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## Duration and frequency of catheterization in central vein stenosis: A case-control study

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### Abstract

**Introduction.** Placement of the central vein catheterization (CVC) is a major risk factor for central vein stenosis (CVS). Repetitive endothelial exposures to the CVC results in inflammation, microthrombi formation, hyperplasia of the intima, fibrosis and thus development of CVS. The study aimed to find out the correlation between the duration and frequency of CVC in patients with CVS.

**Method.** A matched case-control study was conducted in dr. Cipto Mangunkusumo General Hospital. Samples were taken from the medical record. Multivariate statistical comparisons were done using Chi-square tests.

**Results.** Fifty-four out of 717 patients underwent CVC for hemodialysis had CVS. A total of 32 patients with CVS enrolled in the study with 128 non-CVS patients as a control. Duration of CVC >6 weeks does not increase the risk of CVS ( $p = 0.207$ ), whilst the odds ratio of CVS on the frequency of CVC >2 times is 30 times compared to those underwent <2 times ( $p < 0.001$ ).

**Conclusion.** The frequency of CVC >2 times increased the risk of CVS. Longer duration of CVC for hemodialysis did not increase CVS rate.

**Keywords:** *central vein catheter, hemodialysis, stenosis*

### Introduction

Central venous catheter (CVC) for hemodialysis access is a major factor in central venous stenosis. Clinical manifestation includes upper limb and facial edema, collateral venous dilatation of the face, neck, and chest, and ulceration and tissue damage.<sup>1-5</sup> Schumacher et al. (1989) reported the incidence of central venous stenosis in a population of patients undergoing routine hemodialysis are 14%, 23–29% in the US and Canada, whilst to date, remains no data in Indonesia.<sup>6</sup>

Previous studies show predisposing factors for central venous stenosis (CVS) after CVC placement for hemodialysis access depends on the type of catheter (short term, long term, diameter), duration of catheter use, and location of catheter placement (subclavian vein, jugular vein). MacRae et al. (2005) showed the prevalence of central venous stenosis by 41% in 133 patients with hemodialysis catheter dysfunction.<sup>7</sup> Repeated contact with blood vessel walls can cause inflammation, muscle cell migration and thrombus formation which can alter the flexibility of blood vessels and increase blood vessel intraluminal pressure. The process resulted in the occurrence of central venous stenosis.<sup>7</sup> The aim of this study was to investigate the correlation between duration and frequency of CVC as risk factors for CVS.

### Method

A case-control design study conducted to determine the correlation of duration and frequency of CVC as risk factors of CVS in dr. Cipto Mangunkusumo General Hospital, Jakarta. Those with first inserted short-term CVC between January 2013 to December 2015 were included in the study. Meanwhile, those diagnosed with lymphoma or bronchogenic carcinoma were excluded. Despite the subject's characteristics, the comorbid and sites of insertion were recorded, and the occurrence of stenosis. Multivariate statistical comparisons using Chi-square tests were done. Further multivariate logistic regression to explore the risk ratio (RR) and the related 95% confidence intervals. All statistical analysis was performed using SPSS for Windows Ver. 20 and  $p < 0.001$  was considered statistically significant.

### Results

Out of 717 subjects underwent CVC placement for hemodialysis, a total of 54 subjects were diagnosed with CVS. A matched case-control study was done on a total of 32 case subjects and 128 subjects as control. Matching was based on age (>45 years) and gender (males) with a ratio of 1:4.

Table 1. Incidence of central venous stenosis in dr. Cipto Mangunkusumo General Hospital 2013–2015

Variable	n	Percent
CVS	54	7.53
Non-CVS	663	92.7
Total	717	100

Bivariate analysis was performed on the demographic characteristic (Table 2). Diabetes mellitus was found in 5.5% of the non-CVC subjects. Out of 32 CVS subjects, 30 had hypertension (93.7%) and out of 128 non-CVS subjects, 108 had hypertension (84.3%). The location of CVC placement in the subclavian vein has significantly increased the risk for CVS ( $p < 0.001$ ). Out of 50 subjects observed, 20 subjects had weight loss during the observation. From 20 subjects who had hospital malnutrition, one

subject was from those who did not proceed to surgery, while the rest were those who had undergone surgery. This hospital malnutrition incidence was smaller compared to the previous research conducted in 2007, in which the incidence was 52%. The characteristics of the subjects with and without hospital malnutrition were compared in table 2.

Table 2. Demographic characteristics of CVS patients in chronic kidney disease patients with central venous access in dr. Cipto Mangunkusumo General Hospital 2013–2015

Characteristics	CVS n (%)	No CVS n (%)	p
Age group			
– $\leq 45$ years	–	–	
– $> 45$ years	32	128	
Gender			
– Male	32	128	
– Female	–	–	
Comorbid			
– Diabetes	0 (0%)	7 (5.5%)	0.102
– Hypertension	30 (93.7%)	108 (84.3%)	
Sites the CVC			
– Subclavian vein	28 (59.6%)	19 (40.4%)	$< 0.001$
– Internal jugular vein	4 (3.5%)	109 (96.5%)	

A multivariate analysis (binary logistic regression test) on the duration and frequency of CVC as a predictor of CVS was performed. CVS was found in 25 subjects (22.5%) on subjects with a catheter duration  $> 6$  weeks and 7 subjects (13.7%) in subjects with catheter duration  $< 6$  weeks. The analysis shows that catheter duration is not statistically significant as a risk factor for CVS ( $p = 0.207$ ) at

95% confidence level. A significant association was found between the frequency of CVC insertion and CVS ( $p < 0.001$ ) at 95% confidence level. Subjects underwent CVC insertion  $> 2$  times were 30 times compared to those underwent CVC  $< 2$  times (Table 3).

Table 3. Analysis of factors related to CVS occurrence in chronic kidney disease patients with CVC.

	CVS (%)	No CVS (%)	OR	CI 95%	p
Duration of catheter use					
– $> 6$ weeks	25 (22.5%)	84 (77.5%)	1.9	0.8–4.7	0.207
– $< 6$ weeks	7 (13.7%)	44 (86.3%)			
Frequency of catheter insertion					
– $> 2$ times					
– $< 2$ times	28 (53.8%)	24 (46.2%)	30	9.7–94.6	$< 0.001$
	4 (4%)	104 (96%)			

The multi-regression analysis was done on the jugular vein placement location and the frequency of CVC. It shows that both variables are significantly related to CVS ( $p < 0.001$ ). The odds ratio of jugular vein catheter placement was 81 and the odds ratio of the frequency of catheter placement was 62.799 (Table 4). Meaning, both variables are proven to be a significant risk factor for CVS.

Table 4. Multi regression analysis

	CVS (%)	No-CVS (%)	p Value	OR (CI 95%)
Frequency of catheter placement $> 2$ times	32 (20%)	128 (80%)	$< 0.001$	62.799 (11.194 – 352.302)

## Discussion

Arteriovenous fistula has been the recommended access for long-term hemodialysis because it provides the least complications compared to arteriovenous graft and CVC. However, CVC as hemodialysis access is unavoidable due to emergency access required for the hemodialysis.<sup>1,3,14</sup> It is important to minimize the use of CVC through the construction of an arteriovenous fistula before the chronic kidney disease continues to stage 5. Unfortunately, most subjects in this study were those who came requiring emergency hemodialysis.

CVS defined as stenosis or occlusion of the subclavian vein or brachiocephalic vein or superior vena cava,<sup>20</sup> interferes with the hemodialysis circuit leading to venous hypertension and access flow

dysfunction and may result in loss of access.<sup>1,5,8</sup> The CVS diagnosed based on the symptoms and venographic findings. The most common symptoms of CVS are swelling of the ipsilateral arm where the CVC were placed, chest, neck and face.<sup>5,8-11</sup> The prevalence of CVS in this study is lower (7.53%) compared to the study in The USA and Canada (23–29%). In our institution, all patients came with severe symptoms.

In this study, there were 32 subjects enrolled and 128 subjects as control; in a ratio of 1:4. Matching is based on age (>45 years) and gender (males). Hypertension was found in 93.7% subjects in CVS and 84.3% subjects in non-CVS. This was found consistent with the reports that more than 90% of subjects undergoing hemodialysis due to chronic kidney disease suffer from hypertension. Only 5.5% of subjects suffering from diabetes mellitus in this study, whereas in Asian populations with chronic kidney disease undergoing hemodialysis reported more than 60% had diabetes mellitus.<sup>20</sup>

There was a significant association between the frequency of central venous catheter insertion and the occurrence of CVS. There is a 30-fold risk of CVS occurring in patients with central venous catheter placement >2 times compared with those with <2 times. This is consistent with the study of MacRae (2005) reported the incidence of CVS occurs in the insertion more than 1 time.<sup>12</sup> Repeated central venous catheter placement triggers venous wall injury, and followed by the inflammatory processes, thrombus formation, and changes in venous wall histology. The inflammatory process as the body responds to the catheter as a foreign material leading to migration and proliferation of smooth muscle cells to the intimal layer that in turn, leading to venous thickening. Repetitive frictions of the catheter against the venous wall and blood turbulence also cause thickening of the venous wall and platelet accumulation. The veins losing vascular tone leading to CVS.<sup>5,9</sup>

There was no significant association found between the duration of use of a central venous catheter and the occurrence of CVS. While the study by McRae (2005) stated that patients who experienced CVS had a longer duration of dialysis duration, which was 43 months compared to 34 months.<sup>7</sup> The finding is consistent with the study of Hernandez (1998) who stated CVS is more common in longer usage, namely 49 days compared to 29 days.<sup>12</sup> The pathogenesis of CVS in the longer duration of central venous catheter use is similar to pathogenesis at the frequency of repeated insertions. Structural changes in the venous wall last from 24 hours after endothelial denudation with platelet microthrombus formation. This response continues so that smooth muscle cells are layered in the injured area.<sup>5,9</sup> Another risk factor that can cause CVS is the placement location in the subclavian vein.<sup>12,17,20</sup>

## Conclusion

There was a significant correlation ( $p < 0.001$ ) between central venous catheter insertion on the subclavian vein (59.6%) with the occurrence of CVS, compared with internal jugular vein insertion (3.5%).

## Disclosure

Author disclose there was no conflict of interest.

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