Journal of Infection and Public Health 16 (2023) 1023–1032

Contents lists available at ScienceDirect

Journal of Infection and Public Health

journal homepage: www.elsevier.com/locate/jiph

Review

Early identification of local infections in central venous catheters for hemodialysis: A systematic review

José Luis Cobo-Sánchez [a,b,1], Ian Blanco-Mavillard [c,d,e,*,1], Noelia Mancebo-Salas [f,1], Susana Moya-Mier [a], Faustino González-Menéndez [a], Cristina Renedo-González [a], Mercedes Lázaro-Otero [a,g], Raquel Pelayo-Alonso [a], Zulema Gancedo-González [a,h], Joan Ernest de Pedro-Gómez [c,d]

[a] Hospital Universitario Marqués de Valdecilla – IDIVAL, Santander, Spain
[b] Clínica Mompía School of Nursing, Universidad Católica de Ávila, Mompía, Spain
[c] Department of Nursing and Physiotherapy, Universitat de les Illes Balears, Palma, Spain
[d] Care, Chronicity and Evidence in Health Research Group (CurES), Health Research Institute of the Balearic Islands (IdISBa), Palma, Spain
[e] Implementation, Research and Innovation Unit, Hospital de Manacor, Manacor, Spain
[f] Dirección General de Servicios Sociales. Consejería de Familia, Juventud y Política Social, Comunidad de Madrid, Madrid, Spain
[g] Faculty of Nursing, Universidad de Cantabria, Santander, Spain
[h] Escoles Universitaries Gimbernat, Nursing School, Universitat Autonoma Barcelona, Barcelona, Spain

ARTICLE INFO

Article history:
Received 14 December 2022
Received in revised form 29 March 2023
Accepted 11 April 2023

Keywords:
Hemodialysis
Central Venous Catheter
Local Infection
Exit Site Infection
Tunnel Infection
Early Diagnosis
Nursing Assessment
Systematic Review

ABSTRACT

Background: The use of central venous catheters (CVC) is associated with higher morbidity and mortality, related to infectious complications, contributing to poorer clinical outcomes and increased healthcare costs. According to the literature, the incidence of local infections related to CVC for hemodialysis is highly variable. This variability is related to differences in definitions of catheter-related infections.
Objective: To identify signs and symptoms for determining local infections (exit site and tunnel tract infections) used in the literature in tunnelled and nontunnelled CVC for hemodialysis.
Design: Systematic review
Methods: Structured electronic searches were conducted in five electronic databases, from 1 January 2000–31 August 2022, using key words and specific vocabulary, as well as manual searches in several journals. Additionally, vascular access clinical guidelines and infection control clinical guidelines were reviewed.
Results: After validity analysis, we selected 40 studies and seven clinical guidelines. The definitions of exit site infection and tunnel infection used in the different studies were heterogeneous. Among the studies, seven (17,5 %) used the definitions of exit site and tunnel infection based on a clinical practice guideline. Three of the studies (7.5 %) used the Twardowski scale definition of exit site infection or a modification. The remaining 30 studies (75 %) used different combinations of signs and symptoms.
Conclusions: Definitions of local CVC infections are highly heterogeneous in the revised literature. It is necessary to establish a consensus regarding the definitions of hemodialysis CVC exit site and tunnel infections.
Registration: PROSPERO (CRD42022351097).

* Correspondence to: Hospital Manacor, Implementation, Research, and Innovation Unit, Carretera de Manacor-Alcudia s/n, Manacor 07500 Spain.
E-mail address: ianblanco@hmanacor.org (I. Blanco-Mavillard).
[1] These authors contributed equally to this study and shared first authorship.

https://doi.org/10.1016/j.jiph.2023.04.012

Contents

Introduction

Chronic kidney disease is a major public health problem worldwide. Its prevalence ranges from 7 % to 12 % [1] and nearly 700 million people around the world are affected [2]. When the glomerular filtration rate is < 15 mL/min/1.73 m2, renal replacement therapy must be initiated. Approximately 9.7 million people, globally, are currently receiving this type of treatment [2]. Dialysis is the most widely used treatment for chronic kidney disease, and 90 % of these patients undergo hemodialysis [3].

All clinical practice guidelines on hemodialysis recommend the internal arteriovenous fistula (autologous or prosthetic) as the ideal vascular access, due to its lower rate of complications compared to central venous catheters [4–8]. Nevertheless, central venous catheters are commonly accepted as an alternative to arteriovenous fistulas, as they can be used immediately after implantation. The need to allow time for the maturation of arteriovenous fistulas, and the resulting uncertainty about when hemodialysis treatment can be started, contribute to the high frequency and prolonged duration of central venous catheters use [9]. Approximately 70–80 % of incident hemodialysis patients initiate treatment via a central venous catheter [10,11]. Among prevalent patients, however, the use of a central venous catheter is less frequent, representing 30–40 % [10,11].

The use of central venous catheters is associated with higher morbidity and mortality related to infectious complications, and may contribute to poorer clinical outcomes and increased healthcare costs [12–15].

According to the literature, the incidence of bacteremia related to the hemodialysis catheter is highly variable (from 1.6 to 6.18/1000 catheter-days for tunneled catheters and from 1.4 to 8.3/1000 catheter-days for non-tunneled catheters) [16,17]. Similarly, the incidence of exit site infection ranges from 0.35 to 8.3/1000 catheter-days for tunneled catheters, and from 8.2 to 16.75/1000 catheter-days for non-tunneled catheters [16–19]. The variability in these results is due to the lack of consensus on the definition and intrinsic variability in terms of management adherence considering the best available evidence.

Several clinical practice guidelines for vascular access and scientific societies recommend central venous catheters exit site be assessed by nurses in each hemodialysis session to identify early any signs of local infection [4,5,20]. A correct early identification of signs and symptoms of infection in the exit site and tunnel prevents catheter-related infections, either local (exit site, subcutaneous tunnel) or bacteraemias.

The aim of this review was to identify signs and symptoms for determining local infections (exit site and tunnel tract infection) in tunneled and not tunneled central venous catheters for hemodialysis used in the literature to establish a consensus definition through future research.

Material and methods

The protocol for the systematic review was registered and prospectively made available in an international prospective register of systematic reviews (PROSPERO 2022 CRD42022351097) [21]. Our review was performed and reported based on the recommendations made by the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) statement [22].

Review question

What are the signs and symptoms for determining local infections (exit site and tunnel tract infection) in tunneled or non-tunneled central venous catheters for hemodialysis?

Inclusion criteria

An electronic search was conducted for any studies on adult patients (age ≥18 years) with a central venous catheter (tunneled or non-tunneled) as hemodialysis vascular access, in studies that presented data on signs and symptoms for determining local infections (exit site and tunnel tract infection) in tunneled or non-tunneled central venous catheters for hemodialysis.

This review included randomized-controlled trials, non-randomized interventional studies (quasi-experimental), observational studies with pre- and post-guideline/intervention implementation and protocols of randomized-controlled trials and systematic reviews. In addition, vascular access clinical guidelines from nephrology and vascular access scientific societies and infection control clinical guidelines were revised to include their central venous catheter-related definitions for local infections. In addition, we revised titles from relevant journals on nephrology care: Enfermería Nefrológica, Journal of Renal Care and Nephrology Nurses Journal. Also, references cited by included studies and previous reviews were screened to detect other potentially relevant studies. Searches were

limited to English, Spanish and Portuguese, and to the last 22 years (2000–2022).

Exclusion criteria

Non-human studies were excluded. Non-primary studies such as review articles, commentaries, letters to the editor and interviews were also excluded. Similarly, we excluded any case studies and publications outside of peer-reviewed or independently validated papers. Narrative review studies were not considered eligible, although a revision of included studies was also performed. Studies that did not include a definition of local infection (exit site and tunnel tract infection) were excluded.

Searches

The search strategy was piloted in February 2020 in a single database to ensure sensitivity and specificity. An expert librarian from the University was consulted during this phase. The final searches were developed by the first author in March 2020 and then reproduced by a second researcher to ensure the validity of the results. A new search was developed by the first author on September 1, 2022, to review final articles.

Search strategy

Five electronic databases were searched from 1 January 2000–31 August 2022: MEDLINE (via PubMed), CINAHL (via OVID), CUIDEN (Spanish care database), Cochrane Library (including CENTRAL Trials) and Web of Science (via WOS). Structured searches were conducted of published studies using specific subject headings or vocabulary (medical subject headings -MeSH- and health sciences descriptors -DeCS-), as well as free terms or key words. The search terms for the PICO question were “hemodialysis”, “central venous catheter”, “infection”, “exit site” and “subcutaneous tunnel”. These terms will be combined with Boolean operators, “OR” to combine intradomain terms and “AND” to combine inter-domain terms. Marginal terms such as “peritoneal dialysis” were combined with “NOT” to ensure accuracy of the results. Searches were limited to adults and by language (English and Spanish). The full search strategies for these databases and their results are provided in Table 1.

Study selection

After the electronic searches, two independent and blinded reviewers assessed eligibility by study titles in every database and included in a reference manager. Duplicates were removed, and abstracts were then revised by two independent and blinded authors, discarding any study that did not meet the inclusion criteria. The remaining studies were included in a full-text review, in which any studies that failed include a definition of local infection (exit site and tunnel tract infection) were excluded. The full-text articles were assessed by two independent and blinded reviewers for eligibility. Data extraction was revised by the first author to detect disagreements. We used an ad hoc form in this phase. Disagreements were resolved by consensus of the six reviewers who took part in this process.

Data extraction and synthesis

Two independent reviewers conducted data extraction from all included studies and registered in a review form. Every study was then discussed within a group of six reviewers. First, a descriptive analysis of published studies was conducted, which included date of publication, country, aim, study design, sample size, catheter type, setting, definition of local infections (exit site and tunnel tract infection).

Appraisal

Two authors independently assessed the quality of the studies. We used the Newcastle-Ottawa validated tool for the evaluation of internal validity of longitudinal observational studies [23], the CONSORT check list for randomized-controlled trials [24], the CASP check list for experimental studies [25] and the Strobe statement check list for cross-sectional studies [26]. The AGREE reporting checklist was used to evaluate clinical practice guidelines [27].

Results

The electronic searches produced a total of 256 titles. Three additional reports were identified by direct searches in specialized journals in the field of renal care and another two articles were identified from the reference lists of previous studies. Additionally, three vascular access clinical guidelines and two infection control clinical guidelines were included. After the selection process, 47 titles were selected and included in our review: 40 studies and seven clinical guidelines. The study selection process and causes for rejection are described in Fig. 1.

General study characteristics

All selected studies were published after 2008 and conducted in different European countries [28–44], Asian countries [14,45–50], Australia [51,52], Brazil [53,54], South Africa [55], Canada [56–59] and the United States [60–66]. Twenty-three studies were observational, twelve were clinical trials, four were quasi-experimental and there was one systematic review. Twenty-nine studied tunneled catheters, four examined non tunneled catheters and seven analyzed both (tunneled and non-tunneled catheters). Thirty studies took

Table 1
Search strategies used for all databases and results.

Database	Search strategy	Results
CINAHL	(exit site OR insertion site OR tunnel) AND (hemodialysis AND central venous catheter AND infection) Limiters – Published Date: 2000/01/01–2022/08/31	44
Medline	(“haemodialysis”[All Fields] OR “renal dialysis”[MeSH Terms] OR (“renal”[All Fields] AND “dialysis”[All Fields]) OR “renal dialysis”[All Fields] OR “hemodialysis”[All Fields]) AND (“catheters”[MeSH Terms] OR “catheters”[All Fields] OR “catheter”[All Fields]) AND (exit[All Fields] AND site[All Fields]) NOT (“peritoneum”[MeSH Terms] OR “peritoneum”[All Fields] OR “peritoneal”[All Fields]) AND (“2000/01/01”[PDAT]: “2022/08/31”[PDAT])	169
Cochrane Library	“hemodialysis” in Title Abstract Keyword AND “central venous catheter” in Title Abstract Keyword AND “infection” in Title Abstract Keyword AND “exit site” in Title Abstract Keyword NOT “peritoneal” in Title Abstract Keyword – (Word variations have been searched) with Cochrane Library publication date from Jan 2000 to Aug 2022	37 (3 systematic reviews and 34 clinical trials)
Cuiden	hemodiálisis AND catéter AND infección AND (orificio de salida OR tunel) with publication date from Jan 2000 to Jan 2020	6

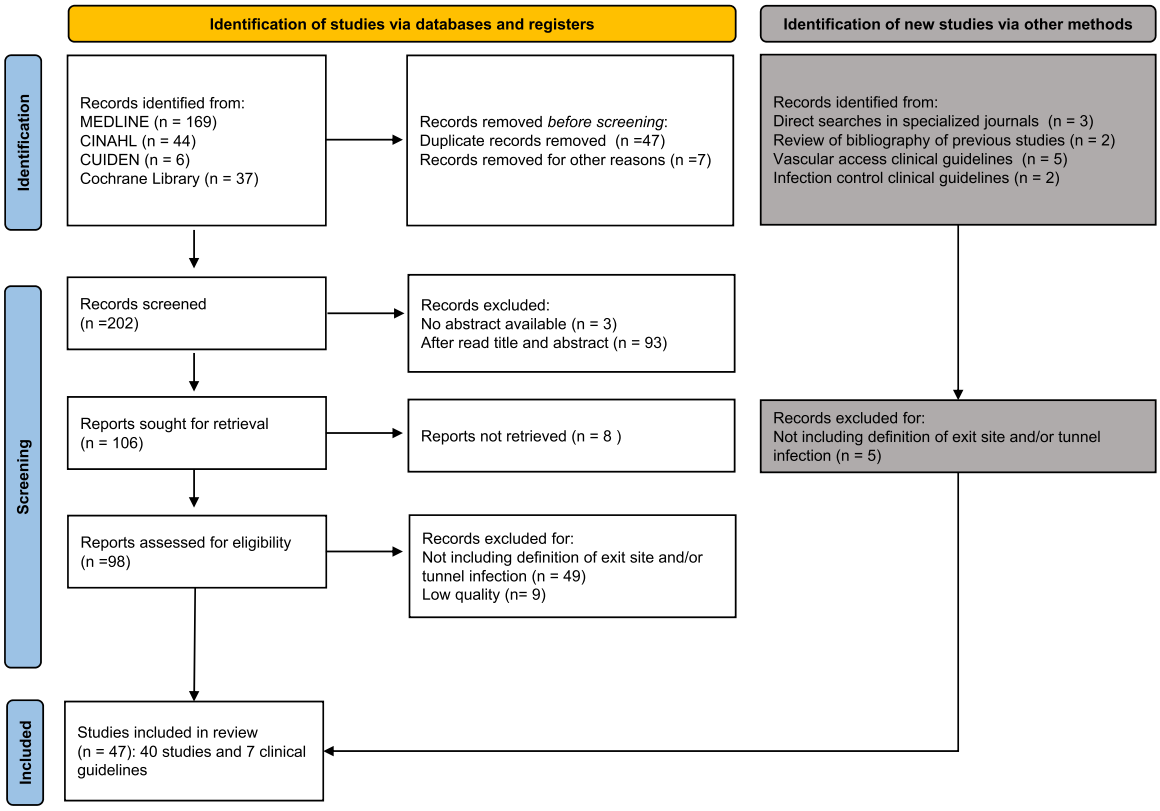

Fig. 1. A flowchart of the inclusion process of studies used in the systematic review (adjusted from the PRISMA 2020 flowchart). PRISMA: Preferred Reporting Items for Systematic Reviews and Meta-Analyses.

place at hospitals, three at dialysis centers and seven took place at both (hospitals and dialysis centers), with a final sample of 12,419 patients. Table 2 summarizes the main characteristics of these studies and definitions of exit site infection and/ or tunnel infection.

Seven clinical practice guidelines were included: two from The National Kidney Foundation's Kidney Disease Outcomes Quality Initiative (KDOQI) (2006 [5] and the 2019 update [67]), one from the Spanish Multidisciplinary Group on Vascular Access (GEMAV) [20], one from the Canadian Society of Nephrology (CSN) [68], one from the European Society for Vascular Surgery (ESVS) [69] and two from control infection societies: Centers for Disease Control and Prevention (CDC) [70] and Infectious Diseases Society of America (IDSA) [71] guidelines. Table 3 presents the definitions of exit site infection and tunnel infection based on the clinical guidelines included in this review.

Definitions of exit site infection and tunnel infection

The definitions of exit site infection and tunnel infection used in the different studies were heterogeneous. Twenty-three studies only defined the exit site infection, whereas 17 studies included definitions of exit site infection and tunnel infection. All clinical guidelines included definitions of both exit site infection and tunnel infection.

Among the studies, seven (17,5 %) used the definitions of exit site and tunnel infection from some clinical practice guideline: three from the CDC guideline [36,37,45], one from the IDSA guideline [28] and three from the KDOQI guidelines (two from 2006 and one from the 2019 update) [42,54,61]. Three of the studies (7.5 %) used the Twardowski scale definition of exit site infection [29,52] or a modification of the same [51]. The remaining 30 studies (75 %) used different combinations of signs and symptoms to determine the presence of exit site and/or tunnel infection.

Table 4 shows the frequency of the different signs and symptoms used, both in the studies and in the clinical practice guidelines, to determine the presence of exit site and/or tunnel infection. In most of the documents, a diameter ≥ 2 cm was used for erythema, induration and tenderness. Positive culture was used in 26 of the studies (57.77 %) to determine local infectious complications.

Discussion

To our knowledge, this is the first systematic review to identify signs and symptoms for determining local infections (exit site and tunnel tract infection) in tunneled and non-tunnelled central venous catheters for hemodialysis.

Our review shows that many studies used the exit site and/or tunnel infection as the dependent variable, although without including a definition of the same in the methods section (49 out of 98 studies, i.e., approximately 50 % of the studies selected for review were excluded on these grounds). Ignoring the definition of a dependent variable in a research study could introduce bias, specifically if the missing results did not occur at random. Missing definitions could create invalid and misleading comparisons between centres and types of intervention.

The studies reviewed from the electronic searches showed a low adherence, with definitions of exit site and tunnel infection proposed by nephrology, vascular access and/or scientific societies for infection control. All clinical practice guidelines indicate a positive culture as the gold standard; however, only 57.77 % of the revised studies used positive culture to determine exit site infection and 31.91 % to determine tunnel infection. Clinical guidelines are important tools to ensure that health practices are evidence-based. Nevertheless, the literature refers that only 14 % of clinically useful research findings are adopted in everyday practice after an average delay of approximately 17 years [72]. A study analyzing the quality of

Table 2
Articles included in the review of electronic databases and other methods with exit site infection and tunnel infection definition.

Author, Year (Country)	Aim	Study design	Catheter type	Setting	Sample size	Exit site infection (ESI) and tunnel infection (TI) definition
Al-hwiesh, 2008 (Saudi Arabia) [45]	To evaluate the efficacy of antibiotic-lock therapy using a combination of vancomycin and gentamycin as a prophylaxis against tunneled central catheters-related bacterial infection in hemodialysis patients.	RCT	T	H	69	ESI and TI: The CDC definitions for infections.
Al-Solaiman et al., 2011 (USA) [60]	To quantify infections in such patients, to characterize their clinical presentations, and to evaluate factors determining need for hospitalization.	O	T	H	172	ESI: Presence of purulent exudate in the exit site, together with positive culture of the exudate and negative blood cultures.
Battistella et al., 2011 (Canada) [56]	To determine whether the low rate of central venous catheters -related infection achieved by topical polyantibiotic ointment use during a randomized controlled trial would be observed during long-term prophylaxis as part of routine clinical care.	O	T	H	228	ESI: Purulent discharge at exit site or erythema, tenderness, induration (2 of 3) at exit site with a positive culture of serous discharge. TI: Purulent discharge or aspirate from a tunnel or pocket site not contiguous with exit site or erythema, tenderness, induration (2 of 3) at a tunnel or pocket site not contiguous with exit site with a positive culture of serous discharge or aspirate from that site.
Bouza et al., 2014 (Spain) [28]	To assess the validity of Gram stain and superficial culture for anticipating catheter exit-site infection and hemodialysis catheter–related bloodstream infection.	O	T	H	75	ESI: Based on the intravascular catheter infection guidelines of the Infectious Diseases Society of America.
Bueloni et al., 2019 (Brazil) [53]	To compare the efficacy of lock solution using a combination of cefazolin and gentamicin versustaurolidine and citrate in reducing catheter-related bloodstream infections in patients undergoing hemodialysis and to identify any adverse effects.	O	T	DC	127	ESI: The presence of purulent discharge or erythema and edema at the exit site below the cuff.
Campos et al., 2011 (Brazil) [54]	To compare a solution of minocycline and EDTA with the conventional unfractionated heparin for the prevention of catheter-related bacteremia in hemodialysis patients during a period of 90 days.	RCT	T	H	204	ESI and TI: Definitions of K/DOQI Clinical Practice Guidelines for Vascular Access
Chen et al., 2019 (Taiwan) [46]	To analyze the impact of routine locking solutions on the incidence of catheter-related bloodstream infections and exit site infection, in preserving catheter function, and on the rate of all-cause mortality in patients undergoing hemodialysis.	SR	B	B	4832	ESI: The development of a purulent redness around the exit site that did not result from residual stitches
Evans et al., 2014 (USA) [61]	To explore the effect of a prescribed showering protocol on catheter-related bloodstream infections rates, tunnel infection rates, and exit site infection rates in individuals undergoing incenter hemodialysis and using an hemodialysis catheter; and to evaluate the effect of not using a catheter exit site dressing on catheter-related bloodstream infections, tunneled catheter infections, and exit site infections.	RCT	T	B	47	ESI: Inflammation confined to the area surrounding the catheter exitsite, not extending superiorly beyond the cuff because the catheter is tunnelled with the exit site having exudates. The culture of catheter exudate has been confirmed to be positive (KDOQI, 2006). TI: The catheter tunnel superior to the cuff is inflamed, painful, and may have drainage through the exit site that is culture positive (KDOQI, 2006). There is presence of tenderness, erythema, or induration over 2 cm from the exit site along the subcutaneous tract of the tunnel with or without evidence of bloodstream infection.
Gupta et al., 2016 (India) [47]	To examine clinical and bacteriological profiles of hemodialysis patients developing catheter-related bloodstream infections, the antibiotic susceptibility of the bacteria isolated from these patients and determine nasal carriage of S. aureus in the study subjects.	O	NT	H	127	ESI: positive semi-quantitative culture of the purulent drainage material obtained from the exit site accompanied with redness and crusting.
Harwood et al., 2008 (United Kingdom) [29]	To examine predictors of positive central venous catheters exit-site infections.	O	T	H	52	ESI: Classification of PD exit sites of Twardowski & Prowant.
Heidempergher et al., 2021 (Italy) [42]	To assess the effect of stricter infection prevention policies adopted during the COVID-19 pandemic on central venous catheters infection rates.	O	T	H	215	ESI and TI: definitions of update KDOQI 2019 guideline.
Hughes et al., 2011 (Australia) [51]	To determine the percentage of opaque dressings currently used for central venous catheters exit sites that remained intact between dialysis episodes, and to explore whether altered dressing integrity is associated with specific demographic or clinical characteristics.	O	B	DC	34	ESI: A modified Twardowski scale was used to standardize color and scab/crust as an assessment of healed, healthy exit site, or whether trauma or infection was present at the exit site.

(*continued on next page*)

Table 2 (*continued*)

Author, Year (Country)	Aim	Study design	Catheter type	Setting	Sample size	Exit site infection (ESI) and tunnel infection (TI) definition
Jaberi et al., 2014 (Canada) [57]	To evaluate the viability and effectiveness of a technique of temporary catheter externalization of a tunneled hemodialysis catheter that allows for preservation of the primary venous access site during treatment of tunnel or exit-site infections in catheter- dependent hemodialysis patients with central venous stenosis and limited venous access options.	O	B	H	26	ESI: inflammation, exudate, or pain localized to the area surrounding the catheter exit site without extension superiorly beyond the cuff. TI: Inflammation, exudate, or pain overlying the catheter tunnel superior to the cuff with or without exit-site drainage.
Kaze et al., 2014 (South Africa) [55]	To investigate the adverse outcomes of non-tunneled hemodialysis catheters and determinants in chronic hemodialysis patients receiving care at the Yaoundé General Hemodialysis center, Cameroon.	O	NT	H	81	ESI: development of a purulent exudate at the site with or without a positive swab culture.
Koç et al., 2008 (Turkey) [30]	To determine whether we should culture the tip, the proximal portion, or both when a patient demonstrates clinical indicators of infection.	O	B	H	22	ESI and TI: The presence of signs of infection around the tunnel or at the catheter insertion site with or without positive (proximal and/or distal) catheter culture ($> 10^3$ CFU/mL).
Lai et al., 2009 (Taiwan) [48]	In this study, the safety and efficacy of the modified exchange technique to manage dysfunctional tunneled hemodialysis catheters with exit site infection were evaluated.	O	T	H	23	ESI: based on any evidence of infection, including erythema or induration within 2 cm of the exit site, purulent discharge from the exit site with positive culture result, or peri–exit-site tenderness.
MacRae et al., 2008 (Canada) [58]	Pilot study using a randomized design to compare the effect of citrate 4 % and 5000 U/mL heparin in terms of catheter-related bloodstream infections, exit site infections, and thrombotic episodes in a Canadian cohort of prevalent dialysis patients with cuffed catheters.	RCT	T	H	61	ESI: Erythema, tenderness, induration (two of three catheters) at exit site positive exit-site cultures in the absence of other causes.
McArdle et al., 2017 (Australia) [52]	To identify the most effective and safe dressing for hemodialysis central venous catheters exit sites in a tropical region	RCT	T	H	26	ESI: Clinical signs of infection were the presence or absence of crust at the exit site, and the color of the exit site, assessed as per the Twardowski Scale at each dialysis session.
Moran et al., 2012 (USA)[63]	To evaluate the use of gentamicin 320 g/mL in 4 % sodium citrate as a routine catheter lock to prevent catheter clotting and bacteremia.	RCT	T	B	303	ESI: Signs of local infection (erythema and discharge).
Oliveira et al., 2008 (Canada) [59]	To determine if the use of a medical directive that included polysporin double ointment application at central venous catheters exit sites that appeared infected was associated with an increased risk of positive yeast cultures at central venous catheters exit sites in hemodialysis patients.	RCT	T	H	126	ESI: Positive exit site culture.
Onder et al., 2009 (USA) [64]	To investigate if the application of chlorhexidine-based solutions (ChloraPrep®) to the exit site and the hub of tunneled-cuffed hemodialysis catheters would have any beneficial impact on the prevention of catheter-related bloodstream infections and catheter survival times when compared with the use of povidone–iodine solutions.	QE	T	H	59	ESI: the presence of purulent discharge, swelling, erythema and tenderness at the exit site with or without a positive swab culture.
Porazko et al., 2021 (Poland) [44]	This study aimed at comparing the potentially less skin-traumatizing single-suture method of the central tunneled catheters stabilizing with the dominating double suture method with respect to the occurrence of early complications, particularly catheter displacement and prolonged would healing.	QE	T	H	373	ESI and TI: redness, swelling, or discharge.
Porazko et al., 2021 (Poland) [43]	To evaluate the impact of the implementation of the innovative redness, edema, discharge and tenderness, symptoms (REDS) scale (devised by the authors) for the description of the tunnel condition on the frequency of infection in long-term catheter users.	O	T	H	40	ESI: exit site redness and edema, tenderness and discharge, and systemic symptoms (body temperature >38 or <36◦C, chills, hypotonia with systolic blood pressure <90 mmHg, tachycardia >90/min, and unusual patient confusion).
Powell et al., 2010 (United Kingdom) [31]	To assess the outcomes of tunneled hemodialysis catheters inserted by way of occluded or collateral veins.	O	T	H	54	ESI: documented clinical signs of infection (e.g., erythema, tenderness, or induration) appeared within 2 cm of the exit site and were supported by a positive swab culture.
Power et al., 2009 (United Kingdom) [32]	To compare the use of 46.7 % citrate and 5 % heparin catheter locks exclusively in patients with end stage reanl failure and a single type of cuffed twincatheter single-lumen central venous catheters, the tunneled catheter, intended as long-term vascular access.	RCT	T	H	232	ESI: Positive exit site culture. Exit-site swabs were used if there were exudates or crust, redness, or induration at the exit site.

(*continued on next page*)

Table 2 (*continued*)

Author, Year (Country)	Aim	Study design	Catheter type	Setting	Sample size	Exit site infection (ESI) and tunnel infection (TI) definition
Power et al., 2010 (United Kingdom) [33]	To describe a large and comprehensive series with long follow-up of the translumbar route for long-term hemodialysis access.	O	T	H	39	ESI: Exit-site swabs were taken if there was exudate with or without pain, crusting, erythema or induration at the exit site. TI: Tunnel infections were defined by pain, redness or induration along the subcutaneous course of the line, with or without exudates at the exit site.
Power et al., 2014 (United Kingdom) [34]	The authors studied the immediate and long-term performance and complications of two twin-catheter systems, the Tesio catheter and the LifeCath Twin, to inform clinical practice.	RCT	T	H	80	ESI: Exit site swabs were taken if there was exudate with or without pain, crusting, erythema or induration at the exit site.
Şanal et al., 2016 (Turkey) [35]	To investigate the safety and functionality of tunneled transhepatic hemodialysis catheters in chronic hemodialysis patients.	O	T	H	38	ESI: Erythema and induration within a 2 cm radius from the catheter exit site with no signs of bacteremia.
Silva et al., 2008 (Portugal) [36]	To assess the relative merits and benefits of two proactive preventive measures addressing each of these mechanisms, questioning if the benefit of both strategies used in association is additive and assessing the relative contribution of each infection pathway, assuming that an antibiotic ointment would fight contamination through the catheter track and that an antimicrobial lock would block luminal microbial biofilm formation and invasion.	RCT	T	B	141	ESI and TI: CDC criteria, Tunnel or exit site infection—purulent discharge or evidence of inflammation of the exit site and/or tunnel (erythema, tenderness, induration).
Silva et al., 2012 (Portugal) [37]	To test safety and effectiveness of citrate. A prospective, interventional study was conducted to assess the safety and efficacy of a 30 % citrate lock in preventing catheter-related bacteremia.	RCT	T	H	157	ESI and TI: CDC criteria, Tunnel or exit site infection—purulent discharge or evidence of inflammation of the exit site and/or tunnel (erythema, tenderness, induration).
Škofic et al., 2009 (Slovenia) [38]	To compare the long-term catheter-related complications associated with temporary untunneled hemodialysis catheters, locked with citrate in the interdialysis period, inserted in critically ill patients with acute kidney injury, between different catheter insertion sites (femoral vs. jugular and subclavian) and catheter types (single-lumen vs. double-lumen).	O	NT	H	290	ESI: local signs of inflammation with purulent discharge and positive exit-site culture.
Sofroniadou et al., 2017 (Greece) [39]	To evaluate the safety and efficacy of an ethanol lock solution in preventing catheter-related bloodstream infections in hemodialysis patients with non-tunneled-uncuffed-catheters.	QE	NT	H	103	ESI: the appearance of erythema, tenderness, and/or induration within 2 cm of the exit site with or without fever or purulent drainage from the exit site while the microbiological exit site infection is the isolation of a microorganism on exudate culture with or without concomitant bloodstream infection criteria.
Sychev et al., 2011 (USA) [65]	To determine whether the dialysis catheter could be salvaged in such patients by treatment with systemic antibiotics and an antibiotic lock.	QE	T	B	2061	ESI: diagnosed in patients with purulent drainage from the exit site with positive wound cultures.
Tacchini-Jacquier and Verloo, 2017 (Switzerland) [40]	To assess and compare the safety performance and other potential complications of a Y-connection and the usual tunneled central venous catheters connection to the hemodialysis machine for blood restitution.	O	T	H	18	ESI: evidence of exudate (with or without pain), crusting, erythema, or induration. TI: pain, redness, or induration along the subcutaneous course of the line, with or without exudates at the exit site.
Wang et al., 2015 (USA) [14]	To report our experience with the patency and complications of translumbar tunneled dialysis catheter at our institution	O	T	H	84	ESI: the presence of new erythema, pain at the exit site and/or purulent drainage around the catheter.
Wang et al., 2016 (China) [49]	We retrospectively reviewed the clinical outcomes and complications of the de novo catheter placement without the delay technique to provide a suitable reference.	O	T	H	164	ESI: evidence of redness, swelling, and drainage from the exit site. TI: purulent discharge from the tunnel, or erythema, induration, and/or tenderness over the catheter tunnel accompanied by a positive culture in the discharge.
Wathanavasin et al., 2021 (Thailand) [50]	To compare the efficacy in lowering rate of catheter loss due to catheter-related thrombosis or catheter-related blood stream infection between sodium bicarbonate and heparin lock in prevalent chronic hemodialysis patients.	RCT	T	DC	118	ESI: hyperemia, induration, and/or tenderness ≥ 2 cm from catheter exit site. TI: identified if the development extended along the subcutaneous tunnel.
Weijmer et al., 2008 (The Netherlands) [41]	To compare the patency and catheter-related complications of this non-tunneled precurved temporary jugular catheter with non-tunneled straight jugular vein catheters. We also related the results to the outcome of tunneled cuffed catheters during this study.	O	B	B	233	ESI: the development of a purulent exudate or redness around the site not resulting from residual stitches.
Zhang et al., 2016 (USA) [66]	Using a registry database, we examined all positive blood cultures by organisms for each type of hemodialysis access over 14 years.	O	B	H	420	ESI: drainage at the exit site (which was cultured) or erythema (not cultured) or both.

Design: RCT randomized clinical trial, O observational, QE quasi-experimental, SR systematic review.
Catheter type: T tunneled, NT non-tunneled, B both (tunneled and non-tunneled).
Setting: H hospital, DC dialysis center, B both (hospital and dialysis center).

Table 3
Clinical practice guidelines definitions of exit site infection (ESI) and tunnel infection (TI) for hemodialysis catheters.

Year	Publisher	Definition of catheter exit site infection and tunnel infection
2019	The National Kidney Foundation's Kidney Disease Outcomes Quality Initiative (KDOQI) [67]	ESI: Hyperemia, induration, and/ or tenderness ≤ 2 cm from catheter exit site. May be associated with drainage from the exit site. It may or may not be associated with bacteremia. If there is exit site drainage, it should be collected and sent for Gram staining, culture and sensitivities. TI: Tenderness, hyperemia, and/ or induration that extends along the subcutaneous tunnel. It may or may not be associated with bacteremia. If there is drainage, it should be collected and sent for Gram staining, culture, and sensitivities.
2018	Spanish Multidisciplinary Group on Vascular Access (GEMAV) [20]	Uncomplicated local infection: Existence of inflammatory signs limited to 2 cm around the cutaneous exit site, not extending superiorly towards the catheter cuff (if tunnelled). May or may not be associated with fever and bacteremia and may be accompanied by purulent drainage through the cutaneous exit site. Complicated local infection: with inflammatory signs extending > 2 cm from the cutaneous exit site and into the subcutaneous catheter tract (tunnelitis). May or may not be associated with fever and bacteremia and may be accompanied by purulent drainage through the cutaneous exit site.
2018	European Society for Vascular Surgery (ESVS) [69]	ESI: The presence of a purulent discharge or erythema, induration/and or tenderness at the catheter exit site with a positive bacteriological culture of the serous discharge. TI: The presence of purulent discharge from the tunnel or erythema, induration and/or tenderness over the catheter tunnel with a positive culture.
2009	Infectious Diseases Society of America (IDSA) [71]	ESI: Hyperemia, induration, and/or tenderness ≤ 2 cm from catheter exit site. May be associated with fever and purulent drainage from the exit site. It may or may not be associated with bacteremia. If there is purulent drainage, it should be collected and sent for Gram staining and culture. TI: Tenderness, hyperemia, and/ or induration that extends > 2 cm from the exit site and along the subcutaneous tunnel. It may or may not be associated with bacteremia. If there is purulent drainage, it should be collected and sent for Gram staining and culture.
2006	The National Kidney Foundation's Kidney Disease Outcomes Quality Initiative (KDOQI) [5]	ESI: Inflammation confined to the area surrounding the catheter exit site, not extending superiorly beyond the cuff if the catheter is tunneled, with exudate culture result confirmed to be positive. TI: The catheter tunnel superior to the cuff is inflamed, painful, and may have drainage through the exit site that is culture positive.
2006	Canadian Society of Nephrology (CSN) [68]	ESI: Catheter exit site infections are characterized by redness, crusting, and exudate at the exit site in the absence of systemic symptoms and negative blood cultures. TI: No available.
2002	Centers for Disease Control and Prevention (CDC) [70]	ESI: Erythema or induration within 2 cm of the catheter exit site, in the absence of concomitant BSI and without concomitant purulence. TI: Tenderness, erythema, or site induration > 2 cm from the catheter site along the subcutaneous tract of a tunneled catheter, in the absence of concomitant bloodstream infection.

Table 4
Signs and symptoms used in the documents included in the review (n = 47), for identification of exit site infection and tunnel infection.

Sign / symptom	Exit site infection		Tunnel infection	
	n	%	n	%
Erythema	30	63.83 %	13	27.66 %
Purulent exudate	20	42.55 %	8	17.02 %
Positive culture	26	57.77 %	15	31.91 %
Exudate / discharge (not specific type)	16	34.04 %	9	19.15 %
Induration	13	27.66 %	4	8.51 %
Tenderness	13	27.66 %	12	25.53 %
Crust / Crusting	8	17.02 %	-	-
Pain / Painful	6	12.77 %	7	14.89 %
Fever	5	10.64 %	1	2.13 %
Inflammation	5	10.64 %	5	10.64 %
Hyperemia	4	8.51 %	3	6.38 %
Swelling	3	6.38 %	2	4.26 %
Bloody exudate	2	4.26 %	1	2.13 %
Purulent exudate expressed with manipulation of catheter	2	4.26 %	-	-
Scab / dry scab	2	4.26 %	-	-
Edema	2	4.26 %	-	-
Serous exudate	1	2.13 %	1	2.13 %
Dressing fell off at home	1	2.13 %	-	-
Pruritis	1	2.13 %	-	-
Obvious abscess	1	2.13 %	1	2.13 %
Excoriation of peri-exit site skin	1	2.13 %	-	-
Exuberance/granulation or 'proud flesh'	1	2.13 %	-	-
Chills	1	2.13 %	-	-
Hypotonia	1	2.13 %	-	-
Unusual patient confusion	1	2.13 %	-	-
Cuff visible	-	-	1	2.13 %

health care in the US showed that only 50 % of people are receiving recommended preventive care, with 70 % of patients receiving appropriate acute care, however only 60 % are receiving recommended reasonable chronic care [73].

Among the studies with a definition and clinical practice guidelines, these were highly heterogeneous regarding the definition of exit site and tunnel infection. Most studies and guides used erythema, purulent exudate, any other type of exudate, induration, and tenderness at the exit site to identify exit site infection which are present in around 30 % of cases. Moreover, tunnel infection was mostly identified by erythema and tenderness (around 25 % of revised documents). It is worth highlighting the article by Harwood et al. [29] on infection predictors of the central venous catheter exit site for hemodialysis. Among other variables, this study determined the presence of exit site signs/symptoms with exit site infection determined by culture of peri catheter skin smears and/or exudate. They found that the signs/symptoms that correlated in a statistically significant way were an erythema of less than 5 mm around the exit site ($p = 0.008$), with most of the infected exit sites showing erythema between 1 and 1.5 cm in diameter from the exit site [29]. According to this study, most of the documents included in our review used a diameter ≥ 2 cm for erythema, induration, and tenderness to identify exit site infection. Secondly, they found that negative cultures were significantly correlated with the presence of dry scab at the exit site ($p = 0.03$) [29]. Patients with pain and/or exudate and/or sensitivity presented an almost significant relationship ($p = 0.06$) with microbiological confirmation of exit site infection in this study [29].

The 2019 update to the National Kidney Foundation's Kidney Disease Outcomes Quality Initiative (KDOQI) Clinical Practice

Guideline for Vascular Access indicates the heterogeneity in the definitions of exit site infection in the different clinical practice guidelines on hemodialysis vascular access, and the need to agree on a definition [67]. Future research should be aimed at achieving a consensus among international experts on the combination of signs and symptoms for early identify of local infections in hemodialysis catheters.

Three of the revised studies used the Twardowski scale definition of exit site infection [29,52] or a modification of the same [51]. We consider that the use of this scale is inappropriate because, according to recent studies, it has a high sensitivity (close to 100 %) and a low specificity (around 60 %) [74,75]. Also, Rigo et al. found that the Twardowski scale showed differences according to the patient's race, reporting 53.2 % agreement with the score for African Americans descendants and 65.4 % agreement for others [75]. Future research must validate specific definitions and instruments to identify local infections in central venous catheters for hemodialysis.

Limitations

This review focuses on fully published research, and excludes grey literature and therefore this review may have been subject to publication bias. Also, consider the heterogeneity in the definitions of the studied phenomenon musts in the interpretation of the analysis displayed.

Conclusions

In conclusion, literature refers high heterogeneity in the signs and symptoms used for determining exit site and tunnel tract infection in tunneled or non-tunneled central venous catheters for hemodialysis. Erythema, purulent exudate or exudate / discharge (not specific type), induration and tenderness were the signs and symptoms with low consensus in the literature for determining local infections in central venous catheters for hemodialysis. This review shows the need to reach a consensus on an international definition of the signs/symptoms to determine the presence of local infections (exit site and tunnel infections) in central venous catheters for hemodialysis. Furthermore, validation studies of diagnostic criteria instruments for exit site and tunnel infections in hemodialysis catheters are necessaries.

Funding sources

This work was supported by Marqués de Valdecilla Research Institute (IDIVAL), Spain, grant number NVAL18/05.

CRediT authorship contribution statement

José Luis Cobo-Sánchez, Ian Blanco-Mavillard and Noelia Mancebo-Salas: conceptualised, designed and conducted the literature review; drafted the **manuscript. Susana Moya-Mier, Faustino González-Menéndez, Cristina Renedo-González, Mercedes Lázaro-Otero, Raquel Pelayo-Alonso, Zulema Gancedo-González, Joan Ernest de Pedro-Gómez:** contributed to the design of the review, reviewed and revised the manuscript.

Declaration of Competing Interest

None.

References

[1] Romagnani P, Remuzzi G, Glassock R, Levin A, Jager KJ, Tonelli M, et al. Chronic kidney disease. Nat Rev Dis Prim 2017;3:17088. https://doi.org/10.1038/nrdp.2017.88

[2] Bikbov B, Purcell CA, Levey AS, Smith M, Abdoli A, Abebe M, et al. Global, regional, and national burden of chronic kidney disease, 1990–2017: a systematic analysis for the Global Burden of Disease Study 2017. Lancet 2020;395:709–33. https://doi.org/10.1016/S0140-6736(20)30045-3

[3] Himmelfarb J, Vanholder R, Mehrotra R, Tonelli M. The current and future landscape of dialysis. Nat Rev Nephrol 2020;16:573–85. https://doi.org/10.1038/s41581-020-0315-4

[4] Vanholder R, Canaud B, Fluck R, Jadoul M, Labriola L, Marti-Monros A, et al. Diagnosis, prevention and treatment of haemodialysis catheter-related bloodstream infections (CRBSI): a position statement of European Renal Best Practice (ERBP. NDT 2010;3:234–46. https://doi.org/10.1093/ndtplus/sfq041

[5] Vascular Access. Work Group. Clinical practice guidelines for vascular access. Am J Kidney Dis 2006;48:S176–247 2006. https://doi.org/10.1053/j.ajkd.2006.04.029

[6] Kumwenda M., Mitra S., Reid C. Clinical practice guideline vascular access for haemodialysis 6th Edition. 2015.

[7] Polkinghorne KR, Chin GK, MacGinley RJ, Owen AR, Russell C, Talaulikar GS, et al. KHA-CARI Guideline: vascular access - central venous catheters, arteriovenous fistulae and arteriovenous grafts. Nephrol (Carlton) 2013;18:701–5. https://doi.org/10.1111/nep.12132

[8] Canadian Society of Nephrology (CSN). Report of the Canadian Society of Nephrology Vascular Access Working Group. Semin Dial 2012;25:22–5. https://doi.org/10.1111/j.1525-139X.2011.01009.x

[9] Arhuidese IJ, Orandi BJ, Nejim B, Malas M. Utilization, patency, and complications associated with vascular access for hemodialysis in the United States. J Vasc Surg 2018;68:1166–74. https://doi.org/10.1016/j.jvs.2018.01.049

[10] United States Renal Data System. US Renal Data System 2019 Annual Data Report: epidemiology of kidney disease in the United States. Am J Kidney Dis 2019;75:S1–64. https://doi.org/10.1053/j.ajkd.2019.09.002

[11] Noordzij M, Jager KJ, van der Veer SN, Kramar R, Collart F, Heaf JG, et al. Use of vascular access for haemodialysis in Europe: a report from the ERA-EDTA Registry. Nephrol Dial Transpl 2014;29:1956–64. https://doi.org/10.1093/ndt/gfu253

[12] Stevenson KB, Hannah EL, Lowder CA, Adcox MJ, Davidson RL, Mallea MC, et al. Epidemiology of hemodialysis vascular access infections from longitudinal infection surveillance data: predicting the impact of NKF-DOQI clinical practice guidelines for vascular access. Am J Kidney Dis 2002;39:549–55. https://doi.org/10.1053/ajkd.2002.31405

[13] Taylor G, Gravel D, Johnston L, Embil J, Holton D, Paton S, et al. Incidence of bloodstream infection in multicenter inception cohorts of hemodialysis patients. Am J Infect Control 2004;32:155–60. https://doi.org/10.1016/j.ajic.2003.05.007

[14] Wang K, Wang P, Liang X, Lu X, Liu Z. Epidemiology of haemodialysis catheter complications: a survey of 865 dialysis patients from 14 haemodialysis centres in Henan province in China. BMJ Open 2015;5:e007136. https://doi.org/10.1136/bmjopen-2014-007136

[15] Klevens RM, Edwards JR, Andrus ML, Peterson KD, Dudeck MA, Horan TC, et al. Special report: dialysis surveillance report: National Healthcare Safety Network (NHSN)-data summary for 2006. Semin Dial 2007;21:24–8. https://doi.org/10.1111/j.1525-139X.2007.00379.x

[16] Weijmer MC, Vervloet MG, ter Wee PM. Compared to tunnelled cuffed haemodialysis catheters, temporary untunnelled catheters are associated with more complications already within 2 weeks of use. Nephrol Dial Transpl 2004;19:670–7.

[17] Develter W, De Cubber A, Van Biesen W, Vanholder R, Lameire N. Survival and complications of indwelling venous catheters for permanent use in hemodialysis patients. Artif Organs 2005;29:399–405. https://doi.org/10.1111/j.1525-1594.2005.29067.x

[18] Stevenson KB, Adcox MJ, Mallea MC, Narasimhan N, Wagnild JP. Standardized surveillance of hemodialysis vascular access infections: 18-month experience at an outpatient, multifacility hemodialysis center. Infect Control Hosp Epidemiol 2000;21:200–3. https://doi.org/10.1086/501744

[19] Betjes MGH. Prevention of catheter-related bloodstream infection in patients on hemodialysis. Nat Rev Nephrol 2011;7:257–65. https://doi.org/10.1038/nrneph.2011.28

[20] Ibeas J, Roca-Tey R, Vallespín J, Moreno T, Moñux G, Martí-Monrós A, et al. Spanish Clinical Guidelines on Vascular Access for Haemodialysis. Enferm Nefrol 2018;21:S1–256. https://doi.org/10.4321/S2254-28842018000500001

[21] Cobo-Sánchez J.L., Blanco-Mavillard I., Mancebo-Salas N., Moya-Mier S., González-Menéndez F., Renedo-González C., et al. Early identification of local infections in central venous catheters for hemodialysis: a systematic review. PROSPERO Int Prospect Regist Syst Rev 2022.

[22] Moher D, Liberati A, Tetzlaff J, Altman DG, Altman D, Antes G, et al. Preferred reporting items for systematic reviews and meta-analyses: the PRISMA statement. PLoS Med 2009:6. https://doi.org/10.1371/JOURNAL.PMED.1000097

[23] Wells G.A., Shea B., O´Connell D., Peterson J., Welch V., Losos M., et al. The Newcastle-Ottawa Scale (NOS) for assessing the quality of nonrandomised studies in meta-analyses 2016. https://www.ohri.ca//programs/clinical_epidemiology/oxford.Asp (accessed June 27, 2017).

[24] Schulz KF, Altman DG, Moher D. CONSORT 2010 statement: updated guidelines for reporting parallel group randomised trials. BMJ 2010;340:698–702. https://doi.org/10.1136/BMJ.C332

[25] Santamaría Olmo R. Programa de Habilidades en Lectura Crítica Español (CASPe) | Nefrología. NefroPlus 2017;9:100–1.

[26] Elm E, von, Altman DG, Egger M, Pocock SJ, Gøtzsche PC, Vandenbroucke JP. Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) statement: guidelines for reporting observational studies. BMJ 2007;335:806–8. https://doi.org/10.1136/BMJ.39335.541782.AD

[27] Brouwers MC, Kerkvliet K, Spithof K. The AGREE reporting checklist: a tool to improve reporting of clinical practice guidelines. BMJ 2016:352. https://doi.org/10.1136/BMJ.I1152

[28] Bouza E, Rojas L, Guembe M, Marín M, Anaya F, Luño J, et al. Predictive value of superficial cultures to anticipate tunneled hemodialysis catheter–related bloodstream infection. Diagn Microbiol Infect Dis 2014;78:316–9. https://doi.org/10.1016/j.diagmicrobio.2013.12.008

[29] Harwood L, Wilson B, Thompson B, Brown E, Young D. Predictors of hemodialysis central venous catheter exit-site infections. CANNT J 2008;18:26–35.

[30] Koç O, Peynircioğlu B, Çil BE. Role of culturing from the tip and the tunneled segment of the catheters in tunneled catheter infection. Diagn Inter Radio 2008;14:228–32.

[31] Powell S, Chan TY, Bhat R, Lam K, Narlawar RS, Cullen N, et al. A retrospective comparative study of tunneled haemodialysis catheters inserted through occluded or collateral veins versus conventional methods. Cardiovasc Interv Radio 2010;33:744–50. https://doi.org/10.1007/s00270-009-9703-7

[32] Power A, Duncan N, Singh SK, Brown W, Dalby E, Edwards C, et al. Sodium citrate versus heparin catheter locks for cuffed central venous catheters: a single-center randomized controlled trial. Am J Kidney Dis 2009;53:1034–41. https://doi.org/10.1053/j.ajkd.2009.01.259

[33] Power A, Singh S, Ashby D, Hamady M, Moser S, Gedroyc W, et al. Translumbar central venous catheters for long-term haemodialysis. Nephrol Dial Transpl 2010;25:1588–95. https://doi.org/10.1093/ndt/gfp683

[34] Power A, Hill P, Singh SK, Ashby D, Taube D, Duncan N. Comparison of Tesio and LifeCath twin permanent hemodialysis catheters: The VyTes randomized trial. J Vasc Access 2014;15:108–15. https://doi.org/10.5301/jva.5000202

[35] Şanal B, Nas Ö, Doğan N, Korkmaz M, Hacıkurt K, Yıldız A, et al. Safety and functionality of transhepatic hemodialysis catheters in chronic hemodialysis patients. Diagn Inter Radio 2016;22:560–5. https://doi.org/10.5152/dir.2016.16043.he

[36] Silva JE, Costa T, Baptista A, Ramos A, Ponce P. Catheter-related bacteremia in hemodialysis: which preventive measures to take? Nephron - Clin Pr 2008;110:251–8. https://doi.org/10.1159/000167873

[37] Silva J, Antunes J, Carvalho T, Ponce P. Efficacy of preventing hemodialysis catheter infections with citrate lock. Hemodial Int 2012;16:545–52. https://doi.org/10.1111/j.1542-4758.2012.00691.x

[38] Škofic N, Buturović-Ponikvar J, Kovač J, Premru V, Knap B, Marn Pernat A, et al. Hemodialysis catheters with citrate locking in critically Ill patients with acute kidney injury treated with intermittent online hemofiltration or hemodialysis. Ther Apher Dial 2009;13:327–33. https://doi.org/10.1111/j.1744-9987.2009.00734.x

[39] Sofroniadou S, Revela I, Kouloubinis A, Makriniotou I, Zerbala S, Smirloglou D, et al. Ethanol combined with heparin as a locking solution for the prevention of catheter related blood stream infections in hemodialysis patients: a prospective randomized study. Hemodial Int 2017;21:498–506. https://doi.org/10.1111/hdi.12524

[40] Tacchini-Jacquier N, Verloo H. Point prevalence of complications between the Y connection technique and the usual care technique for blood restitution in patients of an outpatient hemodialysis unit: a comparison. Int J Nephrol Renov Dis 2017;10:159–66. https://doi.org/10.2147/IJNRD.S130738

[41] Weijmer MC, Vervloet MG, Ter Wee PM. Prospective follow-up of a novel design haemodialysis catheter; Lower infection rates and improved survival. Nephrol Dial Transpl 2008;23:977–83. https://doi.org/10.1093/ndt/gfm767

[42] Heidempergher M, Sabiu G, Orani MA, Tripepi G, Gallieni M. Targeting COVID-19 prevention in hemodialysis facilities is associated with a drastic reduction in central venous catheter-related infections. J Nephrol 2021;34:345. https://doi.org/10.1007/S40620-020-00900-3

[43] Porazko T, Stasiak E, Klinger M. The Impact of the Introduction of Innovative REDS Scale for the Evaluation of Central Tunnelled Catheter (CTC) exit site on infection prevention in long-term haemodialyzed patients. Front Surg 2021;8:629367. https://doi.org/10.3389/FSURG.2021.629367

[44] Porazko T, Piersiak A, Klinger M. The efficacy of single suture for exit site wound closure and stabilization of hemodialysis central tunneled catheter. 205031212110198 SAGE Open Med 2021;9. https://doi.org/10.1177/20503121211019889

[45] Al-hwiesh AK. Tunneled catheter-antibiotic lock therapy for prevention of dialysis catheter-related infections: a single center experience. Saudi J Kidney Dis Transpl 2008;19:593–602.

[46] Chen CH, Chen YM, Yang Y, Chang YJ, Lin LJ, Yen HC. Re-evaluating the protective effect of hemodialysis catheter locking solutions in hemodialysis patients. J Clin Med 2019:8. https://doi.org/10.3390/JCM8030412

[47] Gupta S, Mallya SP, Bhat A, Baliga S. Microbiology of non-tunnelled catheter-related infections. J Clin Diagn Res 10. 2016. p. DC24–8. https://doi.org/10.7860/JCDR/2016/19058.8155

[48] Lai CH, Kan CD, Wu HY, Luo CY, Chao CM, Wen JS. Modified exchange technique for management of dysfunctional tunneled hemodialysis catheters in the presence of exit-site infection: a quality improvement report. Am J Kidney Dis 2009;53:112–20. https://doi.org/10.1053/j.ajkd.2008.08.024

[49] Wang J, Nguyen TA, Chin AI, Ross JL. Treatment of tunneled dialysis catheter malfunction: revision versus exchange. J Vasc Access 2016;17:328–32. https://doi.org/10.5301/jva.5000533

[50] Wathanavasin W, Phannajit J, Poosoonthornsri M, Lewsuwan S, Tanateerapong P, Chongthanakorn K, et al. A randomized controlled trial of comparative efficacy between sodium bicarbonate and heparin as a locking solution for tunneled central venous catheters among patients requiring maintenance hemodialysis. Can J Kidney Heal Dis 2021:8. https://doi.org/10.1177/20543581211046077

[51] Hughes K, Gardner A, Mc Ardle J. Audit of factors associated with the intactness of central venous cather exit site dressings. Ren Soc Austral J 2011;7:108–11.

[52] McArdle J, Wicking K, Smyth W, Gardner A. Haemodialysis central venous catheter exit site dressings in the tropics: a crossover randomised controlled trial. Wound Pr Res 2017;25:200.

[53] Bueloni TNV, Marchi D, Caetano C, de Souza Cavalcante R, Mendes Amaral ML, Ponce D. Cefazolin-gentamicin versus taurolidine-citrate for the prevention of infection in tunneled central catheters in hemodialysis patients: a quasi-experimental trial. Int J Infect Dis 2019;85:16–21. https://doi.org/10.1016/J.IJID.2019.05.017

[54] Campos RP, do Nascimento MM, Chula DC, Riella MC. Minocycline-EDTA lock solution prevents catheter-related bacteremia in hemodialysis. J Am Soc Nephrol 2011;22:1939–45. https://doi.org/10.1681/asn.2010121306

[55] Kaze FF, Ashuntantang G, Halle MP, Kengne A-P. Outcomes of non-tunneled non-cuffed hemodialysis catheters in patients on chronic hemodialysis in a resource limited sub-Saharan Africa setting. Ther Apher Dial 2014;18:455–60. https://doi.org/10.1111/1744-9987.12109

[56] Battistella M, Bhola C, Lok CE. Long-term follow-up of the Hemodialysis Infection Prevention with Polysporin Ointment (HIPPO) study: a quality improvement report. Am J Kidney Dis 2011;57:432–41. https://doi.org/10.1053/j.ajkd.2010.10.009

[57] Jaberi A, Hadziomerovic A, Toor SS, Galwa RP, Graham J, Thornhill RE, et al. Externalization of tunneled hemodialysis catheter in patients with tunnel or exit-site infections and limited access options. J Vasc Inter Radio 2014;25:561–6. https://doi.org/10.1016/j.jvir.2013.12.570

[58] MacRae JM, Dojcinovic I, Djurdjev O, Jung B, Shalansky S, Levin A, et al. Citrate 4% versus heparin and the reduction of thrombosis study (CHARTS). Clin J Am Soc Nephrol 2008;3:369–74. https://doi.org/10.2215/CJN.01760407

[59] Oliveira L, Graham J, Lok C, MacFarlane S, Zimmerman D. Risk factors for yeast superinfection in the treatment of suspected exit site infections: a case-control study. J Vasc Access 2008;9:35–8.

[60] Al-Solaiman Y, Estrada E, Allon M. The spectrum of infections in catheter-dependent hemodialysis patients. Clin J Am Soc Nephrol 2011;6:2247–52. https://doi.org/10.2215/CJN.03900411

[61] Evans EC, Hain D, Kear TM, Dork LA, Schrauf C. Hemodialysis catheter outcomes pilot study: no dressing coverage with prescribed showering. Nephrol Nurs J 2014;41:53–64. 72; quiz 65.

[62] Liu F, Heyka R, Navaneethan SD, Bennett S, McLennan G, Arrigain S, et al. Patency and complications of translumbar dialysis catheters. Semin Dial 2015;28:E41–7. https://doi.org/10.1111/sdi.12358

[63] Moran J, Sun S, Khababa I, Pedan A, Doss S, Schiller B. A randomized trial comparing gentamicin/citrate and heparin locks for central venous catheters in maintenance hemodialysis patients. Am J Kidney Dis 2012;59:102–7. https://doi.org/10.1053/j.ajkd.2011.08.031

[64] Onder AM, Chandar J, Billings A, Diaz R, Francoeur D, Abitbol C, et al. Chlorhexidine-based antiseptic solutions effectively reduce catheter-related bacteremia. Pedia Nephrol 2009;24:1741–7. https://doi.org/10.1007/s00467-009-1154-5

[65] Sychev D, Maya ID, Allon M. Clinical management of dialysis catheter-related bacteremia with concurrent exit site infection. Semin Dial 2011;24:239. https://doi.org/10.1111/J.1525-139X.2011.00869.X

[66] Zhang J, Burr RA, Sheth HS, Piraino B. Organism-specific bacteremia by hemodialysis access. Clin Nephrol 2016;86:141–6. https://doi.org/10.5414/CN108633

[67] Lok CE, Huber TS, Lee T, Shenoy S, Yevzlin AS, Abreo K, et al. KDOQI Clinical practice guideline for vascular access: 2019 Update. Am J Kidney Dis 2020;75:S1–164. https://doi.org/10.1053/j.ajkd.2019.12.001

[68] Jindal K, Chan C, Deziel C, Hirsch D, Soroka S, Tonelli M, et al. Hemodialysis clinical practice guidelines for the Canadian Society of Nephrology. J Am Soc Nephrol 2006;17:S1–27. https://doi.org/10.1681/ASN.2005121372

[69] s Choice - vascular access: 2018 clinical practice guidelines of the European Society for Vascular Surgery (ESVS). In: Schmidli J, Widmer MK, Basile C, de Donato G, Gallieni M, Gibbons CP, editors. Eur J Vasc Endovasc Surg, 55. 2018. p. 757–818. https://doi.org/10.1016/J.EJVS.2018.02.001

[70] O'Grady NP, Alexander M, Dellinger EP, Gerberding JL, Heard SO, Maki DG, et al. Guidelines for the prevention of intravascular catheter-related infections. Am J Infect Control 2002;30:476–89. https://doi.org/10.1067/mic.2002.129427

[71] Mermel LA, Allon M, Bouza E, Craven DE, Flynn P, O'Grady NP, et al. Clinical practice guidelines for the diagnosis and management of intravascular catheter-related infection: 2009 update by the Infectious Diseases Society of America. Clin Infect Dis 2009;49:1–45. https://doi.org/10.1086/599376

[72] Balas E, Boren S. Managing clinical knowledge for health care improvement. Yearb Med Inf 2000;1:65–70.

[73] Schuster MA, McGLYNN EA, Brook RH. How good is the quality of health care in the United States? 1998. Milbank Q 2005;83:843–95. https://doi.org/10.1111/J.1468-0009.2005.00403.X

[74] Elamin S, Khaier MEM, Kaballo BG, Abu-Aisha H. Low sensitivity of the exit site scoring system in detecting exit site infections in peritoneal dialysis patients. Clin Nephrol 2014;81:100–4. https://doi.org/10.5414/CN108179

[75] Rigo M, Pecoits-Filho R, Lambie M, Tuon FF, Barretti P, de Moraes TP. Clinical utility of a traditional score system for the evaluation of the peritoneal dialysis exit-site infection in a national multicentric cohort study. Perit Dial Int 2021;41:292–7. https://doi.org/10.1177/0896860820949032