Journal of Indonesian Society for Vascular and Endovascular Surgery
Vol. 1, No. 2, June 2020
pISSN 2715-1204 - eISSN 2715-1239

Original Article

Catheter-Related Bloodstream Infection for End Stage Renal Disease Patients -Evaluation in the Era of Low Budget National Health Insurance Coverage in Indonesia-

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JINASVS 2020;1(2):30-35

Introduction: The use of central venous catheter (CVC) plays an essential role in patient care. The catheter-related bloodstream infection (CRBSI) is one of complications and associated with morbidity and mortality. In Indonesia, the national health coverage for single CVC procedure claim is only US$ 197-286. The aim of this study is to evaluate CRBSI number after subclavian and femoral non-tunnelled catheter insertion for urgent haemodialysis access.

Method: A retrospective study with the simple consecutive sampling was conducted. The inclusion criteria were adult and end stage renal disease (ESRD) patients required urgent haemodialysis access with infection on the site of insertion on the subclavian or femoral access. Exclusion criteria were artery catheter placement, pacing catheter, and another sources of previously infection was defined. Patients were divided into subclavian and femoral access group then we evaluate them retrospectively based on medical record data.

Results: Forty patients with 20 patients were subclavian inserted, and rest were femoral inserted. Infections rate was 7.84%. Demographic showed 55% was male (22/40) & age 51.8±14.3 years. Catheter duration in subclavian and femoral group were 47.7±34.2 and 36.7±18.4 days, respectively. Hospital stays in subclavian and femoral group were 9.9±6.4 and 9.3±7.2 days, respectively. From SIRS criteria, in subclavian group showed the heart rate, respiratory rate, body temperature and white blood cell (WBC) count were 90.1±7.8 x/min, 21.1±2.6 x/min, 37.4±0.8 °C, 15.5.0±7.0 $*10^3$/µL, respectively. For femoral group were 86.8±10.5 x/min, 21.6±4.0 x/min, 36.9±0.6 °C, 14.9±8.4 $*10^3$/µL, respectively. The *p*-values of them were 0.273, 0.612, 0.041, and 0.793 respectively. Eighty percent in subclavian group was first insertion, and for femoral group was 50% (p=0.047). In subclavian group was 10% (2/20) patients had more than three times insertion and femoral group was 25% (5/20) (p=0.225). Creatinine and ureum level in subclavian group were 9.4±5.8 and 155.5±83.6 mg/dL and for femoral group were 11.4±6.2 and 133.6±50.3 mg/dL (p=0.298 and 0.322, respectively). A 62.5% of all patients (25/40) was treated with third generation cephalosporin. The *p*-value for amount of intravenous antibiotic (single, double, triple) between subclavian and femoral group was 0.352. There was no blood culture taken for all patients. Sepsis and death as complication was 10% and 5% from all patients, respectively.

Conclusion: Prolonged use of central venous catheter more than 2 weeks and recurrent procedure were the cause of increasing incidence of CRBSI. Ultrasound guiding is needed to decrease complication. In a low budget system for national health insurance in Indonesia, a good strategy (pre-ESRD arteriovenous fistula, internal jugular vein access, nosocomial infection prevention, and rational antibiotic usage with a rational blood culture) need to be developed to prevent the infection of CRBSI.

Keywords: catheter, infection, prevention, health insurance, Indonesia.
https://doi.org/10.36864/jinasvs.2020.2.008

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INTRODUCTION

Catheter-related bloodstream infection (CRBSI) is defined as the presence of bacteria originating from intravenous catheters. CRBSI is the most common complication, high mortality and high cost of treating complications. Central venous catheter (CVC) insertion is benefit for intravenous fluids, taking blood samples, drugs, nutrition, and hemodynamic monitoring, including haemodialysis access for ESRD patients in emergency setting. CVC insertion has the greatest risk of infection compared to other measures. The CVC procedure is also a source of bacteremia and septicemia for patients in hospital.[1,2]

Infection due to CRBSI hospital treatment ranges from 10% - 20% in the United Kingdom (UK) and is associated with increased length of stay in ICU and mortality.[4] The incidence of CRBSI is related to the type of catheter, the duration of catheter placement and comorbid factors of the patient such as the type of disease and the severity of the disease. The risk of CRBSI occurs 64 times greater in CVC compared with intravenous peripheral catheters. For a short period of CVC (<10 days), which is the most common infection on the outer surface of the catheter and the best prevention of infection is to reduce exposure to extraluminal contamination. Whereas in the long term CVC (>10 days), endo-luminal infections are a source of infection. The incidence of dialysis associated with CRBSI is reported 2.5-5.5 cases per 1000 days or 0.9-2.0 per patient/year.[1-6]

The risk factors of CRBSI is the underlying disease, catheter insertion method, catheter placement, catheter duration and purpose. Other risk factors of CRBSI on dialysis are contamination from dialysis fluids or reuse of dialyzers, catheter duration, increased doses of recombinant erythropoietin used, low haemoglobin levels, low serum albumin, diabetes mellitus, peripheral atherosclerosis, and surgery. [1,3,5]

Several factors play a role in the pathogenesis of CRBSI. The mechanism of CRBSI can occur through 4 pathways, namely skin colonization of the catheter, colonization of the catheter lumen due to contamination, hematogenous spread of the catheter due to other sources of infection, and contamination due to fluid being inserted. Resistance to antibiotics due to the formation of biofilms also plays an important role in the emergence of bacteremia. When the blood culture obtained from the catheter is positive but the blood sample elsewhere is negative, it indicates the colonization of the catheter compared to CRBSI.[2,3,5]

In a study, 64% of the pathogens causing CRBSI were gram positive and 36% were gram negative. The most common pathogens that cause CRBSI are *S. aureus* 40%, *Pseudomonas aureginosa* 16%, negative coagulase *staphylococci* 8%, *E. coli* 8%, *Klebsiella pneumoniae* 8%, and *Acinetobacter baumanii* 4%. Based on Krishnan *et al*. gram-positive *cocci* were around 27% and gram-negative *bacilli* were 56%. Higher gram-negative amounts of CRBSI were reported in western hospitals. In the study of Almuneef *et al.* (2006) a total of 50 CRBSI, 48% were polymicrobial, 32% were due to gram-negative basics, and 10% were due to gram-positive organisms. The most common organisms found were 16% *Klebsiella pneumoniae*, 14% *staphylococci negative coagulase*, and 11% *Pseudomonas aureginosa*.[2,3,5].

METHOD

This was a retrospective study with a data collection from January to August 2019 in Wahidin Sudirohusodo Hospital, Makassar, Indonesia. The inclusion criteria were adult patients, diagnosed with

Table 1. Patients' characteristic

	Subclavian group n=20, n (%) or mean ± SD	Femoral group n=20, n (%) or mean ± SD	*p*-value
Demographic			
Age (years)	51.8 ± 14.3	50.8 ± 12.5	0.816
Male	15 (75)	7 (35)	0.025
Catheter duration (days)	47.7 ± 34.2	36.7 ± 18.4	0.211
Hospital stay (days)	9.9 ± 6.4	9.3 ± 7.2	0.781
Laboratory parameters			
Creatinine (mg/dL)	9.4 ± 5.8	11.4 ± 6.2	0.298
Ureum (mg/dL)	155.5 ± 83.6	133.6 ± 50.3	0.322
AST/SGOT (IU/L)	28.1 ± 26.1	76.4 ± 190.1	0.267
ALT/SGPT (IU/L)	33.8 ± 45.6	40.6 ± 73.6	0.724
Platelets ($10^3/\mu L$)	263.9 ± 94.6	286.3 ± 109.3	0.492
RBC ($10^6/\mu L$)	2.6 ± 0.4	2.8 ± 0.8	0.437
ESR (mm/hour)	-	-	-
CRP (mg/dL)	-	-	-
Comorbidities			
Hypertension	18 (90)	17 (85)	>0.995
Stroke	3 (15)	2 (10)	>0.995
Cardiovascular events	3 (15)	1 (5)	0.605
Lung disease	3 (15)	3 (15)	>0.995
Liver disease	0 (0)	0 (0)	n/a
Diabetes mellitus type 2	5 (25)	7 (35)	0.490
Smoking history	14 (70)	17 (85)	>0.995
Level of consciousness			n/a
GCS 13-15	20 (100)	20 (100)	
GCS 9-12	0 (0)	0 (0)	
GCS 3-8	0 (0)	0 (0)	

ESR, erythrocyte sedimentation rate; CRP, C-reactive protein; GCS, Glasgow Coma Scale

Table 2. Infection parameters, therapeutic, and complications

	Subclavian group n=20, n (%) or mean ± SD	Femoral group n=20, n (%) or mean ± SD	*p*-value
SIRS criteria			
Heart rate (x/min)	90.1 ± 7.8	86.8 ± 10.5	0.273
Respiratory rate (x/min)	21.1 ± 2.6	21.6 ± 4.0	0.612
Temperature (°C)	37.4 ± 0.8	36.9 ± 0.6	0.041
WBC (10^3/μL)	15.5 ± 7.0	14.9 ± 8.4	0.793
CVC insertions			
First time	16 (80)	10 (50)	0.047
Second time	2 (10)	5 (25)	0.225
Third time or more	2 (10)	5 (25)	0.225
Blood culture	0 (0)	0 (0)	n/a
Infiltrate in CXR post insertion	5 (25)	11 (55)	0.053
Antibiotic amounts			0.352
Monotherapy	17 (85)	14 (70)	
Double therapy	1 (5)	4 (20)	
Triple therapy	2 (10)	2 (10)	
Antibiotic regiment			>0.995
Cephalosporin first gen.	0 (0)	2 (10)	
Cephalosporin third gen.	14 (70)	11 (55)	
Carbapenem	2 (10)	1 (5)	
Vancomycin	1 (5)	0 (0)	
Others (penicillins, quinolones, macrolides)	3 (15)	6 (30)	
Complications			>0.995
Sepsis	3 (15)	1 (5)	
Multiple organ damages	0 (0)	0 (0)	
Pulmonary embolism	0 (0)	0 (0)	
Cerebrovascular events	0 (0)	0 (0)	
Death	1 (5)	1 (5)	

CXR, chest x-ray

ESRD who need urgency and/or emergency haemodialysis access, and infection at the CVC insertion point. Exclusion criteria were artery catheter placement, heart pacing catheter, and another sources of previously infection was defined. Patients were divided into subclavian and femoral access group then an evaluation was performed based on medical record data. The numerical data was presented in the mean and standard deviation (SD) for parametric data or median and range for non-parametric data, for categorical data was presented in number and frequency. The statistical evaluation for numerical data was performed with Student t-test and categorical data between two groups was evaluated with Chi-square test. A non-parametric data was evaluated with Mann-Whitney U test and Wilcoxon test. All data were analysed by SPSS 25 (IBM) with a statistically significance *p*-value <0.05.

RESULTS

From January to August 2019, there was 510 non-tunneled CVC insertions in total (63% was femoral access). CRBSI was found in 40 patients then divided into 20 insertions in subclavia and the rest were femoral. There was none in internal jugular vein. The infection rate for CRBSI in present study was 7.84%. The demographics showed 55% of the sample were male (22/40) and the average age was 51.8 ± 14.3 years. The duration of the catheter in subclavia and femoral was 47.7 ± 34.2, and 36.7 ± 18.4 days. The length of hospital stay in subclavia and femoral were 9.9 ± 6.4 and 9.3 ± 7.2 days. Based on the Systemic Inflammatory Response Syndrome (SIRS) criteria in the subclavian group, the heart rate, respiratory rate, temperature and number of white blood cells (WBC) were 90.1 ± 7.8 x / min, 21.1 ± 2.6 x / min, 37.4 ± 0.8 ° C, 15.5.0 ± 7.0 * 10^3/μL. In the femoral group were 86.8 ± 10.5 x / min, 21.6 ± 4.0 x / min, 36.9 ± 0.6 ° C, 14.9 ± 8.4 * 10^3/μL. The *p*-values in the group are 0.273, 0.612, 0.041, and 0.793. Eighty percent (80%) of the subclavian group was the first insertion and femoral was 50% (*p* = 0.047), Table I, II.

In the subclavian group 10% (2/20) insertion has been more than three times and in the femoral 25% (5/20) with a *p*-value of 0.225. The comorbidities accompanying when performed on femoral insertion were stroke 2 patients, 1 patient heart disease, 3 patients lung disease, no liver disorders and 7 type 2 diabetes mellitus patients. Whereas in subclavian group were 3 stroke patients, 3 heart problems, 3 lung disease, no liver disorders, and 5 type 2 diabetes mellitus patients. Hypertension was predominant in both groups, Table I, II.

The *p*-value for antibiotic use (single, double, triple) between the two groups was 0.352. Blood culture was not taken for all patients. Sepsis and death as complications were 10% and 5% of all patients, Table II.

Besides the WBC count, we evaluated also the AST (aspartate transaminase), ALT (alanine transaminase), differential WBC (neutrophils segment, lymphocytes, basophils, monocytes, and eosinophils). Unfortunately, ESR and CRP were not evaluated due to low budget health insurance system. The expense that covered by national health insurance system for a CVC operation was US$ 197 to 286. The median and range for differential WBC in all groups were basophils 0.2 (0-0.5); eosinophils 1.8 (0-7.1); neutrophils segment 82.7 (58.8-93.8); lymphocytes 9.1 (1.3-36.8); and monocytes 5.5 (0.7-

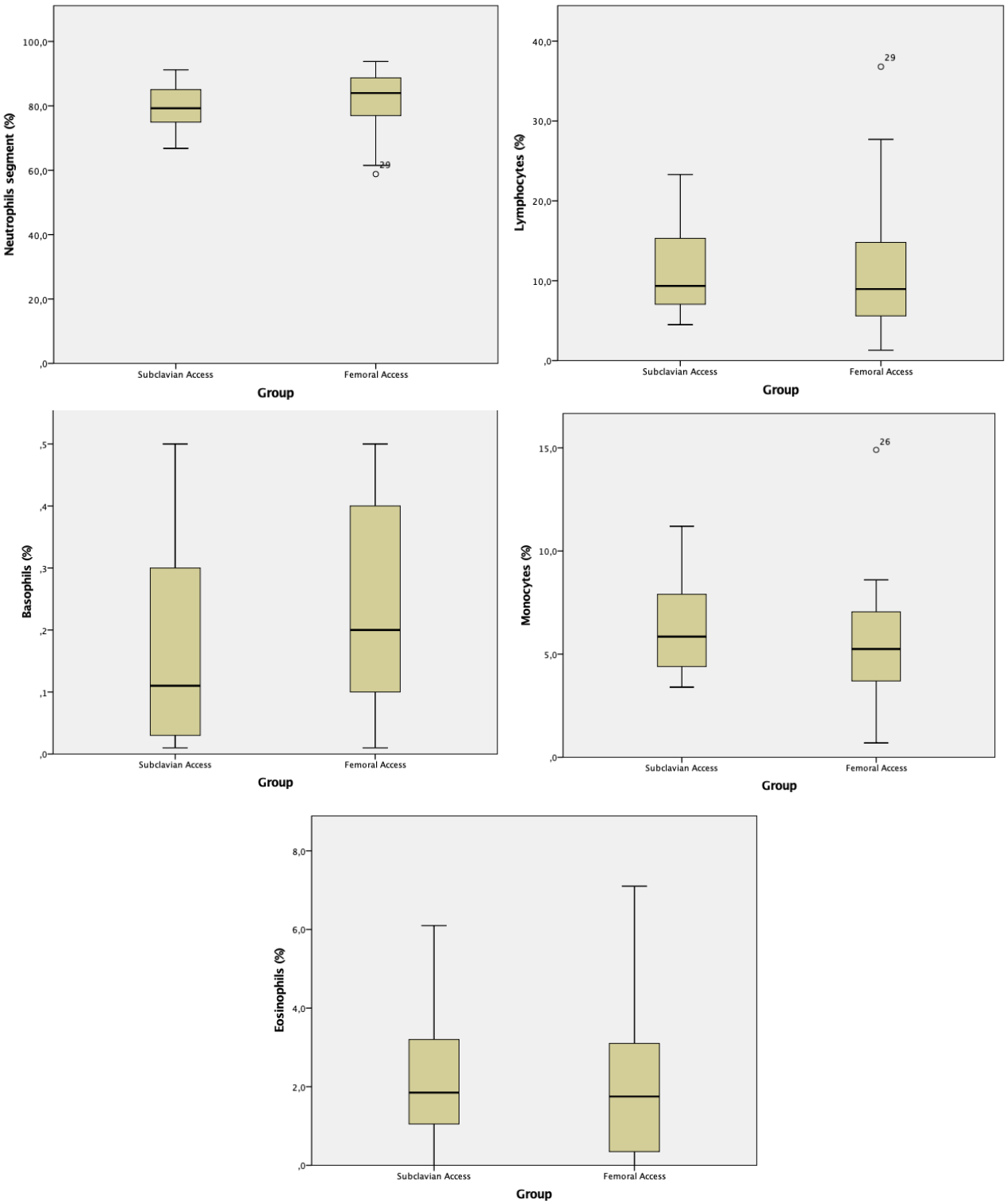

Figure 1. Comparisons of white blood cell elements between groups

14.9), and Figure 1 showed the difference in each group. In femoral group showed higher level for AST and ALT, 76.4 ± 190.1 and 40.6 ± 73.6 IU/L than in subclavian group, with no significant differences, Table 1.

DISCUSSION

In this study, it was found that CRBSI was mostly at the age of the fifth decade. The non-tunneled catheter duration in both groups were prolong use, 47.7 ± 34.2 days in subclavian group and 36.7 ± 18.4 days in femoral group. A non-tunneled catheter lifespan only 5-7 days, and not more than two weeks to achieve the best performance of the catheter and prevent the infection.[14] The prolonged usage of the catheter became the entry of the agent of infection and lead to CRBSI in present study. Furthermore, repeated insertions of catheter was also risk factor for CRBSI. On KDOQI 2019 also states that non-tunneled cental venous catheters (NT-CVC) can be used in emergencies and with a maximum duration

of two weeks due to increased risk of infection and only used in emergencies. This is different from tunneled CVC which can be used for a long time and is used in patients with comorbidities such as age> 85 years, risk of AV fistula failure, phobia of needles, and in patients who are young adults while waiting for a donor transplant. In this study, the use of a catheter with a duration that exceeds the duration. Insertion of haemodialysis CVC can be done in three places, such as internal jugular vein, femoral vein and subclavian vein. To reduce the risk of infection, access via internal jugular should be used, but in this study there are no insertion of the internal jugular vein. In this study insertion did not use ultrasound guiding, whereas based on the study of Zeki Aydin et al the use of ultrasound guiding could reduce the risk of complications such as arterial insertion.[6-13]

The placement of the insertion of non-tunneled catheter also should became a consideration. The first choice is right internal jugular vein, then femoral vein, then left jugular vein, then subclavian vein in a dominant upper extremity.[15] The placement of catheters in present study was inappropriate, and lead to the higher infection rate or CRBSI. A single non-tunneled catheter was around US$ 50-75, and tunneled catheter was around US$ 150-200. With a budget from US$ 197-286, insuranced patient could not choose the best option for their treatment. The non-tunneled catheter became the first choice. The best option for a low cost treatment and preventing the CRBSI was tunneled catheter with a pre-ESRD arteriovenous fistula. The education for patients and healthcare professionals should be improved.

In this research also found no significant difference between the use of antibiotics monotherapy, double and triple. So it is advisable to continue using single antibiotic for CRBSI. To prevent the occurrence of CRBSI intraluminal lock solutions can be used. Several RCTs have examined lock solutions such as gentamicin, cefazolin, cefotaxime, vancomycin, linezolid, vancomycin + gentamicin, cefazolin + gentamicin, cotrimoxazole or antimicrobial CVC locks such as (taurolidine, citrate, ethanol, and EDT). It was found that the incidence of CRBSI with antibiotics or antimicrobial solutions was very effective in reducing the rate of CRBSI.[6,8,13]

In the era of a low budget national health insurance system for central venous catheter placement for ESRD patients should be considered carefully. The pre-ESRD patients should be aware and encouraged to undergo a native arteriovenous fistula operation. The proper laboratory examinations and comorbidities evaluation should be more emphasized.

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CONCLUSION

In a low budget system for national health insurance in Indonesia, a good strategy such as pre-ESRD arteriovenous fistula, internal jugular vein access, nosocomial infection prevention, and rational antibiotic usage with a rational blood culture, need to be developed to prevent the infection of CRBSI.

CONFLICT OF INTEREST

The author states the original work, and there is no conflict of interest in doing this research.

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