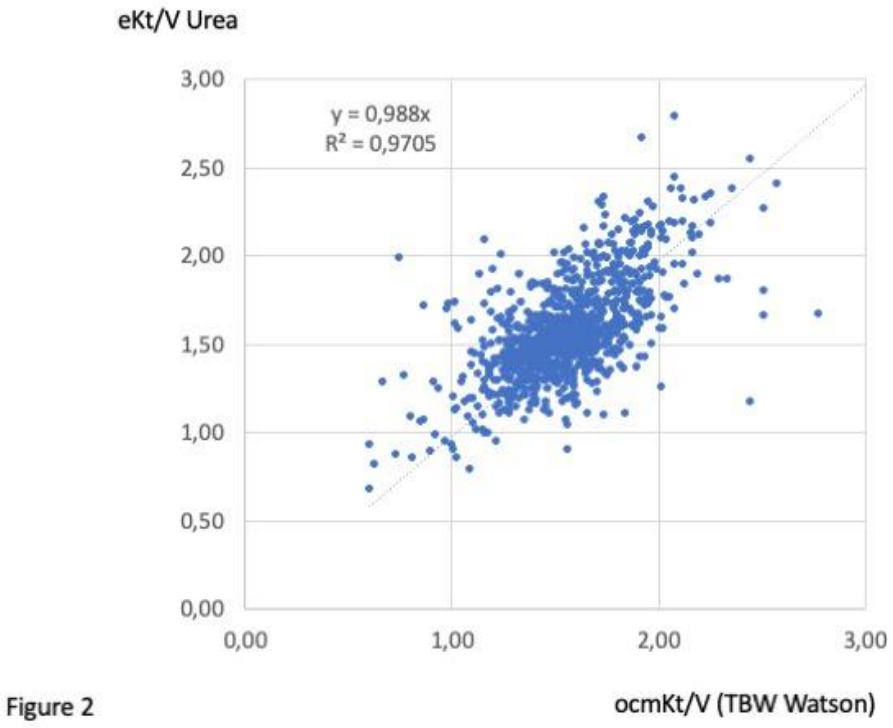

Figure 2

Figure 2. Correlation between ocmKt/V and eKt/V.

3.4. Clinical performances (over a 30-month follow-up)

3.4.1. Cumulative clinical performances comparing DualCath (DCath) and grouped Arterio-Venous Accesses (AVA).

Vascular accesses are grouped as AVAs and DCath and median values of key performance indicators are presented in Table 4. As shown, patients bearing DCath tended to have a smaller body

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weight compared to patients treated through AVA. They also tended to have a slightly lower blood flow and a higher recirculation translating in a slightly and significantly lower dialysis dose delivered for small molecules (Kt/V and Kt) but not for convection volume (22.5 vs 25.4, NS) and percent reduction of ß2M per session (74 vs. 78%, NS). Indeed, the effective dialysis dose achieved with DCath was much higher than that recommended by best practice guidelines. This fact is confirmed by stability over time of nutritional markers such as albumin, prealbumin (transthyretin) or normalized protein catabolic rate (nPCR). CRP and fibrinogen used as indicators of inflammation were similar in all vascular access groups. Additionally, key parameter indicators of dialysis adequacy (fluid volume status, blood pressure, electrolytic control, bone mineral disorder, anemia) were maintained in target for both types of vascular access.

Table 4. Cumulative clinical performances comparing DualCath (DCath) and grouped Arterio-Venous Accesses (AVA) (over a 30-month follow-up).

	AVA	DualCath	*p value*
N patients	41	**27**	
n measures	741	207	
BW (Kg)			
median (IQR)	64,8 [20,7]	60,6 [23,4]	*0,001*
H (%)			
median (IQR)	36,5 [4,5]	36,8 [5,5]	*0,716*
QB (ml/min)			
median (IQR)	400,3 [15,5]	400,3 [18,4]	*0,028*
spKt/V			
median (IQR)	1,90 [0,4]	1,80 [0,3]	*0,001*
eKt/V			
median (IQR)	1,6 [0,32]	1,52 [0,27]	*<,001*
REC VA (%)			
median (IQR)	2,8 [3,6]	7,2 [5,2]	*<,001*
Kt (L/ses)			
median (IQR)	57 [16,1]	52,6 [16]	*0,028*
PR-ß2M (%)			
median (IQR)	78,0 [8,25]	74,0 [4,0]	*0,327*
VUF (l/ses,)			
median (IQR)	25,4 [5,5]	22,5 [6,7]	*0,098*
S-ALB (g/l)			
median (IQR)	35,8 [5,5]	35,6 [6,0]	*0,05*
PRE-ALB (mg/l)			
median (IQR)	300 [120]	300 [150]	*0,437*
CRP (mg/l)			
median (IQR)	6,4 [11,Ø]	4,2 [8,8]	*0,378*
Fib (g/l)			
median (IQR)	4,3 [1,3]	4 [1,5]	*0,065*
nPCR (g/kg/24h)			
median (IQR)	0,9 [0,5]	1,0 [0,5]	*0,173*

(AVA, arteriovenous access; BW, body weight; Ht, hematocrit; Qb, blood flow; REC.VA, vascular access recirculation; PR, percentage of reduction; V_{uf}, total ultrafiltration volume; pre-alb, pre-albumin; nPCR, normalized protein catabolic rate).

3.4.2. Longitudinal follow-up

Two main indicators of dialysis dose delivery including the effective urea clearance throughout the complete session (Figure 3) and the middle and large molecule clearance as reflected by the total ultrafiltration volume (V_{UF}) (Figure 4) were monitored throughout the 30 months of follow-up for the two types of vascular access (AVA, Arterio-Venous Access; DC, DCath) As shown in both cases, dialysis dose delivered was maintained relatively stable over the total observational period. Small molecule clearances were slightly higher with AVA versus DCath, while total ultrafiltration volume, used in that case as a surrogate of middle molecule clearance was not different from DCath.

Serum albumin concentration as an integrated biomarker of dialysis adequacy and safety of the method, nutritional and inflammation status, was also monitored over the 30 months and reported in Figure 5.

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DualCath KT

Kt (l/ses)	AVA	DualCath
n	741	207
Median	56.960	52.560
Mean	56.007	53.985
Std. Error of Mean	0.401	0.981
Std. Deviation	10.911	14.109
IQR	16.100	15.955

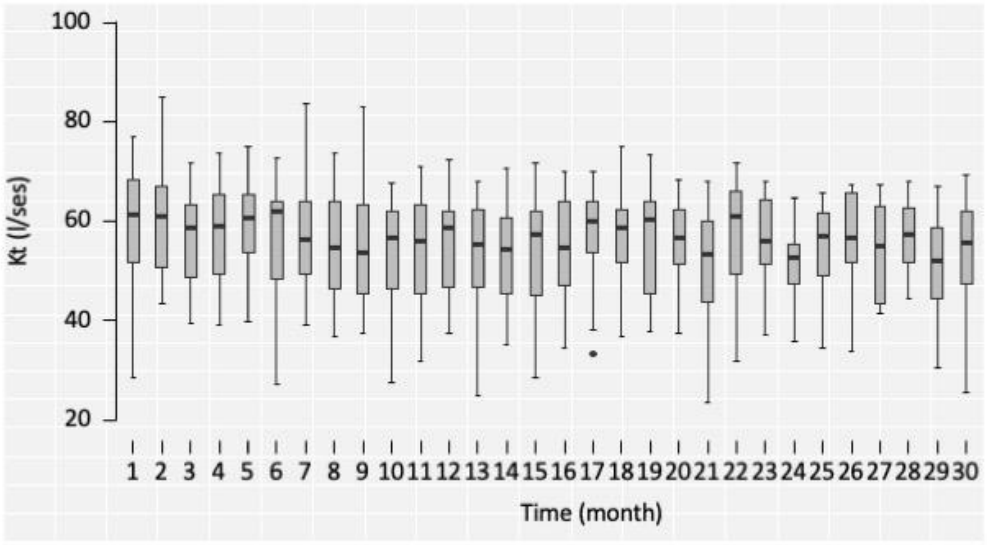

Figure 3A

AVA Kt

Kt (l/ses)	AVA	DualCath
n	741	207
Median	56.960	52.560
Mean	56.007	53.985
Std. Error of Mean	0.401	0.981
Std. Deviation	10.911	14.109
IQR	16.100	15.955

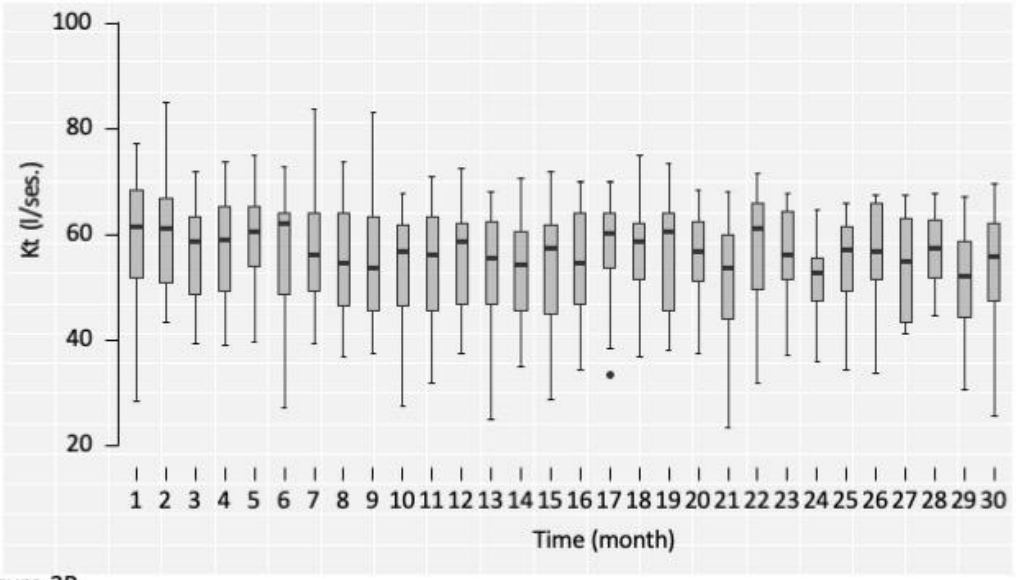

Figure 3B

Figure 3. Effective urea clearance ($_{dp}$Kt, expressed in liters per session) over the 30 months of follow-up in A) DCath and B) AVA.

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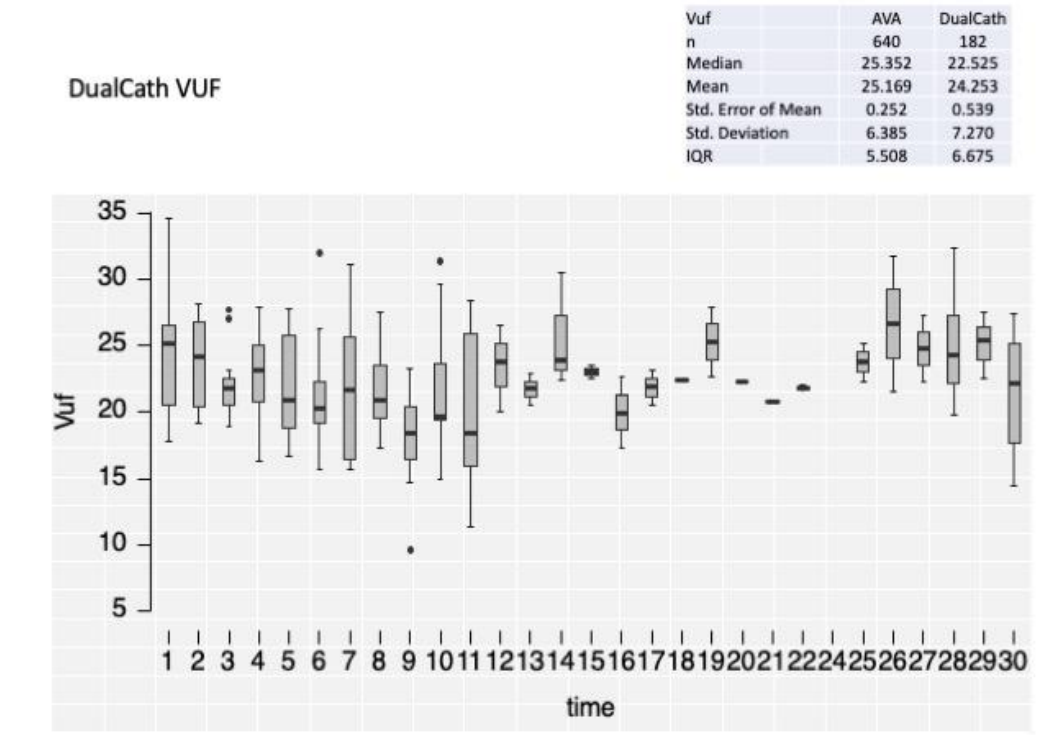

Figure 4A

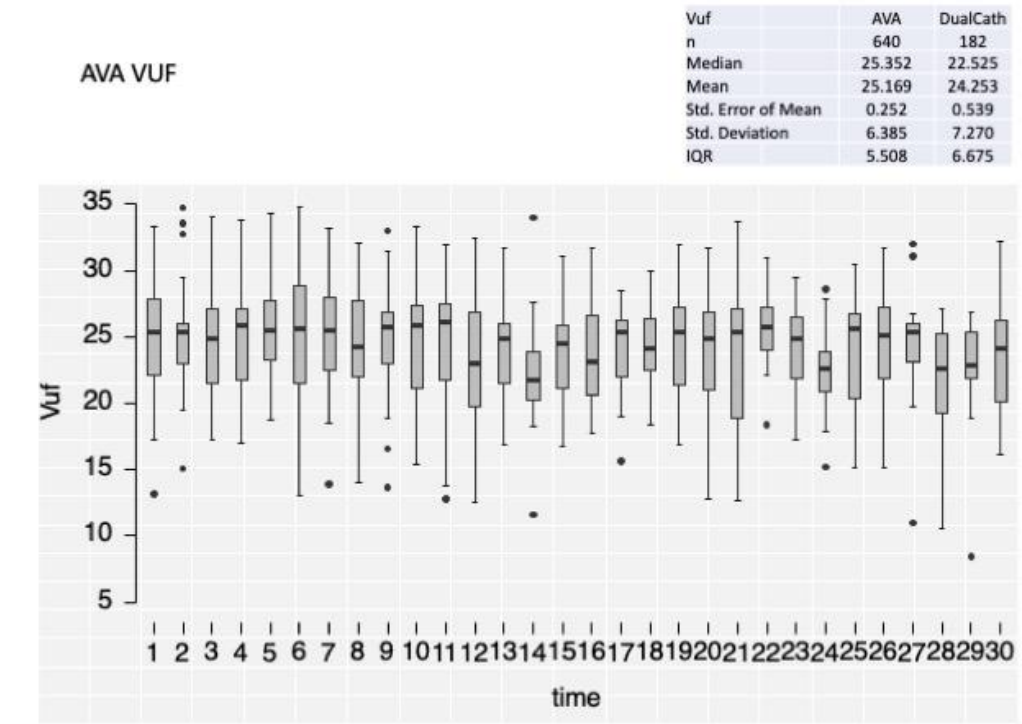

Figure 4B

Figure 4. Convective volume (expressed in liters per session) over the 30 months of follow-up in A) DCath and B) AVA.

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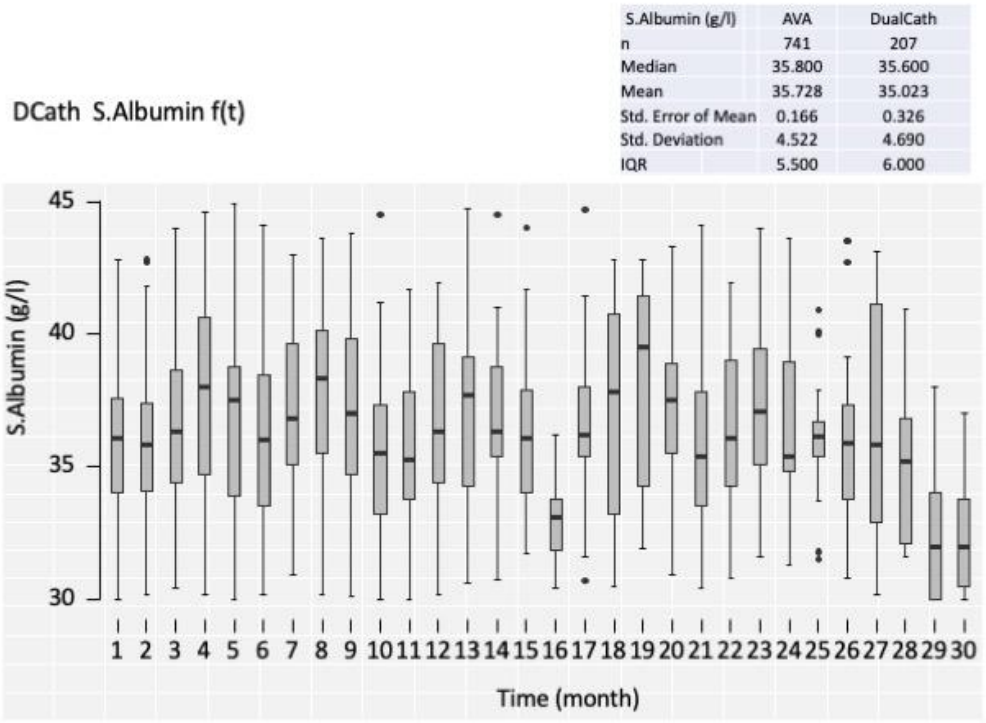

Figure 5A

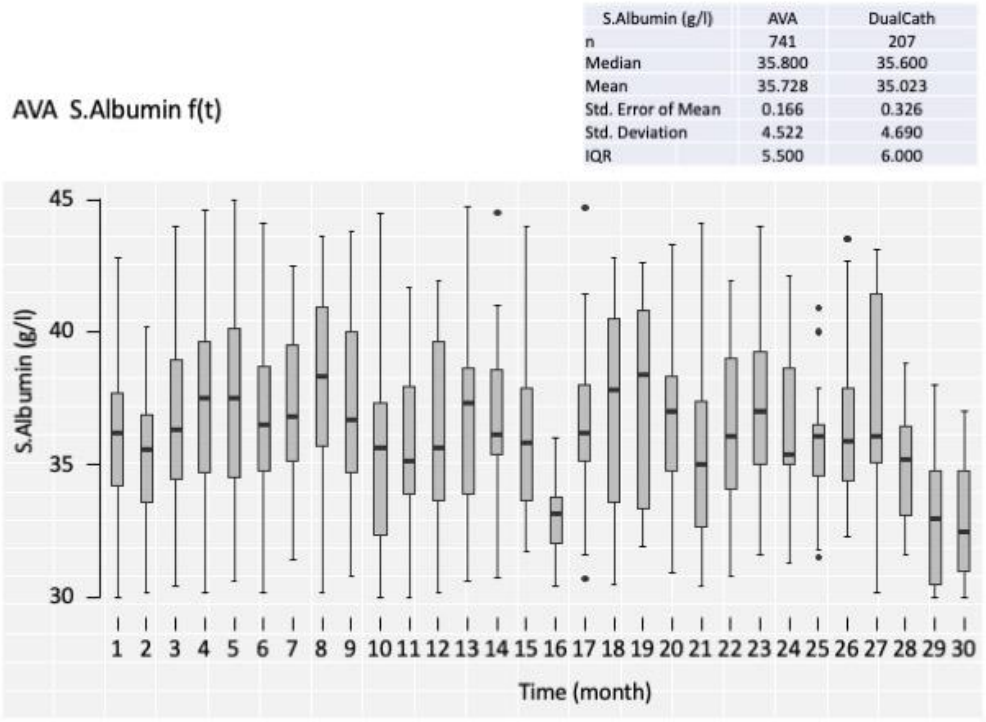

Figure 5B

Figure 5. Serum albumin over the 30 months of follow-up in A) DCath and B) AVA.

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4. Discussion

Main findings of our study:

In this retrospective study consisting of 68 maintenance dialysis patients, we assessed precisely clinical performances delivered throughout tunneled central venous catheters (DCath) and compared them to various arteriovenous accesses (AVA) used routinely in our dialysis facility. For this purpose, we used monthly quality control measures with 30 months followed-up. As most original finding of our study is the fact that DCath were shown to deliver high blood flow (400 ml/min) and achieved high volume hemodiafiltration on a regular basis with comparable results to AVA. As second finding, the study highlighted the fact that dialysis dose delivered, either for small sized molecules (total urea clearance) or middle-sized molecules (total ultrafiltration volume and β2M reduction rate) was almost similar with DCath and AVA, was higher than the targets recommended by clinical best practice guidelines and remained stable over time up to 30 months. The main difference relies on the fact that recirculation with DCath was significantly higher (≈7%) than AVA resulting in a total urea clearance with DCath slightly lower than AVA. Interestingly, this recirculation didn't impact the total ultrafiltration volume which remained almost similar with DCath and AVA. In all cases, dialysis performances and key performance indicators were not affected while DCath were used as mainstream vascular access.

Literature comparison:

This finding is in quite contrast with previous studies reporting that tunneled CVC tends to be associated with a reduction of dialysis dose delivered due to the limited blood flow and increase in vascular access recirculation, but also precluding use of high volume hemodiafiltration[21,39,40]. In fact, the apparent superiority of DCath compared to other tunneled central venous catheters relies on three main components: firstly, to the geometry and the design of cannulas that are specifically engineered (two independent cannulas, adjustable to patient anthropometry, with side holes at the tips) to provide high blood flow with relatively low blood flow resistance; secondly, to the careful way of inserting and positioning tips in central venous system at time of implantation, mainly at junction of superior vena cava and right atrium for internal jugular vein site, but alternatively in inferior vena cava for femoral site; thirdly, to the strict and careful catheter handling protocol consisting in using locking solutions (antithrombotic, fibrinolytic) to maintain or restore catheter flow permeability[41].

Each of these components has been clearly documented in the scientific literature[13]. Two single cannulas made of soft silastic with adequate inner lumen (≥ 2 mm) and distal side holes tend to provide higher and more sustainable blood flow during dialysis session than double lumen semi-rigid polyurethane conventional catheters[12,13,21,42]. Tips positioning at the junction of superior vena cava and right atrium also tend to reduce risk of poor blood flow occurring during dialysis session due to the hypovolemia associated with the ultrafiltration[43]. In addition, side holes present at the tips of catheters keep lines in the core flow of the vein and prevent sucking vein walls. Higher flow achieved with side holes catheters has been challenged in some studies by thrombosis and infectious risk[14,15].

Silastic cannulas made of soft rubber tend to be the most hemocompatible material reducing platelet adhesion, catheter thrombosis risk and bacterial adhesion[44]. This mechanistic interpretation of phenomenon has been illustrated in some catheter flow modeling studies from simulation in silico experiment[45]. Another important factor relies on the strict implementation of best practices catheter handling developed by nursing team[46]. Aside strict aseptic conditions applied to catheter handling, a new science of catheter locking solution has been developed and has been shown to be very efficient in maintaining catheter lumen patency[47-50]. It is not our intent to review catheter locking practices, but we refer readers interested to recent comprehensive reviews on this topic. In our unit, locking solutions have been always at the heart of catheter care practices. We moved from conventional heparin locking solution to more personalized and adaptative locking solutions involving more citrate-based solutions and/or fibrinolytic solutions guided by blood flow and/or pressure regime changes in the recent time.

 doi:10.20944/preprints202306.0758.v1

Strength and weakness of our study:

Strength of our study relies on the precise quantification and comparison of dialysis performances achieved with DCath compared to conventional arteriovenous accesses (AVF, AVG) used to deliver high volume hemodiafiltration in a relatively large number of dialysis patients followed up for 30 months. This is in clear contrast with a previous large cohort study showing that high volume HDF (>21 l) was achieved in 33% of prevalent patients[51]. Safety and risk assessment associated with DCath use is currently assessed in another multicenter study.

Our study has weaknesses that we want to highlight. Firstly, this is a single center study performed by well-trained physicians and nursing team dedicated to vascular access management and therefore transferability to larger centers may be questionable. Secondly, the number of patients may appear limited, but this is due to the academic hospital-based dialysis facility with large turnover of patients. Thirdly, a comparative economic evaluation between DCath and AVA was not done in this study.

Implications for clinical practices:

As our study indicates, the use of tunneled CVC is not associated with worst vascular access scenario in dialysis patients. As such, by means of DCath, we were able to perform high volume hemodiafiltration with high blood flow in all patients for sustained period up to 30 months. This is a quite reassuring finding, since it makes possible to consider treating fragile patients (i.e., elderly, diabetic, cardiac) or patients without AVF or AVG by most efficient convective-based treatment modalities, currently high volume hemodiafiltration. In other words, tunneled central venous catheter should not be considered as a limiting factor in providing most efficient treatment modality provided the right tunneled CVC is used.

Conclusion

As shown through this study, high-flow DCath tunneled two single lumen silicone catheters may be used in dialysis-dependent chronic kidney disease patients to deliver high volume hemodiafiltration like arteriovenous accesses. Although, results obtained with DCath tended to be slightly lower than those achieved with arteriovenous accesses, they remained far above best practice guidelines, indicating that DCath were not compromising optimal clinical performances. In addition, clinical performances of DCath remained stable and achieved in a consistent manner over time. These results support the notion that design and geometry of the two silicone cannulas are optimal, and that the strict adherence to best catheter practices is clue to success in tunneled central venous catheter use.

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