

## Survival of tunneled hemodialysis catheters after percutaneous placement\*

Ewa Weber<sup>1</sup>✉, Tomasz Liberek<sup>1</sup>, Wojciech Wołyniec<sup>2</sup>, Marcin Gruszecki<sup>3</sup> and Bolesław Rutkowski<sup>1</sup>

<sup>1</sup>Department of Nephrology, Transplantation and Internal Medicine, Medical University of Gdańsk, Gdańsk, Poland; <sup>2</sup>Department of Occupational and Internal Medicine, <sup>3</sup>Department of Radiology Informatics and Statistics, Medical University of Gdańsk, Gdańsk, Poland

**Background.** Tunneled catheters are becoming increasingly used as a permanent dialysis access. Easy way of insertion and good long-term patency make them competitive to fistulas in some groups of patients. **Methods.** Late complications and survival of 180 tunneled catheters inserted from June 2010 to December 2013 in 171 unselected hemodialysis patients were analyzed. **Results.** The cumulative time of observation was 2103.5 patient-months and median observation was 9 months (range of 0.5–45 months). Only 19 out of 180 catheters were removed due to complications (12 for infections, 4 due to malfunction and 3 because of mechanical damage). Majority of catheters were removed electively: 27 after maturation of arterio-venous fistula (AVF), 4 after kidney transplant, 5 after transfer to peritoneal dialysis and 3 due to the recovery of renal function. At the end of the observation, 58 catheters were still in use and 64 patients had died with functioning catheter. When censored for elective catheter removal and patient death, 88.2% of catheters survived for 1 year. Catheter survival was significantly better in older patients (over 65 years, in comparison to patients <65 years,  $p=0.046$ ). **Conclusions.** Nearly 90% of all inserted catheters gave reliable dialysis access as long as it was needed. Among them, over 30% of the inserted catheters were in use at the end of the observation period, and over 30% of patients had died with a functioning catheter. The results of tunneled catheters survival are encouraging and they should be taken into consideration during decision-making on vascular access, especially in the older patients.

**Key words:** hemodialysis, tunneled catheter, survival

**Received:** 19 July, 2015; **revised:** 02 November, 2015; **accepted:** 16 December, 2015; **available on-line:** 02 February, 2016

### INTRODUCTION

The number of patients with chronic kidney disease (CKD) necessitating dialysis is constantly growing. This is due to the rising prevalence of chronic diseases like diabetes and hypertension being the most common causes of renal failure and, importantly, due to the increasing availability of renal replacement therapy in the developing countries. Thus, each year, increasing numbers of patients reach the final stage of a renal disease and start a renal replacement therapy (Kramer *et al.*, 2009). Nearly 70% of all patients on renal replacement therapy are treated by the maintenance hemodialysis (Camins, 2013).

By far, the best vascular access for hemodialysis (HD) is native arterio-venous fistula (AVF), as it has low rate of infection and thrombotic complications. The KDOQI (Kidney Disease Outcome Quality Initiative (Vascular Access Work Group, 2006) guidelines set goal that more than 50% of patients should start hemodialysis therapy with matured native fistula. Similarly, less than 10% of prevalent hemodialysis patients should be maintained on central catheters as their permanent dialysis access. However, cross-sectional data from the Dialysis Outcome and Practice Patterns Study (DOPPS) show that among participating European countries and the US, the percentage of patients using catheters for their chronic dialysis access ranged from 9.9 to 28.2 and was in the rise (Rayner *et al.*, 2004). In the most recent study reporting data from 10 national European registries (Noordzij *et al.*, 2014), the percentage of patients starting dialysis with tunneled hemodialysis catheter (THC) increased from 58 to 68, between the years of 2005 and 2009. At the same time, usage of THCs in prevalent patients increased from 28% to 32%.

Despite efforts to increase the use of fistula as dialysis access like the “fistula first” initiative (Lok, 2007), it appears that tunneled catheters are becoming increasingly used as a provisional or permanent dialysis access. In some cases, use of the catheter may be regarded as the best, or indeed, the only way to continue dialysis. The number of such patients is rising with aging populations starting dialysis and being dialyzed for longer time, which in some patients inevitably leads to mounting of vascular access complications and increasing difficulties in new fistula creation. Many patients come to nephrologists with advanced uremia and need urgent start of dialysis with no time to create and develop AVF. In such patients, tunneled catheter serves as a “bridge” to a more permanent dialysis access. Importantly, in some countries, fistula creation may be a subject to logistic or financial limitations, which may jeopardize access to vascular surgery (Sampathkumar *et al.*, 2011).

✉ e-mail: eweber@gumed.edu.pl

\*Majority of the results was reported as a poster at the 52 ERA-EDTA Congress, London 05.2015 and the 9th Congress of Vascular Access Society, Barcelona 04.2015

**Abbreviations:** AVF, arterio-venous fistula; CKD, chronic kidney disease; HD, hemodialysis; KDOQI, Kidney Disease Outcome Quality Initiative; DOPPS, Dialysis Outcome and Practice Patterns Study; THC, tunneled hemodialysis catheter; IJV, right internal jugular vein; MOS, sternocleidomastoid muscle; CARI, Caring for Australasians with Renal Impairment; EBPG, European Best Practice Guidelines; chest A-P, chest anterior-posterior

## PATIENTS AND METHODS

We have analyzed complications and survival of tunneled catheters inserted in the Department of Nephrology, Transplantology and Internal Medicine from June 2010 to December 2013. The observation was ended in June 2014. 186 catheters were inserted in 177 unselected patients treated in our dialysis unit and in 13 other dialysis units in the northern Poland.

Right internal jugular vein (IJV) was the preferred vein. If its cannulation was not possible due to skin infection at this site, thrombosis or lack of visible right IJV on ultrasound, left IJV was used for cannulation. Femoral and subclavian veins were used as the next options. In general, 19 or 23 cm catheters (cuff to tip length) were used for right IJV and 23 or 27 cm for left IJV.

Insertions were performed in the treatment room with no immediate fluoroscopy control or in the coronary angiography suite. Before the insertion, the jugular vein was identified by ultrasound and its localization was marked on the skin. Low, lateral access for both right and left internal jugular vein (IJV) was preferred. Needle was inserted 2–3 cm above the clavicle, behind the clavicular head of the sternocleidomastoid muscle (MOS) and directed towards the sternal notch and below the muscle. If this approach was unsuccessful, the standard median approach through the middle of the MOS triangle was used. Insertion was performed under local anesthesia with 1% lignocaine. Catheter insertion was performed with standard Seldinger technique with the use of the peel-away sleeve. After insertion, catheter function was checked with the 10 cc syringe and heparin was instilled into both arms (5000 IU/ml). Small wound at catheter insertion site was sutured and covered with dressing, as was the exit site. Chest A–P and lateral x-rays were taken to assess possible complications and catheter position. Hemodialysis was usually postponed until the next day to avoid bleeding related to general heparinization. No routine antibiotic prophylaxis was used for insertion procedure. All insertions were performed by the same team of nephrologists.

Catheter insertion was considered as primary when it was the first vascular access in a patient starting hemodialysis (with the exception for one temporary catheter inserted previously). Secondary insertions were performed in patients who lost function of their existing vascular access (both AVF and catheters) and in patients starting dialysis with the failing grafts.

The blood cultures were taken from the catheter and peripheral vein only if clinical or laboratory symptoms of possible infection (fever, purulent discharge or skin changes around the catheter exit site, increased C reactive protein or procalcitonin) were present. The number of blood drawings was different, depending on the clinical situation of a given patient, cultured under aerobic and anaerobic conditions.

Catheter related sepsis was defined as a simultaneous incidence of clinical signs and positive blood culture from the catheter and/or from the peripheral vein.

The presence of catheter related sepsis did not cause the automatic removal of the catheter. In each case, the decision to remove the catheter was taken individually, taking into consideration the clinical situation of the patient and severity of the infection. The removal of the catheter was more likely with the relapsing infections.

**Statistical analysis.** Variables with normal distribution were compared between groups using Student's *t* test and Mann-Whitney test was used for variables with-

out normal distribution. Survival analysis was performed with the Kaplan–Meyer method, unadjusted survival was compared with log-rank test. In catheter survival analysis, only catheter removal for complications (infection, loss of function and mechanical damage, including inadvertent removal of the catheter by the patient) was considered as the final event, and observations were censored when catheters were removed after successful creation of AVF, transplantation, transfer to peritoneal dialysis, recovery of renal function or at the end of the observation period. Patient death with functional catheter was also regarded as a censored observation.

Data were expressed as the mean  $\pm$  standard deviation, and median and range were used for non-normally distributed variables. The *p* value of  $<0.05$  was interpreted as statistically significant. Statistical analyses were performed with STATISTICA software package (StatSoft, Inc., 2007, Tulsa, OK, USA).

## RESULTS

180 catheters were analyzed in 171 patients. For 6 patients, not enough clinical data were retrieved, and they were considered as lost to follow up. Patients' character-

**Table 1. Patients' and catheters' characteristics**

	N	%
N (catheters)	180	100
Patients age (at insertions)	92/88	51.1/48.9
sex (M/F)		
age (years)	65.2 $\pm$ 14.9 (median 65 y)	
Kidney disease diagnosis		
Glomerulonephritis	47	26.1
Diabetic nephropathy	38	21.1
Hypertensive nephropathy	21	11.7
Interstitial renal disease	13	7.2
ADPKD	10	5.6
Other/undetermined	51	28.3
Catheter insertion primary/ secondary	94/86	52.2/47.8
Catheter type		
Arrow Cannon II	147	81.7
Bard Hemosplit	30	16.7
Covidien Tal Palindrome	3	1.6

istics are given in Table 1.

Arrow Cannon II catheter (with backward tunneling) was used in 147 cases, Bard HemoSplit™ in 30 cases, and Covidien Tal Palindrome™ in 3 cases.

In 133 cases, the catheter was inserted into the right IJV, in 22 cases into the left IJV. Right and left subclavian veins were used in 11 and 2 cases, and right and left femoral veins in 8 and 3 cases, respectively.

Local hematomas and prolonged wound bleeding was the most common complication of the insertion procedure. There was no case of pneumothorax. In 1 case, thoracic duct was punctured with no further consequences. Malposition of the catheter tips occurred in 6 blind insertions (in 4 cases into the azygos vein and in 2 into the right innominate vein), all malpositions were immediately and successfully repositioned under fluoroscopy.

The cumulative time of observation was 2103.5 patient-months and median observation was 9 months (range of 0.5–45 months).

19 catheters were removed for complications, among them the most common cause was infection, with both,

Table 2. Catheter outcome

Catheter outcome	N	%
Removal — catheter related complications	19	10.5
Catheter related sepsis	9	5.0
Malfunction/clotting	4	2.2
Tunnel infection	3	1.7
Mechanical damage	3	1.7
Removal — other	39	21.7
AVF creation	27	15.0
Transfer to peritoneal dialysis	5	2.8
Successful kidney transplant	4	2.2
Recovery of renal function	3	1.7
Alive with functioning catheter	58	32.2
Died with functioning catheter	64	35.6

catheter related sepsis and tunnel or exit site infection. Data on catheter outcome are presented in Table 2.

When censored for death with functioning catheter, 94.2% tunneled THC survived 3 months, 92.0% — 6 months and 88.2%, 85.6% and 81.1% survived 1, 2 and 3 years, respectively (Fig. 1A). The longest observed catheter survival was 45 months. We did not observe differences in catheter survival with respect to sex, catheter type or, interestingly, type of insertion (primary vs. secondary). Diabetes was not a risk factor for catheter loss.

During the observation, 124 patients had no positive blood culture and no symptoms of catheter infection have been recorded. In total, 90 positive blood cultures have been documented in 56 patients. These patients had a significantly greater chance for catheter loss in comparison to patients without infection (Fig 1B). The majority of cultured species (73 isolates) were Gram (+) cocci — (54 *S. epidermidis*, 14 *S. aureus* and 5 *Enterococci*). 17 Gram negative bacteria species were cultured (12 *Enterobacteriaceae*, 2 *Acinetobacter sp.* and 3 *Pseudomonas sp.*). The mean infection rate was 1.42/1000 catheter days or 0.5 episode/year.

There were no differences in survival between catheters introduced through the right or left internal jugular veins, but catheters inserted into jugular veins had a significantly better survival in comparison to the ones in femoral veins ( $p=0.024$ ) (Fig. 1C).

Catheter survival was significantly better in older patients. Patients over 65 years old had marginal, but significant superior catheter survival when compared to younger patients (Fig. 1D). As 65 years was the median age in our study group, both age subgroups had a similar number of patients.

## DISCUSSION

It is widely accepted that AVF or graft are the best accesses for hemodialysis, and tunneled catheters are

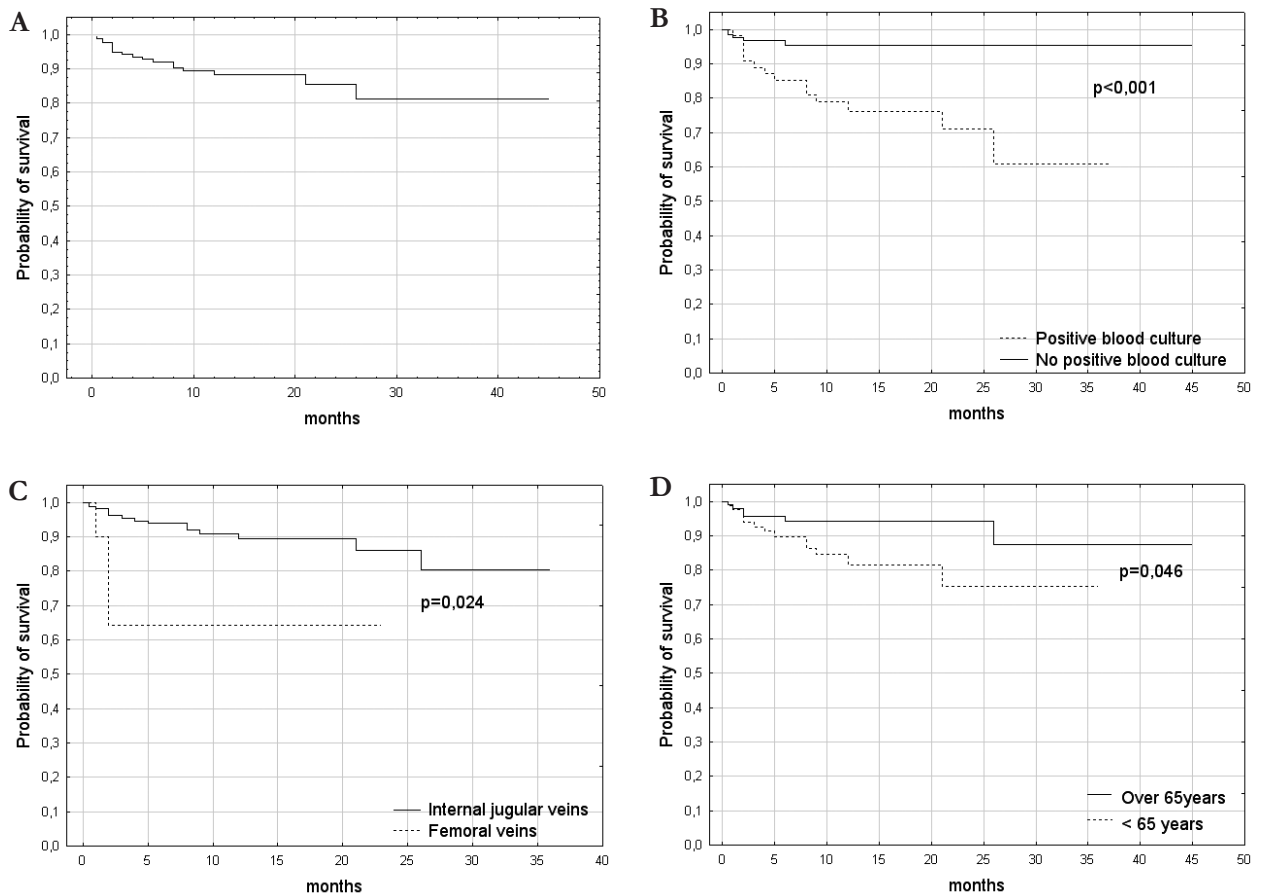


Figure 1. Kaplan-Meier survival curves after censoring for death with functioning catheter, elective catheter removal and catheters functioning at the end of the study.

(A) Overall THCs survival. (B) Significantly inferior survival of THCs in patients with at least one positive blood culture obtained during study ( $p < 0.001$ , log rank test). (C) Significantly inferior survival of THCs inserted into femoral veins ( $n=11$ ) in comparison to catheters in jugular veins ( $n=155$ ) ( $p=0.024$ , log rank test). (D) Superior survival of THCs in elderly patients (over 65 years) in comparison to younger patients ( $p=0.046$ , log rank test).



universally regarded as the less optimal option of vascular access for HD. High rate of catheter related infection or thrombosis results not only in unsatisfactory catheter survival but also in increased mortality of HD patients dialyzed through THC. The superiority of AVF over other forms of dialysis accesses has been supported by numerous recommendations and guidelines' setting bodies: KDOQI (Vascular Access Work Group, 2006), EBPG (European Best Practice Guidelines)(Tordoir *et al.*, 2007), CARI (Caring for Australasians with Renal Impairment) (Polkinghorne *et al.*, 2013). While they are widely accepted, it has to be remembered that they are based purely on observational studies, and at least part of the observed differences in catheter survival and mortality could be explained by the case-mix. In this respect, catheters are used predominantly in patients who start dialysis in an unplanned way, often without any previous nephrological care or in the oldest and most comorbid patients, where fistula creation and maturation may be impeded by numerous complications.

Our data present late complications and catheter survival in a large, unselected population of HD patients, inserted by a nephrologist, both as the first access in patients starting dialysis, or with failed previous access. The large number of catheter insertions and a relatively high percentage of catheter insertion in new dialysis patients were, at least in part, due to the problems in functioning of vascular surgery services, which were relatively overloaded and underfunded, and fistula operation, both creation and repair, could not get the desired priority.

In our 4-year study, only 10.5% of catheters were removed for complications. The most important reason for catheter removal was catheter related sepsis and the positive blood culture was the most important risk factor for the catheter loss. Catheters were also removed due to malfunction related to thrombosis or mechanical damage, including inadvertent catheter removal by the patient. Importantly, nearly 90% of all inserted catheters served the patients well, being a reliable dialysis access until the creation and maturation of AVF, kidney transplantation, transfer to peritoneal dialysis or recovery of the renal function. Among them, over 30% of inserted catheters were in use at the end of the observation and over 30% of patients had died with a functioning catheter.

Previous studies usually reported similar (Mandolfo *et al.*, 2014) or less favorable catheter survival (Sampathkumar *et al.*, 2011; Little *et al.*, 2001; Ewing *et al.*, 2002; Shingarev *et al.*, 2013). In one of the largest studies reporting outcome of 573 catheters, only 47% of THCs had survived for 1 year. However, the main reason for non-elective removal was catheter non-function (69%) and authors reported the use of lower concentrations of heparin (1000 IU/ml) in their study (Little *et al.*, 2001). Similarly, in another study (Shingarev *et al.*, 2013), where 1000 IU/ml heparin locks were used for anticoagulation, catheter malfunction was also the most common reason for removal, with rather low overall THC survival.

In some other studies (Sampathkumar *et al.*, 2011; Little *et al.*, 2001), similarly to the study presented here, the most important reason for catheter loss was catheter related infection. Importantly, in our report catheter related infection rate was rather low at 1.42 episodes/1000 catheter-days, while the previously reported infection rate was 1.7–5.2 episodes/1000 catheter days (Ewing *et al.*, 2002; Ervo *et al.*, 2001). This finding may explain a very good survival rates observed in our study. Nevertheless, in the present analysis, catheter related infections remained the main reason for catheter removal and were

a significant risk factor for catheter loss. However, it appears that with the implementation of meticulous catheter care and with the use of new antibacterial catheter locks, a substantial progress in this area can be expected (Tan *et al.*, 2014; Weijmer *et al.*, 2005; Campos *et al.*, 2011; Labriola *et al.*, 2008). One may draw a parallel to the situation observed in peritoneal dialysis where with the perfected line connections, implementation of reliable exchange procedures and improvement in patient training, an impressive reduction in peritonitis rate has been achieved. It could be expected that similar progress will happen, or in fact is observed now, in lowering of infection rate and improved outcome of tunneled hemodialysis catheters.

Importantly, in our study, and also other studies (Canaud *et al.*, 1998; Hernandez-Jaras *et al.*, 2004; Murea *et al.*, 2014; Drew *et al.*, 2014; Claudeanos *et al.*, 2015), THC survival seems to be superior in the older population. This appears to be an especially important finding as fistula creation in older population may be technically more difficult and more often complicated by fistula non-maturation (Lok *et al.*, 2006). A relatively recent large meta-analysis suggested that elderly patients have 70% increased risk of fistula failure at 1 year, in comparison to younger patients (Lazarides *et al.*, 2007).

## CONCLUSIONS

In our opinion, the key factor in catheter function and survival is the expertise and dedication of the team performing catheter insertion and rigorous catheter care in the dialysis units. Careful pre-implantation assessment of the access point with the use of ultrasound, proper choice of the catheter length with respect to body size and insertion side, together with the adherence to strict aseptic technique during catheter insertion, care and HD connections seem to be the cornerstones of the success.

In the light of the increasing age of dialysis population, the expansion of dialysis in the developing countries where vascular surgery facilities may not be able to serve the growing number of HD patients, and with better outcomes achieved with THCs, we should not discriminate against dialysis catheters, but use them wisely to achieve the best outcomes for the patients.

## Conflict of interest

None to declare

## REFERENCES

- Camins BC (2013) Prevention and treatment of hemodialysis-related bloodstream infections. *Semin Dial* **26**: 476–481. <http://dx.doi.org/10.1111/sdi.12117>.
- Campos RP, do Nascimento MM, Chula DC, Riella MC (2011) Minocycline-EDTA lock solution prevents catheter-related bacteremia in hemodialysis. *J Am Soc Nephrol* **22**: 1939–1945. <http://dx.doi.org/10.1681/ASN.2010121306>.
- Canaud B, Leray-Moragues H, Garrigues V, Mion C (1998) Permanent twin catheter: a vascular access option of choice for hemodialysis in elderly patients. *Nephrol Dial Transplant* **13** (Suppl 7): 82–88.
- Claudeanos KT, Hudgins J, Keahey G, Cull DL, Carsten CG (2015) Fistulas in octogenarians: are they beneficial? *Ann Vasc Surg* **29**: 98–102. <http://dx.doi.org/10.1016/j.avsg.2014.10.002>.
- Drew DA, Lok CE, Cohen JT, Wagner M, Tangri N, Weiner DE (2014) Vascular access choice in incident hemodialysis patients: a decision analysis. *J Am Soc Nephrol* **26**: 183–191. <http://dx.doi.org/10.1681/ASN.2013111236>.
- Ervo S, Cavatorta F, Zollo A (2001) Implantation of permanent jugular catheters in patients on regular dialysis treatment: ten years' experience. *J Vasc Access* **2**: 68–72.
- Ewing F, Patel D, Petherick A, Winney R, McBride K (2002) Radiological placement of the Ash Split hemodialysis catheter: a prospec-

- tive analysis of outcome and complications. *Nephrol Dial Transplant* 17(4):614-9.
- Hernández-Jaras J, García-Pérez H, Torregrosa E, Pons R, Calvo C, Serra M, Orts M, Rius A, Camacho G, Bernat A, Sánchez-Canel JJ (2004) Outcome of tunneled hemodialysis catheters as permanent vascular access. *Nefrología* 24: 446-452.
- Kramer A, Stel V, Zoccali C, Heaf J, Ansell D, Grönhagen-Riska C, Leivestad T, Simpson K, Pálsson R, Postorino M, Jager K (2009) An update on renal replacement therapy in Europe: ERA-EDTA Registry data from 1997 to 2006. *Nephrol Dial Transplant* 24: 3557-3566. <http://dx.doi.org/10.1093/ndt/gfp519>.
- Labriola L, Crott R, Jadoul M (2008) Preventing hemodialysis catheter-related bacteremia with an antimicrobial lock solution: a meta-analysis of prospective randomized trials. *Nephrol Dial Transplant* 23: 1666-1672.
- Lazarides MK, Georgiadis GS, Antoniou GA, Stamos DN (2007) A meta-analysis of dialysis access outcome in elderly patients. *J Vasc Surg* 45: 420-426.
- Little MA, O'Riordan A, Lucey B, Farrell M, Lee M, Conlon PJ, Walshe JJ (2001) A prospective study of complications associated with cuffed, tunneled hemodialysis catheters. *Nephrol Dial Transplant* 16: 2194-2200.
- Lok CE, Allon M, Moist L, Oliver MJ, Hemal Shah H, Zimmerman D (2006) Risk equation determining unsuccessful cannulation events and failure to maturation in arteriovenous fistulas (REDUCE FTM I). *J Am Soc* 17: 3204-3212.
- Lok CE. (2007) Fistula first initiative: advantages and pitfalls. *Clin J Am Soc Nephrol* 2: 1043-1053.
- Mandolfo S, Acconcia P, Bucci R, Corradi B, Farina M, Rizzo MA, Stucchi A (2014) Hemodialysis tunneled central venous catheters: five-year outcome analysis. *J Vasc Access* 15: 461-465. <http://dx.doi.org/10.5301/jva.5000236>.
- Murea M, James KM, Russell GB, Byrum GV, Yates JE, Tuttle NS, Bleyer AJ, Burkart JM, Freedman BI (2014) Risk of catheter-related bloodstream infection in elderly patients on hemodialysis. *Clin J Am Soc Nephrol* 9: 764-770. <http://dx.doi.org/10.2215/CJN.07710713>.
- Noordzij M, Jager KJ, van der Veer SN, Kramar R, Collart F, Heaf JG, Stojceva-Taneva O, Leivestad T, Buturovic-Ponikvar J, Benítez Sánchez M, Moreso F, Prütz KG, Severn A, Wanner Ch, Vanholder R, Ravani P (2014) Use of vascular access for hemodialysis in Europe: a report from the ERA-EDTA Registry. *Nephrol Dial Transplant* 29: 1956-1964. <http://dx.doi.org/10.1093/ndt/gfu253>.
- Polkinghorne KR, Chin GK, MacGinley RJ, Owen AR, Russell Ch, Talaulikar GS, Vale E, Lopez-Vargas PA (2013) KHA-CARI Guideline: Vascular access — central venous catheters, arteriovenous fistulae and arteriovenous grafts. *Nephrology* 18: 701-705. <http://dx.doi.org/10.1111/nep.12132>.
- Rayner HC, Besarab A, Brown WW, Disney A, Saito A, Pisoni RL (2004) Vascular access results from the dialysis outcomes and practice patterns study (DOPPS): performance against kidney disease outcomes quality initiative (K/DOQI) clinical practice guidelines. *Am J Kidney Dis* 44 (5 Suppl 2): 22-26.
- Sampathkumar K, Ramakrishnan M, Sah AK, Sooraj Y, Mahaldhar A, Ajeshkumar R (2011) Tunneled central venous catheters: Experience from a single center. *Indian J Nephrol* 21: 107-111 <http://dx.doi.org/10.4103/0971-4065.82133>.
- Shingarev R, Barker-Finkel J, Allon M (2013) Natural history of tunneled dialysis catheters placed for hemodialysis initiation. *J Vasc Interv Radiol* 24: 1289-1294. <http://dx.doi.org/10.1016/j.jvir.2013.05.034>.
- Tan M, Lau J, Guglielmo BJ (2014) Ethanol locks in the prevention and treatment of catheter-related bloodstream infections. *Ann Pharmacother* 48: 607-615. <http://dx.doi.org/10.1177/1060028014524049>.
- Tordoir J, Canaud B, Haage P (2007) EBPG on Vascular Access. *Nephrol Dial Transplant* 22 (Suppl 2): ii88-117.
- Vascular Access Work Group (2006) Clinical practice guidelines for vascular access. *Am J Kidney Dis* 48 (Suppl 1): S248-S273.
- Weijmer MC, van den Dorpel MA, Van de Ven PJ, ter Wee PM, Jos van Geelen JACA, Groeneveld JO, van Jaarsveld BC, Koopmans MG, le Poole CY, Schrandt-Van der Meer AM, Siegert CEH, Stas KJF, for the CITRATE Study Group (2005) Randomized, clinical trial comparison of trisodium citrate 30% and heparin as catheter-locking solution in hemodialysis patients. *J Am Soc Nephrol* 16: 2769-2777.