ORIGINAL ARTICLE

UDC: 616.61-08-06
https://doi.org/10.2298/VSP160205332K

Risk factors for catheter-related infections in patients on hemodialysis

Faktori rizika od nastanka infekcija povezanih sa kateterom kod bolesnika na hemodijalizi

Violeta Knežević*, Tatjana Djurdjević Mirković*, Dušan Božić*, Gordana Stražmešter Majstorović*, Igor Mitić*, Ljiljana Gvozdenović†

Clinical Center of Vojvodina, *Clinic for Nephrology and Clinical Immunology, †Clinic for Anesthesiology and Intensive Care, Novi Sad, Serbia

Abstract

Background/Aim. Catheter-related infections are a significant morbidity and mortality cause in patients on hemodialysis. The objective of this study was to determine the incidence, to analyze risk factors and to identify etiological causes of catheter-related infections in these patients. **Methods**. The study was carried out at the Clinic for Nephrology and Clinical Immunology of the Clinical Centre of Vojvodina, from August, 2012 to May, 2015. One hundred and thirteen patients on chronic hemodialysis participated in the study. The risk factors of catheter-related infections in the infected patients were to those in the control group, as follows: demographic and laboratory parameters, co-morbidities and the use of immunosuppressive therapy, the length of hemodialysis treatment, urgent catheter placement, the position and placement difficulties, the number of insertions and catheter maneuvering, the existence of permanent vascular access in maturation or without a vascular access in the course of catheter positioning, catheter life, surgical procedures (≤ 30 days from catheter placing), the length of hospitalization and isolated infection causes. **Results**. One hundred and ninety-seven catheters were placed in 113 patients, among which 182 of them temporary. The total number of catheter days was 17.842, the incidence of infections was 3.53/1,000 catheter days. During the monitoring period, 63 catheter-related infections were diagnosed, 54 (85.7%) with temporary and 9 (14.3%) with permanent catheters. Multivariate logistic regression analysis (with border values/levels determined by receiver operating characteristic – ROC analysis) determined independent predictors of catheter-related infections in the following order: hemoglobin levels < 95 g/l ($p < 0.001$) and albumin levels < 33 g/l ($p = 0.041$), catheter duration of > 90 days ($p = 0.004$), > 2/day catheter maneuvering ($p = 0.011$) and the duration of hospitalization of > 15 days ($p = 0.003$). The main pathogen was *Staphylococcus spp.* Coagulase negative. **Conclusion**. Intensifying of prevention measures and infection control would significantly reduce the frequency of catheter-related infections and the number of hospitalizations. The timely creation of a native arteriovenous fistula would decrease the use of hemodialysis catheters.

Key words:
renal dialysis; catheter-related infections; risk factors.

Apstrakt

Uvod/Cilj. Infekcije povezane sa kateterom i dalje predstavljaju značajan uzrok morbiditeta i mortaliteta kod bolesnika na hemodijalizi. Cilj ovog ispitivanja je bio da se utvrdi incidencija, analiziraju faktori rizika i identifikuju etiološki uzročnici kateter infekcija kod ovih bolesnika. **Metode.** Ispitivanje je sprovedeno na Klinici za nefrologiju i kliničku imunologiju Kliničkog centra Vojvodine u periodu od avgusta 2012. do maja 2015. godine. Ispitivanjem je bilo obuhvaćeno 113 bolesnika lečenih hroničnim hemodijalizama. Upoređivani su faktori rizika od infekcija povezanih sa kateterom kod bolesnika sa dokazanom infekcijom u odnosu na kontrolnu grupu. Analizirani su demografski i laboratorijski parametri, komorbiditeti i upotreba imunosupresivne terapije, dužina dijaliziranja, urgentno plasiranje, pozicija i otežano plasiranje katetera, broj mesta insercije i manipulacija kateterom, postojanje trajnog vaskularnog pristupa u maturaciji ili bez vaskularnog pristupa tokom plasiranja katetera, dužina trajanja katetera, hiruške intervencije (≤ 30 dana od plasiranog katetera), dužina hospitalizacije i izolovani uzročnici infekcija. **Rezultati**. Kod 113 bolesnika plasirano je 197 katetera, od kojih su 182 bila privremena. Ukupni broj dana katetera iznosio je 17,842, a incidencija infekcija je bila 3.53 slučajeva na 1,000 kateter dana. Tokom perioda praćenja potvrđene su 63 kateter-povezane infekcije, 54 (85.7%) privremenih i 9 (14.3%) trajnih katetera. Multivarijantnom logističkom regresionom analizom (granične vrednosti određene *receiver operating curve* – ROC analizom), kao nezavisni prediktori kateter-povezanih infekcija dobijeni su: vrednost hemoglobina < 95 g/l ($p < 0.001$) i albumina <

Correspondence to: Violeta Knežević, Clinical Center of Vojvodina, Clinic for Nephrology and Clinical Immunology, Hajduk Veljkova 1–7, 21 000 Novi Sad, Serbia. E-mail: vknezevic021@gmail.com

33g/l (p = 0.041), trajanje katetera > 90 dana (p = 0.004), > 2/dan manipulacije kateterom (p = 0.011) i trajanje hospitalizacije > 15 dana (p = 0.003). Najčešći uzročnik je bio *Staphylococcus spp.* koagulaza negativan. **Zaključak**. Intenziviranje mera prevencije i kontrole infekcija bi znatno smanjilo učestalost kateter-povezanih infekcija i broj hospitalizacija. Pravovremeno kreiranje nativne arteriovenske fistule smanjilo bi upotrebu dijaliznih katetera.

Ključne reči:
bubreg, dijaliza; kateter, povezane infekcije; faktori rizika.

Introduction

The number of patients at the end-stage of renal disease in the need of renal replacement therapy is rising in Europe and the world [1]. At the end of 2013, 5,775 patients were on renal replacement therapy, and the majority of them was on hemodialysis – 4,480 [2]. The quality of life and survival expectancy of those patients depend on the duration of functional vascular approaches (VA) [3]. Since the artery-vein fistula (AVF), which was depicted back in 1966 by Braescia and Cimino, has the longest survival rate and the least complication frequency, it should, whenever it is possible, be the first choice for VA [1]. Hemodialysis catheters are used for quick establishing of an adequate VA, when urgent hemodialysis is indicated in time of maturation of AVF and in patients in whom all other VA have been exhausted [1, 4]. Despite the priorities of AVF, nearly 80% of those patients start treatment with the dialysis catheters [3]. The previous papers have shown that VA is the major risk factor for the infection occurrence in the patients undergone hemodialyses. It is concluded that they suffer from a lesser risk of infections with AVF and artery-venous graft (AVG), and from a greater risk with temporary or permanent catheters [5]. The frequency of catheter-related infections ranges from 1.0 to 5.5 episodes in 1,000 catheter days [6–8]. In relation to the patients with the permanent VA, the ones who are dialyzed via catheters are hospitalized two to three times more due to infections [9]. The catheter infections cause a significant morbidity rate as well as the mortality increase for more than 50% in relation to the patients with the native AVF [10]. Besides, metastatic infections are present in 5% to 10% of patients with catheter sepsis in the form of osteomyelitis, endocarditis, septic arthritis and epidural abscess [11]. The risk infection factors related to catheters are the make and the position of catheters, and those related to patients are comorbidities, patients' hygienic conditions [12]. The most frequent etiological culprits of infections are gram-positive microorganisms, although bacteremia can be caused by gram-negative microorganisms as well. These patients are at risk of infections caused by hospital multi-resistant cultures that are less susceptible to many antibiotics [13]. The isolation of etiological agent and determining of antibacterial susceptibility profile are important to obtain a better prognosis [14].

The objective of this research was to determine the incidence rate, to analyze risk factors and to identify etiological causes of catheter-related infections in patients on chronic dialysis.

Methods

The research was conducted retrospectively at the Clinic for Nephrology and Clinical Immunology of the Clinical Centre of Vojvodina from Aug, 2012 to May, 2015. It included 113 hospitalized patients over 18 years of age on chronic dialysis treated for 4 hours, three times a week. The kind of dialysis was bicarbonate on polysulphate capillary membrane of the surface of 1.1 to 1.3 m^2, blood flow of 250–300 mL/min. The research involved the patients who had undergone an urgent temporary catheter placement (with or without AVF) in order to start an active treatment for renal insufficiency and the patients with replaced or permanent catheters due to maturation or loss of the existing permanent vascular access fistula and graft (AVF, AVG). The patients who were excluded from the research are: the patients with acute renal insufficiency, the patients from other hemodialysis centres temporarily dialyzed at our centre, the ones who started dialysis at home, the ones transferred from peritoneum dialysis to hemodialysis as well as transplant patients with no graft.

The risk factors for catheter-related infections were compared between the examined group and the control group of patients with no infections in the course of the research period. Since several patients had more infections on different catheter positions, every new infection of the placed catheter was analyzed. If one catheter in the course of the same hospitalization caused several infections, only the first infection entered the statistical data. Some patients had a temporary catheter placed for a longer period due to inability of permanent vascular placement (VP), and in such cases, the duration of temporary and permanent catheters was determined. Defining of urgently placed catheters meant quick solving of vascular access from vital indications in the patients with or without AVF/AVG in maturation. Placing difficulties caused swelling and hematomas or bleeding at the spot of catheter placement.

The following was analyzed: demographical and laboratory parameters, comorbidities, the use of immunosuppressive therapy, the length of dialyzing, urgent placing, the position and difficulty positioning, the number of insertion spots as well as catheter maneuvering, the existence of permanent vascular access in maturation or without vascular access during catheter placement, the length of catheter use, surgical procedures (≤ 30 days of catheter placement), the duration of hospitalization and the isolated infection causes.

Temporary catheters with two lumens were placed by an anesthesiologist by a modified Seldinger method, whereas the permanent ones were administered by vascular surgeons who, after the placement, drew catheter subcutaneously, i.e. tunneled it along the anterior rib cage wall using the aseptic technique [15]. After placing a non-tunneled catheter, prior turning it on, 10 mL of blood was aspirated from every rod, then every lumen was widened with 10 mL of 0.9% NaCl. In

tunneled catheters, the procedure was the same, only the widening of the catheter was 40 ml 0,9% NaCl (especially in femoral catheters which are longer). At the end of dialysis, after turning off, the procedure was repeated, and then the catheter lumens were aseptically locked with heparin. While determining the heparin volume, the values prescribed by producers and inscribed at every catheter lumens were carefully taken into account. Then, the exit was cleaned by benzine, Codane (uncolored alcohol solution) and Octanisept (Octenidine tenoxi ethanol) along with bandaging.

In the monitored period, all places of catheter insertion were checked, the swabs of the exit place and blood cultures were examined. Every time when infection was suspected, 3 sets of 7–10 mL of blood cultures were taken by vein puncture and from the lumens of dialytic catheters. Himedia Hi-Combi Dual Performance Medium HiSafe Blood Culturing System 40 mL was used for hemocultures. They were processed by standard laboratory technique and with the help of BacT/Alert 3D (Bact/Alert, bioMerienx, Marcy l Etoile France) of the automatic system for continual monitoring of hemocultures. After aseptic catheter removal, the tip of catheter of 5 cm was processed in a sterile lab container by standard microbiological method.

The diagnosis of catheter-related infections was defined by at least one blood culture and the culture from the catheter tip with the same pathogen along with clinical manifestations of the infection with no evidence of the other infection source [16].

If it was a bacteria that makes normal skin flora (*Staphylococcus spp*. Coagulase negative, etc.), the infection was included in the research only when the same microorganism was isolated in two blood cultures along with clinical manifestation of infection [17]. Demographic and laboratory data were collected along with medical documentation of the Clinic for Nephrology and Clinical Immunology. The following laboratory parameters were analyzed: hemoglobin, iron, ferritin, albumin, calcium and phosphorus. The analyses (Hg, Erci and Het) were done on the BECKMAN COULTER machine by HmX method impendence and flow citometry. The serum concentrations of calcium and phosphorus were processed by photometric method. Albumin serum was determined by a photometric color test on the OLYMPUS analyzer by using Beckman Coulter kits (Ireland). Iron levels and ferritin were processed on the Architech c8000 analyzer by Abbott company with commercial sets of the same company (Wiesbaden, Germany). Ferritin leves were obtained by the immunoturbimetric method, while iron by the colometric method.

In the course of this analysis, numerical data were shown by the mean value, standard deviation and median, whereas descriptive variables by absolute and relative numbers. The following statistical methods were used: χ^2, *t*-test, Mann-Whitney U test, receiver operating characteristic (ROC) analysis and multivariate logistic regression analysis.

Results

One hundred and ninety-seven catheters were placed in 113 patients, 182 of which were temporary. The total number of catheters was 17,842, with the infection incidence of 3.53 cases in 1,000 catheter days (the number of days of temporary ones was 14,521, and of permanent ones was 3,321, with the infection incidence of 3.72 and 2.71 cases in 1,000 catheter days). In the course of the monitoring period, 63 catheter-related infections were diagnosed, 54 (85.7%) temporary and 9 (14.3%) permanent catheters. Thirty-five patients (19.2%) had one infection, while 19 (10.4%) two or more infections. Nine (60%) patients using permanent catheters had two or more infections. During the monitoring period, 9 patients had their temporary catheters replaced by permanent ones, 3 patients had two permanent catheters grafted. Univariate analysis of catheter-related infection risk factors showed that the infection catheter group in relation to the control group had statistically significantly lower levels of hemoglobin, iron, albumin ($p < 0.005$): longer period of dialyzing, higher mean value of catheter duration (median 85:79), more insertion spots, a greater number of catheter maneuvering and a bigger number of hospital days (Tables 1 and 2). Multivariate logistic regression analysis (forward conditional model) of univariate significant risk factors for infection occurrence (border values determined by ROC analysis), as independent predictors of catheter-related infections, were singled out as follows: hemoglobin levels < 95 g/L ($p < 0.001$), albumin levels < 33g/L ($p = 0.041$), catheter life of > 90 days ($p = 0.004$), > 2/day catheter maneuvering ($p = 0.011$) and the length of hospitalization of > 15 days ($p = 0.003$) (Table 3).

Table 4 shows isolated causes of catheter infections. Gram-positive microorganisms were isolated in 55 (87,3%) patients. The most common pathogen was Coagulase-negative staphylococci 42.8%, then *Staphylococcus aureus* 31.7%, *Enterococcus faecalis* 7.9%, *Enterococcus spp*. 3.2% and *Enterococcus faecium* 1.6%. Gram negative (*Proteus mirabilis* and *Klebsiela pneumonia* 2%) and polymicrobic microorganisms were isolated in 6.3% patients.

Discussion

Catheter-related infections and sepsis are linked to a high morbidity rate and hospitalization, high treatment costs and a poor survival rate [17]. The previous studies dealt with diverse numerous risk factors related to catheter infections. According to literature, the use of central venous catheter, the most frequent risk factors for catheter-related infections in hemodialytic patients were: female gender, diabetes, anemia, hipoalbuminemia, urgent catheter placing, inadequate hygiene of hands prior catheter maneuvering and previous hospitalization [7, 18–20]. The infection incidence in our study was 3.53 cases in 1,000 catheter days (temporary 3.72; permanent 2.71 cases in 1,000 catheter days), similar to the results of certain previous studies [6, 7, 21].

The patients of both groups were of average age > 60 and did not differ in age in relation to catheter-related infections, which was confirmed by some studies opposed to the study by Murea et al. [22] in which the patients aged 75 had 60% less frequent infections [22–24]. However, our patients diagnosed with infection suffered from a significantly higher

Table 1

Risk factors with dialysis catheter infections (univariate analysis)

Risk factors	Catheter infections n = 63	No catheter infections n = 134	*p*
Gender (M/F), n/n	24/21	48/20	0.095
Age (years), $\bar{x} \pm SD$	63.4 ± 12.7	63.1±10.04	0.912
< 65, n (%)	34 (31.5)	74 (68.5)	
65–75, n (%)	12 (26.1)	34 (73.9)	0.392
≥ 75, n (%)	17 (39.5)	26 (60.5)	
DD (months), $\bar{x} \pm SD$	43.0 ± 44.6	23.4 ± 26.1	0.004*
Co-morbidities, n (%)			
hypertension	58 (92.1)	120 (89.6)	0.766
coronary disease	7 (11.1)	22 (16.4)	0.444
cardiomyopathy	43 (68.3)	79 (59.0)	0.273
acute brain stroke	14 (22.2)	18 (13.4)	0.176
diabetes mellitus	28 (44.4)	50 (37.3)	0.425
DSD	32 (50.8)	58 (43.3)	0.405
PAOD	6 (9.5)	6 (4.5)	0.288
HOPD	3 (4.8)	7 (5.2)	0.597
malignant disease	1 (1.6)	11 (8.2)	0.059
Hemoglobin (g/L), $\bar{x} \pm SD$	93.1 ± 9.1	106.2 ± 10.5	< 0.001*
Iron (µg/L), $\bar{x} \pm SD$	9.5 ± 5.9	11.2 ± 6.1	0.026*
Ferritin (µg/L), $\bar{x} \pm SD$	742 ± 594	668 ± 605	0.211
Calcium (mmol/L), $\bar{x} \pm SD$	2.21 ± 0.23	2.27 ± 0.21	0.055
Phosphorus (mmol/L), $\bar{x} \pm SD$	1.83 ± 1.37	1.77 ± 0.41	0.328
Albumin (g/L), $\bar{x} \pm SD$	32.4 ± 5.8	35.8 ± 5.4	< 0.001*

DD – dialysis duration; DSD – digestive system diseases ; PAOD-peripheral artery occlusive disease; HOPD – chronic obstructive pulmonary disease; M/F – male/female; *$p < 0.05$.
$\bar{x}$ – mean; SD – standard deviation; n (%) – number (percentage) of patients.

Table 2

The risk factors in dialysis catheter infections (univariate analysis)

Risk factors	Catheter infections n = 63	No catheter infections n = 134	*p*
Position of temporary/permanent catheter, n/n			
v. jugularis	35/5	93/2	0.201/0.174
v. subclavia	10/2	25/4	
v. femoralis	9/2	10/0	
Catheter duration (days), $\bar{x} \pm SD$	120.8 ± 98.0	77.3 ± 74.0	
< 30, n (%)	11 (22.9)	37 (77.1)	
30–90, n (%)	24 (27.3)	64 (72.7)	0.017*
> 90, n (%)	28 (45.9)	33 (54.1)	
Number of catheter insertions			
1, n (%)	38 (33.9)	74 (66.1)	
2, n (%)	6 (15.8)	32 (84.2)	
≥ 3, n (%)	19 (40.4)	28 (59.6)	
Urgent catheter placement , n (%)	19 (30.2)	55 (41.0)	0.189
AVF[a] , n (%)	26 (26.0)	74 (74.0)	
AVG[a] , n (%)	3 (25.0)	9 (75.0)	
No access[b] n (%)	34 (40.0)	51 (60.0)	
Catheter maneuvering difficulties, n (%)	13 (20.6)	13 (9.7)	0.059
Catheter maneuvering ≥ 3/days, n (%)	14 (22.2)	14 (10.4)	0.026*
Surgical procedures, n (%)	25 (39.7)	46 (34.3)	0.283
Length of hospitalization, (days) $\bar{x} \pm SD$	34.62 ± 33.7	23.37 ± 25.2	0.010*
Immunosuppressive therapy, n (%)	0 (0.0)	7 (5.2)	0.064

AVF – arteriovenous fistula; AVG-arteriovenous graft; [a] Permanent vascular access in maturation; [b] No permanent vascular access or the loss of it; *$p < 0.05$.
$\bar{x}$ – mean; SD – standard deviation; n (%) – number (percentage) of patients.

Table 3

Risk factors with dialysis catheter infections (multivariate analysis)

Risk factors	Beta	SD	*p*	OR
Hemoglobin < 95 g/L	2.505	0.410	< 0.001	12.2
Albumin < 33 g/L	0.808	0.395	0.041	2.2
Catheter duration > 90 days	1.188	0.418	0.004	3.3
Catheter maneuvering > 2/day	1.403	0.551	0.011	4.1
Hospitalization duration > 15 days	1.177	0.402	0.003	3.2
Model constant	-3.683	0.526	< 0.001	0.02

SD – standard deviation; *p* – probability; OR – odds ratio.

Tabela 4

Frequency of isolated pathogens

Pathogen	n (%)
Gram positive microorganisms	55 (87.3)
Staphylococcus species Coagulase-negative	27 (42.8)
Staphylococcus aureus	20 (31.7)
Enterococcus faecalis	5 (7.9)
Enterococcus species	2 (3.2)
Enterococcus faecium	1 (1.6)
Gram negative microorganisms	4 (6.3)
Proteus mirabilis	2 (3.2)
Klebsiela pneumoniae	2 (3.2)
Polymicrobic flora	4 (6.3)

medium length of hospitalization, which can be explained by exhaustion of permanent vascular approaches along with a more frequent need to replace temporary catheters and eventually the need to replace them with permanent ones. The frequency of the monitored stages and disorders was similar to other developed countries [25]. The patients of the advanced age have complex changes of the immune system and very often conjoint chronic diseases such as systemic hypertension and diabetes [26]. Grothe et al. [27] have shown that diabetic and hypertonic patients have 22% more chances to develop catheter infection. Since it is well-known that diabetes leads to impaired immune system and in combination with immunosuppressive uremia, it can lead to a higher risk of bacteremia; the link between diabetes and catheter infections is confirmed in certain studies [7, 27]. While some authors highlight that simultaneous renal insufficiency and surgical procedure, hematological malignancies, neutropenia that lasts longer than 8 days and presence of coalesced immunodeficiency have a role in infection development, some others did not validate this connection [23, 28]. In our study, we did not link comorbid states and the use of immunosuppressive therapy with dialytic catheter infections, as opposed to significantly lower values of hemoglobin, iron and albumin in relation to the control group of patients, which corresponds with previous study results [7, 14, 20]. The lower hemoglobin levels can be related to the risk of iron overload, which increases the colonization of bacteria and weakens the phagocyte function [29]. Hypoalbuminemia is frequent in dialytic patients due to malnutrition and it contributes to the occurrence of bacterial infection [30]. Lukowsky et al. [31] have shown that one third of deaths in the first 90 days of hemodialysis was related to hypoalbuminemia < 35 g/l. Multivariate analysis showed that the albumin levels of < 33 g/L and hemoglobin levels of < 95 g/L are significantly independent predictors of temporary catheter infection, which refers to a compulsory hypoalbuminemia and anemia correction in order to decrease infections. We have not found the difference between the patients with or without catheter infection in relation to ferritin values, which corresponds with the study results in which the infections of temporary and permanent vascular approaches were analyzed [7, 21].

In terms of the planned VA treating, the risk of catheter-related bacterial infections increases 2.21 times in urgent cases when it is necessary to place or replace a catheter within 24 hours [20]. In 37.6% of catheters that were urgently placed (with or without AVF/AVG in maturation), we did not diagnosed significantly more infections, which is a slightly lower percentage in relation to the same results of other studies [14, 32, 33].

According to the literature data, the most widespread position of temporary catheters is in interior jugularis vein, which is shown in both groups of our patients [14, 34]. Although vascular access societies and the European Best Practice Guidelines (EBPG) for hemodialysis advise on using the right jugularis vein as the way to place tunneled vascular catheters, the most widespread of these catheters in our infected patients was the jugularis vein, as opposed to subclavia vein in the control group [35]. It was not established that the catheter position was a significant risk factor for temporary or permanent catheter-related infections. In earlier studies, the greatest frequency of infections was with temporary femoral catheters, followed by jugularis then the access under clavicle. According to Caylan et al. [20] the position of temporary catheters in femoral vein creates 2.14 times bigger risk for catheter-related infections occurrence. However, the results of recent studies do not link the insertion spot of temporary and permanent catheters to a higher risk of infections [36–38].

Other analyzed risk factors include, according to univariate analysis, a greater number of insertion spots and frequent catheter maneuvers. Catheter maneuvering > 2/day was established by multivariate analysis, creates 4.1 times bigger risk of catheter-related infection occurrence. Caylan et al. [20] concluded that inadequate hygiene of hands immediately before catheter maneuvering created higher risk that maneuvering itself ≥ 3/day. Catheter placing difficulty was not a significant factor for catheter infections in our patients, which was shown by Gauna et al. [14]. During hospitalization of the catheter placed patients, we have not found that a permanent VP in maturation or its loss influenced infection occurrence. A big comprehensive recent analysis has shown that starting catheter dialysis long before AVF predicts, that a continual use of catheter as a dialytic access during one year increasea a infection risk. Over 13% of all patients had at least one positive blood culture in the first year of starting dialysis, and the risk infection was 3 times higher in the patients with catheter in relation to AVF [39].

The use of vascular catheters in Serbia is smaller the one in Dialysis Outcomes anal Practice Patterns Study

(DOPPS) countries, where they are used as a permanent access in 4–18% patients, if we exclude Japan with 1% of the patients, although it is bigger than those recommended by the Vascular Access Society and European Guide [35, 40]. The explanation was similar to the findings from previous years: permanent catheters are positioned in a small number of reference centres, procurement discontinuity, the existence of patients with exhausted vascular access, numerous comorbidities and a short survival expectancy period [2]. In relation to the above mentioned, it is not unexpected that infection occurs in cases of significantly shorter catheter use in comparison to the control group, which is depicted in most studies, except for one where no statistical significance was found [5–7, 41, 42]. Fram et al. [19] analyzed the duration of temporary and permanent vascular access by using three periods (0–30, 30–180, > 180 days) and concluded that the infection incidence is significantly higher up to 30 days, which highlights the need to careful implementation of prevention measures in the course of catheter positioning [19]. Napalkov et al. [43] showed that most infections caused by temporary catheters occurred in the first 90 days, notably, that the incidence rate was 5.1/1,000 catheter days, and that the infection risk was higher up to 6 months from catheter positioning, which leads to a conclusion that catheter treatment should be intensified in the mentioned period. It was concluded by multivariate analysis that in the period of > 90 days, the risk of infection is 3.3 times higher, but the sample of permanent catheters in our patients was relatively small and some temporary catheters were used as permanent vascular access. According to the valid recommendations, catheters should not be changed in order to prevent infections, but it is necessary to decrease their use by ensuring matured AVF. Besides a smaller infection risk, we are fully aware of other advantages of permanent catheters in relation to temporary ones. Permanent catheters are better than temporary ones even in intensive care units if catheter is expected to stay longer than 3 weeks [44].

The implementation of immunosuppressive therapy and surgical interventions (≤ 30 days from catheter positioning), were not related to infections in our patients, which corresponds with the results of two other studies [14, 20].

The duration of hospitalization was a significant risk factor for the occurrence of infections in our patients, notably the infection risk increased 3.2 times in the period of hospitalization of > 15 days. The previously mentioned risk factor for dialytic catheter infections was confirmed in certain studies [42, 45–47].

Most infections were a result of gram positive microorganisms (87.3%), which is confirmed by most studies, although the presence was from 33% to 72.8% [7, 8, 19–21]. Two most common isolated gram-positive pathogens were *Staphylococcus Spp*. Coagulase negative and *Staphylococcus aureus*, which was not surprising considering that both of them have skin origin. The sum data from 1992 to 1999 indicate that *Staphylococcus Spp*. Coagulase negative is the most isolated pathogen for hospital-catheter-related infections (37%), followed by (13.5%) [48]. In comparison to more recent studies, the most common isolated pathogens were *Staphylococcus aureus* and *Staphylococcus epidermis* [5, 7–9, 13, 14]. In our patients, *Staphylococcus* was isolated in (31.7%) cases after *Staphylococcus spp*. Coagulase negative (42.8%), and according to the percentage of incidence, it corresponds with the results of most studies [7, 19–21]. Isolated *Staphylococcus aureus* is potentially lethal, and the annual frequency of its incidence in dialysis patients is between 6 and 27% [49, 50]. Mokrzycki et al. [51] have shown that the infection of tunneled catheters caused by this pathogen causes more than 3 times higher risk of complications due to infection, as well as 4 times higher risk of recurrent bacterial infection or death within 3 months in relation to other pathogens. However, two studies have shown that *Staphylococcus aureus* is the most frequent gram positive microorganism, although the most present ones were gram-negative bacteria isolated from blood culture [14]. Gram-negative microorganisms were isolated in 26.9 (56%) cases, while fungus was less common [7, 8, 19–21]. The infections caused by gram-negative bacteria are difficult to treat due to high resistance and they can cause nosocomial infections and are frequently linked with high mortality rate [52]. Polymicrobial pathogens can be present in 9.5–11% of catheter-related bacterial infections [22]. In our study, a slightly lower percentage of gram-negative bacteria and polymicrobial pathogens were isolated (6.3%). This study had certain limitations that were typical in retrospective data collecting character. Since it is an intersection study, the data on VA patients that had been treated by chronic dialyses were not included.

Conclusion

The levels of hemoglobin of < 95g/L, and albumin of < 33 g/L, the duration of catheter treatment of > 90 days, > 2/day manipulations and the length of catheter hospitalization of > 15 days are independent predictors of catheter-related infections. Anemia correction, better nourishment, reduced rate of dialysis catheters by timely AVF introducing along with enhancing prevention measures and infection control recommended by official guidelines and adjusted to the conditions of hemodialysis unit by multidisciplinary team supervised by epidemiologists would significantly lower the frequency of catheter-related infections and the number of hospitalizations.

R E F E R E N C E S

1. *Pantelias K, Grapsa E.* Vascular access today. World J Nephrol 2012; 1(3): 69−78.
2. *Serbian Nephrologist Association.* Annual report on dialysis and kidney transplant treatments in Yugoslavia, 2010. Belgrade: Serbian Nephrologist Association; 2013.
3. *Xue H, Ix JH, Wang W, Brunelli SM, Lazarus M, Hakim R,* et al. Hemodialysis access usage patterns in the incident dialysis year and associated catheter-related complications. Am J Kidney Dis 2013; 61(1): 123−30.
4. *Wadelek J.* Haemodialysis catheters. Anestezjol Intens Ter 2010; 42(4): 213−7.
5. *Taylor G, Gravel D, Johnston L, Embil J, Holton D, Paton S.* Canadian Hospital Epidemiology Committee. Canadian Nosocomial Infection Surveillance Program. Prospective surveillance for primary bloodstream infections occurring in Canadian hemodialysis units. Infect Control Hosp Epidemiol 2002; 23(12): 716−20.
6. *Katneni R, Hedayati S.* Central venous catheter-related bacteriemia in chronic hemodialysis patients: Epidemiology and evidence-based management. Nat Clin Pract Nephrol 2007; 3(5): 256−66.
7. *Fysaraki M, Samonis G, Valachis A, Daphnis E, Karageorgopoulos DE, Falagas ME,* et al. Incidence, clinical, microbiological features and outcome of bloodstream infections in patients undergoing hemodialysis. Int J Med Sci 2013; 10(12): 1632−8.
8. *Saran AK, Sabry A, Alghareeb A, Molhem A. Central* Venous Catheter-Related Bacteremia in Chronic Hemodialysis Patients: Saudi Single Center Experience. Eur J Gen Med 2013; 10(4):208-213.
9. *Jaber BL.* Bacterial infections in hemodialysis patients: Pathogenesis and prevention. Kidney Int 2005; 67(6): 2508−19.
10. *Astor BC, Eustace JA, Powe NR, Klag MJ, Fink NE, Coresh J.* CHOICE Study. Type of vascular access and survival among incident hemodialysis patients: the Choices for Healthy Outcomes in Caring for ESRD (CHOICE) Study. J Am Soc Nephrol 2005; 16(5): 1449−55.
11. *Allon M.* Dialysis catheter-related bacteremia: treatment and prophylaxis. Am J Kidney Dis 2004; 44(5): 779−91.
12. *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 Plus 2010; 3(3): 234−46.
13. *Colville LA, Lee AH.* Retrospective analysis of catheter-related infections in a hemodialysis unit. Infect Control Hosp Epidemiol 2006; 27(9): 969−73.
14. *Gauna TT, Oshiro E, Luzio YC, Paniago AM, Pontes ER, Chang MR.* Bloodstream infection in patients with end-stage renal disease in a teaching hospital in central-western Brazil. Rev Soc Bras Med Trop 2013; 46(4): 426−32.
15. *Aydin Z, Gursu M, Uzun S, Karadag S, Tatli E, Sumnu A*, et al. Placement of hemodialysis catheters with a technical, functional, and anatomical viewpoint. Int J Nephrol 2012; 2012: 302826.
16. *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): 1−45.
17. *Saad TF.* Bacteremia associated with tunneled, cuffed hemodialysis catheters. Am J Kidney Dis 1999; 34(6): 1114−24.
18. *Nguyen DB, Lessa FC, Belflower R, Mu Y, Wise M, Nadle J*, et al. Invasive methicillin-resistant Staphylococcus aureus infections among patients on chronic dialysis in the United States, 2005-2011. Clin Infect Dis 2013; 57(10): 1393−400.
19. *Fram D, Okuno PF, Taminato M, Ponzio V, Manfredi SR, Grothe C*, et al. Risk factors for bloodstream infection in patients at a Brazilian hemodialysis center: A case-control study. BMC Infect Dis 2015; 15: 158.
20. *Caylan R, Yilmaz G, Sozen EE, Aydin K, Koksal I.* Incidence and risk factors for bloodstream infections stemming from temporary hemodialysis catheters. Turk J Med Sci 2010; 40(6): 835−41.
21. *Resić H, Ajanović S, Kukavica N, Ćorić A, Mašnić F, Bećiragić A.* Infections of tunnelized catheters in patients on hemodialysis: one clinic experience. Acta Med Croatica 2012; 66(Suppl 2): 17−21. (Croatian)
22. *Murea M, James KM, Russell GB, Byrum GV, Yates JE, Tuttle NS*, et al. Risk of Catheter-Related Bloodstream Infection in Elderly Patients on Hemodialysis. Clin J Am Soc Nephrol 2014; 9(4): 764−70.
23. *Taylor G, Gravel D, Johnston L, Embil J, Holton D, Paton S.* Canadian Nosocomial Infection Surveillance Program. Canadian Hospital Epidemiology Committee: Incidence of bloodstream infection in multicenter inception cohorts of hemodialysis patients. Am J Infect Control 2004; 32(3): 155−60.
24. *Sedlacek M, Gemery JM, Cheung AL, Bayer AS, Remillard BD.* Aspirin treatment is associated with a significantly decreased risk of Staphylococcus aureus bacteremia in hemodialysis patients with tunneled catheters. Am J Kidney Dis 2007; 49(3): 401−8.
25. DOPPS 2010. Dialysis Outcomes and Practice Patterns Study Program. Annual Report; 2010. Available from: www.dopps.org/ProgramHome/NewsPress.aspx
26. *Barros MB, Francisco PM, Zanchetta LM, César CL.* Trends in social and demographic inequalities in the prevalence of chronic diseases in Brazil. PNAD: 2003-2008. Cien Saude Colet 2011; 16(9): 3755−68. (Portuguese)
27. *Grothe C, da Belasco SA, de Bittencourt CA, Vianna LA, de Sesso CC, Barbosa DA.* Incidence of bloodstream infection among patients on hemodialysis by central venous catheter. Rev Lat Am Enfermagem 2010; 18(1): 73−80.
28. *Yilmaz G, Koksal I, Aydin K, Caylan R, Sucu N, Aksoy F.* Risk factors of catheter-related bloodstream infections in parenteral nutrition catheterization. JPEN J Parenter Enteral Nutr 2007; 31(4): 284−7.
29. *Boelaert JR, Daneels RF, Schurgers ML, Matthys EG, Gordts BZ, Van Landuyt HW.* Iron overload in haemodialysis patients increases the risk of bacteraemia: a prospective study. Nephrol Dial Transplant 1990; 5(2): 130−4.
30. *Cianciaruso B, Brunori G, Traverso G, Panarello G, Enia G, Strippoli P*, et al. Nutritional status in the elderly patient with uraemia. Nephrol Dial Transplant. 1995; 10 (Suppl 6): 65−8.
31. *Lukowsky LR, Kheifets L, Arah OA, Nissenson AR, Kalantar-Zadeh K.* Patterns and predictors of early mortality in incident hemodialysis patients: New insights. Am J Nephrol 2012; 35(6): 548−58.
32. *Souza RA, Oliveira EA, Silva JM, Lima EM.* Avaliação do acesso vascular para hemodiálise em crianças e adolescentes: um estudo de coorte retrospectivo de 10 anos. J Bras Nefrol 2011; 33: 422−30.
33. *Ethier J, Mendelssohn DC, Elder SJ, Hasegawa T, Akizawa T, Akiba T*, et al. Vascular access use and outcomes: An international perspective from the Dialysis Outcomes and Practice Patterns Study. Nephrol Dial Transplant 2008; 23(10): 3219−26.
34. *Jones SM, Ravani P, Hemmelgarn BR, Muruwe D, Macrae JM.* Morphometric and biological characterization of biofilm in tun-

neled hemodialysis catheters. Am J Kidney Dis 2011; 57(3): 449−55.
35. Vascular Access Society. 2013. Home Page, Guidelines, 10. Central venous access. Guidelines10.3. [cited 2013 Sep 10]. Available from: http://www.vascularaccesssociety.com
36. *Weijmer MC, Vervloet MG, Wee PM.* Prospective follow-up of a novel design haemodialysis catheter; lower infection rates and improved survival. Nephrol Dial Transplant 2008; 23(3): 977−83.
37. *Premužić V*, *Tomašević B*, *Eržen G*, *Makar K*, *Brunetta-Gavranić B*, *Francetić I*, et al. Temporary and permanent central venous catheters for hemodialysis. Acta Med Croatica 2014; 68(2): 167−74. (Croatian)
38. *Marik PE*, *Flemmer M*, *Harrison W*. The risk of catheter-related bloodstream infection with femoral venous catheters as compared to subclavian and internal jugular venous catheters: A systematic review of the literature and meta-analysis. Crit Care Med 2012; 40(8): 2479−85.
39. *Xue H, Ix JH, Wang W, Brunelli SM, Lazarus M, Hakim R,* et al. Hemodialysis access usage patterns in the incident dialysis year and associated catheter-related complications. Am J Kidney Dis 2013; 61(1): 123−30.
40. (FFCL) Dashboard (May 2015). Available from: http://esrdncc.org/wp-content/uploads/2015/08/FFCL-Dashboard-May2015.xlsx
41. *Lee T, Barker J, Allon M.* Tunneled cateters in hemodialysis patients, reason and subsequent outcomes. Am J Kidney Dis 2005; 46(3): 501−8.
42. *Samani S, Saffari M, Charkhchian M, Khaki A.* Incidence and risk factors of bloodstream catheter-related infections in hemodialysis patients. Comp Clin Pathol 2015; 24(2): 275−9.
43. *Napalkov P, Felici DM, Chu LK, Jacobs JR, Begelman SM.* Incidence of catheter-related complications in patients with central venous or hemodialysis catheters: A health care claims database analysis. BMC Cardiovasc Disord 2013; 13: 86.
44. III. NKF-K/DOQI Clinical Practice Guidelines for Vascular Access: update 2000. Am J Kidney Dis 2001; 37(1 Suppl 1): S137−81.
45. *Gonçalves EA, Andreoli MC, Watanabe R, Freitas MC, Pedrosa AC, Manfred SR,* et al. Effect of temporary catheter and later referral on hospitalization and mortality during the first year of hemodialysis treatment. Artf Organs 2004; 28(11): 1043−9.
46. *Engemann JJ, Friedman JY, Reed SD, Griffiths RI, Szczech LA, Kaye KS*, et al. Clinical outcomes and costs due to Staphylococcus Aureus bacteremia among patients receiving long-term hemodialysis. Infect control hosp. Epidemiol 2005; 26(6): 534−9..
47. *Mesiano ER, Merchan-Hamann E.* Bloodstream infections among patients using central venous catheters in intensive care units. Rev Lat Am Enfermagem 2007; 15(3): 453−9.
48. *Mermel LA.* Prevention of intravascular catheter-related infections. Ann Intern Med 2000; 132(5): 391−402.
49. *Danese MD, Griffiths RI, Dylan M, Yu HT, Dubois R, Nissenson AR.* Mortality differences among organisms causing septicemia in hemodialysis patients. Hemodial Int 2006; 10(1): 56−62.
50. *Nissenson AR, Dylan ML, Griffiths RI, Yu HT, Dean BB, Danese MD,* et al. Clinical and economic outcomes of Staphylococcus aureus septicemia in ESRD *patients receiving hemodialysis. Am J Kidney Dis 2005; 46(2): 301−8.*
51. *Mokrzycki MH, Zhang M, Cohen H, Golestaneh L, Laut JM, Rosenberg SO.* Tunnelled haemodialysis catheter bacteraemia: Risk factors for bacteraemia recurrence, infectious complications and mortality. Nephrol Dial Transplant 2006; 21(4): 1024−31.
52. *Al Mohajer M, Darouiche RO.* Sepsis syndrome, bloodstream infections and device-related infections. Med Clin N Am 2012; 96: 1203−23.

Received on February 5, 2016.
Accepted on June 13, 2016.
Online First November, 2016.