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The Impact of Initial Vascular Access on Long-term Mortality in Hemodialysis Thai Patients

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Background: End-stage kidney disease (ESKD) patients are significantly at risk of higher mortality than the general population. While cardiovascular disease and infection are the major causes of death in ESKD patients on hemodialysis (HD), the impact of vascular access type on long-term mortality in the Thai population remains unclear.

Objective: To find an association between types of vascular access and long-term mortality in HD Thai patients.

Methods: A multicenter, retrospective cohort of HD patients with a 55-month follow-up (November 2015 to December 2020) was conducted. Patients' baseline characteristics, and HD profiles were reviewed. A logistic regression model and survival analysis were used to test the association and survival probability of each type of vascular access and mortality.

Results: Of 196 HD patients over 55 months, the proportions of initial vascular access included 46.94% of arteriovenous fistula (AVF), 27.55% of arteriovenous graft (AVG), and 25.51% of tunneled dialysis catheter (TDC). The overall mean all-cause mortality in this cohort was 29.1%. Compared with AVF, TDC was associated with increased mortality (adjusted OR, 3.18; 95% CI, 1.37 - 7.37; $P < .05$) while the association between AVG and mortality was borderline significant (adjusted OR, 2.29; 95% CI, 0.96 - 5.46; $P > .05$).

Conclusions: TDC as initial vascular access for incident HD Thai patients was associated with increased all-cause mortality at 55 months compared with functioning AVF.

Keywords: Hemodialysis, Mortality, Tunneled dialysis catheter, Vascular access

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Introduction

End-stage kidney disease (ESKD) is the terminal stage of chronic kidney disease when the kidney function is permanently lost, leading to renal replacement therapy. The prevalence of ESKD varied across the geographic region, with an estimated prevalence of 4.9 to 7.1 million.[1] Patient with ESKD, despite receiving timely dialysis, have worse overall survival compared with the general population.[2] The major causes of death in these patients are cardiovascular disease, infection, and withdrawal from dialysis.[3, 4] Additionally, dialysis-related risk factors, including dialysis adequacy and dialysis vintage, are associated with overall mortality in ESKD patients. However, it is unclear whether a factor of a dialysis access type is also associated with long-term mortality. According to the Kidney Disease Outcome and Quality Initiative (KDOQI) 2019, further studies are required to make recommendations on the choice of hemodialysis vascular access type based on the association with overall mortality.

For hemodialysis (HD), there are 3 types of HD vascular access which are arteriovenous fistula (AVF), arteriovenous graft (AVG), and tunneled dialysis catheter (TDC). Each type of vascular access has its unique advantages and disadvantages. AVF, despite a high rate of failure to mature, is superior to other types of access for better patency rate, longer access survival rate, and lower complications once matured.[5-9] AVG offers similar characteristics to AVF but has higher complications, particularly thrombosis and access loss. While TDC requires no maturation time and is available for immediate use, however, it is associated with high infection rates, inflammation, thrombosis, and central venous stenosis. Those unique benefits and risks of different types of HD vascular access may potentially affect the mortality in HD patients. Recent studies found that AVF as initial vascular access was associated with a higher survival rate than AVG or TDC.[10-12] However, the data in the Thai HD population is limited.

We conducted this study to find an association between types of initial dialysis vascular access and long-term mortality in Thai HD patients. To the best of our knowledge, this is the first study on the association between types of vascular access and long-term mortality conducted in the Thai HD population.

Methods

Participants and Study Design

This study was a multicenter retrospective cohort of patients receiving maintenance HD at Somdech Phra Debaratana Medical Center and Queen Sirikit Medical Center, Faculty of Medicine Ramathibodi Hospital, Mahidol University, and Bhumirajanagarindra Kidney Institute Hospital, Thailand. The enrollment period of the study was from November 2015 to March 2016. Patients at the age of 18 to 90 years with ESKD who received maintenance HD for more than one week were included in the study.

Patient's baseline characteristics (age, gender, body mass index [BMI], comorbidities, residual urine volume), HD profiles (dialysis vintage, mode of HD, HD frequency, amount of ultrafiltration), types of initial vascular access, and laboratory parameters at the beginning of the cohort were collected from medical records. All laboratory tests were performed at the hospital's central laboratory. A delivered dose of dialysis (Kt/V urea), using a single-pool urea kinetic model, was used as a dialysis efficacy parameter in our study.

The study endpoint of each patient was the date of the last HD session of December 31, 2020. The reason for cessation of HD, such as death, kidney transplantation, hospital transfer, or loss to follow-up, was confirmed with direct patient contact on every patient.

Ethics

This study was approved by the Human Research Ethics Committee from Faculty of Medicine Ramathibodi Hospital, Mahidol University. The approval number was MURA2021/1038, on December 27, 2021.

Statistical Analysis

Continuous data was reported using the mean with standard deviation (SD) or median with interquartile range (IQR) as appropriate, while categorical data was reported using frequency with percentage.

Baseline characteristics between different types of vascular access were compared using one-way analysis of variance (ANOVA) for continuous data and the exact probability test for categorical data.

Associations between types of vascular access and mortality were analyzed using a logistic regression model. A univariate analysis method was first introduced to calculate a *P* value of the study variables. Types of vascular access and potential confounding factors (study variables with *P* value < .1 from the univariate analysis) were further tested using a multivariable analysis method.

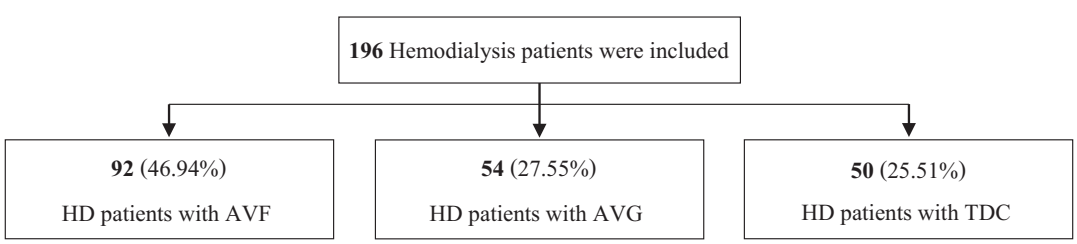
Association between survival probabilities of each type of vascular access and time since dialysis initiation was demonstrated with Kaplan-Meier curves. A log-rank test was used to test the statistical difference between each survival function. A 2-tailed *P* value of less than .05 was considered statistically significant.

All statistical analyses were performed using SPSS version 24.0 (IBM SPSS Statistics for Windows, Version 24.0. Armonk, NY: IBM Corp; 2016).

Results

A total of 196 patients were enrolled, 46.94% had AVF, 27.55% had AVG, and 25.51% had TDC as their initial vascular accesses, respectively (Figure 1). The follow-up duration since the initiation of HD was 55 months. The mean age was 68 years, 52.6% were female, and the mean BMI was 22.4 kg/m^2. Most patients had conventional HD, and half had HD thrice weekly. Age, underlying cerebrovascular disease, serum albumin, and ultrafiltration were significantly different among the three types of vascular access. Our cohort's overall mortality rate was 29.1%, which resulted from infection, cardiovascular death, malignancy, and other causes as 11.7%, 10.7%, 4.1%, and 2.6%, respectively. Eleven patients (5.6%) underwent kidney transplantation. The all-cause mortality rates based on types of vascular access were 20.7% in AVF, 27.8% in AVG, and 46% in TDC (Table 1).

Figure 1. Flow Chart Shows the Distribution of ESKD Patients by Types of Vascular Access



Abbreviations: AVF, arteriovenous fistula; AVG, arteriovenous graft; ESKD, end-stage kidney disease; TDC, tunneled dialysis catheter.

Table 1. Baseline Characteristics and Outcomes According to Types of Vascular Access

Characteristic	Total (N = 196)	Types of Vascular Access			*P* Value*
		AVF (n = 92)	AVG (n = 54)	TDC (n = 50)	
Age, mean (SD), y	68.5 (13.1)	64.8 (13.1)	70.0 (11.5)	73.9 (12.8)	< .001
Female, No. (%)	103 (52.6)	41 (44.6)	30 (55.6)	32 (64)	.08
BMI, mean (SD), kg/m^2	22.4 (4.2)	22.2 (4.0)	23.3 (4.4)	21.8 (4.4)	.19
Hypertension, No. (%)	184 (93.9)	83 (90.2)	54 (100)	47 (94)	.06

Table 1. Baseline Characteristics and Outcomes According to Types of Vascular Access (Continued)

Characteristic	Total (N = 196)	Types of Vascular Access			*P* Value*
		AVF (n = 92)	AVG (n = 54)	TDC (n = 50)	
Diabetes, No. (%)	112 (57.1)	46 (50)	34 (63)	32 (64)	.16
Smoker, No. (%)	43 (21.9)	24 (26.1)	14 (25.9)	5 (10)	.06
Coronary artery disease, No. (%)	65 (33.2)	29 (31.5)	14 (25.9)	22 (44)	.13
Cerebrovascular disease, No. (%)	18 (9.4)	4 (4)	5 (9.6)	9 (18)	.03
Dialysis vintage, median (IQR), mo	21 (20)	26 (18)	20 (21)	21 (21.3)	.20
Residual urine volume, median (IQR), mL	0 (1100)	0 (915)	0 (1305)	0 (760)	.71
Hemodiafiltration, No. (%)	24 (12.2)	12 (13)	6 (11.1)	6 (12)	.94
3x week dialysis, No. (%)	95 (48.5)	46 (50)	25 (46.3)	24 (48)	.91
Ultrafiltration, mean (SD), L	2.3 (1.0)	2.5 (1.1)	2.3 (0.9)	2.0 (0.9)	.02
Hemoglobin, mean (SD), g/dL	11.0 (1.4)	11.1 (1.5)	11.1 (1.1)	10.9 (1.5)	.70
Serum albumin, mean (SD), g/dL	3.7 (0.4)	3.7 (0.4)	3.8 (0.4)	3.6 (0.4)	.04
Serum calcium, mean (SD), mg/dL	9.2 (0.7)	9.1 (0.6)	9.3 (0.7)	9.3 (0.8)	.26
Serum phosphorus, mean (SD), mg/dL	4.6 (1.4)	4.6 (1.4)	4.8 (1.3)	4.3 (1.5)	.23
Serum iPTH, median (IQR), pg/mL	355 (452.9)	409.8 (484.6)	306.2 (332.8)	294.8 (497.1)	.27
Serum B_2-microglobulin, mean (SD), ug/mL	31.2 (9.8)	32.0 (9.7)	30.5 (8.5)	30.3 (11.3)	.57
hsCRP, median (IQR), mg/L	0.16 (0.5)	0.21 (0.6)	0.1 (0.4)	0.2 (0.6)	.63
spKt/V, mean (SD)	2.1 (0.4)	2.1 (0.4)	2.1 (0.4)	2.1 (0.4)	.87
nPCR, mean (SD)	1.0 (0.3)	1.0 (0.3)	1.1 (0.4)	1.0 (0.3)	.65

Abbreviations: AVF, arteriovenous fistula; AVG, arteriovenous graft; BMI, body mass index; hsCRP, high sensitivity C-reactive protein; iPTH, intact parathyroid hormone; IQR, interquartile range; nPCR, normalized protein catabolic rate; SD, standard deviation; spKt/V, single-pool Kt/V; TDC, tunneled dialysis catheter.

* Significance threshold, $P < .05$.

According to the univariate analysis (Table 2), when compared with AVF, TDC was significantly associated with increased all-cause mortality (Odds ratio [OR], 3.27; 95% Confidence interval [CI], 1.54 - 6.94; $P = .02$). Association between AVG and mortality was nonsignificant (OR, 1.48; 95% CI, 0.68 - 3.23; $P = .33$). While an increase in age was associated with increased mortality, BMI and serum albumin were inversely associated with mortality. An association between serum intact parathyroid hormone (iPTH) was also noted, but the effect size was small.

Types of vascular access and other factors with a *P* value of less than .1, including types of vascular access, age, BMI, serum albumin, and serum iPTH were selected for multivariable analysis. TDC was independently associated with mortality (adjusted OR, 3.18; 95% CI, 1.37 - 7.37; $P = .007$), while AVG demonstrated the same direction of association with borderline statistical significance (adjusted OR, 2.29; 95% CI, 0.96 - 5.46; $P = .06$). Kaplan-Meier survival curves of the patients with different types of vascular access were shown with a significant difference between TDC and AVF groups were demonstrated (Figure 2).

In a subgroup analysis of patients over 60 years, TDC was independently associated with mortality compared with AVF (adjusted OR, 2.42; 95% CI, 1.07 - 5.45; $P = .03$). While the effect of AVG and AVF on patients' mortality was comparable (adjusted OR, 1.03; 95% CI, 0.43 - 2.44; $P = .96$)

Table 2. Factors Influencing Mortality in Hemodialysis Patients, Using Univariate and Multivariate Logistic Regression Analysis

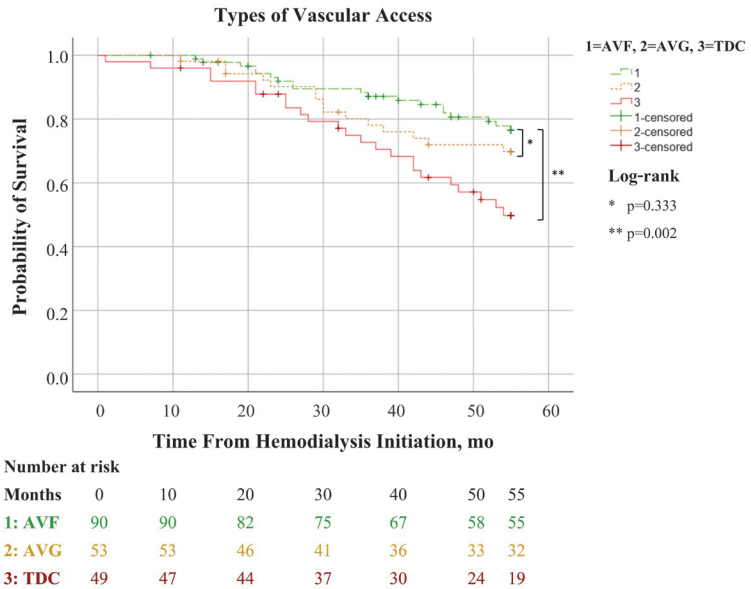
Risk Factor	Mortality			
	Univariate		Multivariate**	
	OR (95% CI)	*P* Value*	OR (95% CI)	*P* Value*
Initial vascular access				
AVF	1.00 [Reference]	NA	1.00 [Reference]	NA
AVG	1.48 (0.68 - 3.23)	.33	2.29 (0.96 - 5.46)	.06
TDC	3.27 (1.54 - 6.94)	.002	3.18 (1.37 - 7.37)	.007
Age, y	1.05 (1.02 - 1.08)	.001	NS	NS
Female	1.23 (0.66 - 2.28)	.52	-	-
BMI, kg/m^2	0.85 (0.78 - 0.93)	.001	0.86 (0.78 - 0.94)	.001
Hypertension	2.13 (0.45 - 10.05)	.34	-	-
Diabetes	0.63 (0.34 - 1.18)	.15	-	-
Smoker	0.68 (0.31 - 1.50)	.34	-	-
Coronary artery disease	1.56 (0.82 - 2.97)	.17	-	-
Cerebrovascular disease	1.28 (0.45 - 3.59)	.65	-	-
Dialysis vintage, mo	1.01 (1.00 - 1.01)	.26	-	-
Residual urine volume, mL	1.00 (0.99 - 1.00)	.15	-	-
Hemodiafiltration	1.26 (0.51 - 3.12)	.63	-	-
3x week dialysis	1.04 (0.56 - 1.92)	.91	-	-
Ultrafiltration	1.00 (1.00 - 1.00)	.78	-	-
Hemoglobin, g/dL	1.07 (0.86 - 1.33)	.56	-	-
Serum calcium, mg/dL	1.18 (0.76 - 1.84)	.46	-	-
Serum phosphorus, mg/dL	0.96 (0.77 - 1.20)	.72	-	-
Serum albumin, g/dL	0.25 (0.11 - 0.59)	.001	0.26 (0.10-0.63)	.003
Serum iPTH, pg/mL	0.99 (0.99 - 1.00)	.03	NS	NS
Serum B_2-microglobulin, ug/mL	1.02 (0.99 - 1.05)	.29	-	-
hsCRP, mg/L	0.92 (0.62 - 1.38)	.68	-	-
spKt/V	0.66 (0.30 - 1.44)	.29	-	-
nPCR	1.64 (0.63 - 4.25)	.31	-	-

Abbreviations: AVF, arteriovenous fistula; AVG, arteriovenous graft; BMI, body mass index; CI, confidence interval; hsCRP, high sensitivity C-reactive protein; iPTH, intact parathyroid hormone; NA, not applicable; nPCR, normalized protein catabolic rate; NS, not significant; OR, odds ratio; spKt/V, single-pool Kt/V; TDC, tunneled dialysis catheter.

* Significance threshold, $P < .05$.

** Adjusted for age, initial vascular access, BMI, serum albumin, iPTH.

Figure 2. Kaplan-Meier Survival Function for Mortality of Hemodialysis Patients, stratified by Types of Vascular Access



Number at risk

Months	0	10	20	30	40	50	55
1: AVF	90	90	82	75	67	58	55
2: AVG	53	53	46	41	36	33	32
3: TDC	49	47	44	37	30	24	19

Abbreviations: AVF, arteriovenous fistula; AVG, arteriovenous graft; ESKD, end-stage kidney disease, TDC, tunneled dialysis catheter.

Discussion

This observational study aimed to explain an association between types of initial vascular access and overall mortality in Thai HD patients. Regarding the patient's baseline characteristics (Table 1), patients with TDC were older, had lower serum albumin, and lower amount of dialysis ultrafiltration when compared with those with AVF and AVG. The number of patients who had prior cerebrovascular disease was highest in the TDC group. The overall mortality rate of HD patients in our cohort was 29.1%, comparable to prior studies. Infection was the most prevalent cause of death, followed by cardiovascular death. Particularly, patients with TDC had the highest overall mortality rate. Our study found that utilization of TDC, lower BMI, and lower serum albumin level were independently associated with higher all-cause mortality in HD patients.

As for the association between the first vascular access and all-cause mortality, our study shows that TDC had higher mortality than AVF. AVG seemed to have a similar trend with higher mortality than AVF with borderline statistical significance. Our findings were consistent with a prospective cohort study of 2666 patients on hemodialysis in the United Kingdom with TDC utilization associated with 7-fold higher odds of death than AVF.[13] The higher all-cause mortality in patients with TDCs, when compared to AVF, might be contributed by catheter-related complications, including infection and non-infection.

Regarding non-infectious complications, catheter dysfunction causing flow dysfunction may result in recirculation. Moreover, it may affect catheter patency and lead to interruption of dialysis and inadequate dialysis. Eventually, this may increase all-cause mortality in patients receiving dialysis via TDCs. TDC has a one-year primary patency rate of 65% to 75%, and the duration of primary catheter function is between 6 to 12 months.[14] When compared with all created AVF with failure to mature included, the one-year primary patency of TDC and AVF are comparable, approximately 60%.[15, 16] However, when compared to only mature AVF, the one-year primary patency of TDC is inferior to mature AVF, approximately 80%.[9, 16] There are several causes of catheter dysfunction, such as fibrin sheath formation and catheter thrombosis. Fibrin sheath formation can be demonstrated in up to 76% of TDC.[17, 18] However, not all fibrin sheaths cause catheter dysfunction; 13% to 57%

cause catheter dysfunction.[19] Another common cause of catheter dysfunction is catheter thrombosis which frequently results in catheter loss. The mean patency rate of the catheter for this problem has been reported 73 to 84 days.[19] Not only a concern of catheter loss, but catheter thrombosis can potentially lead to catastrophic consequences threatening patients' safety, such as pulmonary embolism, loss of vascular access in the relevant vein, and central venous occlusion.[20]

Regarding infectious complications, catheter-related infection is a notorious complication of dialysis catheter utilization. This may directly contribute to patient mortality. Dialysis catheter has approximately 10 times higher bacteremia than AVF.[21,22] Moreover, long-term use of TDC may trigger an immune reaction and lead to chronic inflammation as evidence of elevated C-reactive protein.[23-25] However, our study shows that C-reactive protein levels in each type of vascular access were similar. These catheter-related complications may either directly or indirectly increase the overall mortality of patients utilizing TDCs.

Apart from vascular access, our study found that higher BMI and higher serum albumin were associated with lower overall mortality (Table 2). In general, BMI is a useful and practical anthropometric tool for determining nutritional status. Data from meta-analyses showed that BMI and albumin levels in HD patients were inversely associated with overall mortality.[26,27] Having BMI between 25 to 29.9 kg/m^2 was a protective factor of survival in HD patients. However, the protective effect has not been verified in those with BMI greater of equal to 30 kg/m^2.[28] Serum albumin is another highly predictive biomarker used in establishing a diagnosis of malnutrition in HD patients.[29] Persistent systemic inflammation in ESKD patients results in a decrease in serum albumin, which may predict their overall prognosis and mortality.[30] Our study emphasizes that BMI and serum albumin can be potential predictors for mortality in HD patients.

Nevertheless, our study has some limitations. Firstly, the decision of choosing vascular access for incident HD patients might be based on patient statuses such as baseline cardiopulmonary status, life expectancy, or patient preference. There was no information regarding those decisions available to explore. This makes our study subject to selection bias. Secondly, not all patients stayed on the same vascular access initially created for the long-term. At some point, patients starting with TDC might switch to permanent vascular access, either AVF or AVG, once matured. The other way around, patients with permanent vascular access might have a vascular problem and need to use TDC temporally. The data on switching types of vascular access and during for each vascular access utilization was not available in our study. Moreover, factors that potentially influence physician decision on type of vascular access selection, such as the timing of nephrologist or vascular surgeon referral before vascular access creation, socioeconomic status, and medical insurance or coverage were not identified. Accordingly, our study can only make a point that first dialysis access with TDC for incident HD patients may be associated with higher mortality at 55 months. The data regarding the sources of infection in our cohort was not available. Finally, other factors that might have confounded with patient's mortality, including frailty score, history of diabetic complication, or parathyroidectomy, were not collected; further prospective studies are required to confirm this association and explore its potential contributing factors.

Conclusions

TDC as initial vascular access for incident HD Thai patients was associated with increased all-cause mortality at 55 months compared with functioning AVF. While AVG may increase the 5-year mortality as borderline statistical significance.

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ผลของชนิดหลอดเลือดสำหรับการฟอกเลือดหรือเส้นฟอกเลือดขั้นต้นต่ออัตราการเสียชีวิตระยะยาวในผู้ป่วยคนไทยที่เป็นโรคไตเรื้อรังระยะสุดท้ายที่ได้รับการฟอกเลือดด้วยเครื่องไตเทียม

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บทนำ: โรคไตวายเรื้อรังระยะสุดท้ายเป็นปัญหาสำคัญที่นำไปสู่การเสียชีวิตของผู้ป่วย แม้ว่าสาเหตุการเสียชีวิตของผู้ป่วยส่วนใหญ่เกิดจากการติดเชื้อ หรือโรคหัวใจ อย่างไรก็ตาม ผลของชนิดหลอดเลือดสำหรับการฟอกเลือดหรือเส้นฟอกเลือดต่ออัตราการเสียชีวิตระยะยาวในคนไทยยังไม่เป็นที่แน่ชัด

วัตถุประสงค์: เพื่อศึกษาผลของความสัมพันธ์ระหว่างชนิดของหลอดเลือดหรือเส้นฟอกเลือดกับอัตราการเสียชีวิตระยะยาวของผู้ป่วยไทยที่ได้รับการฟอกเลือด

วิธีการศึกษา: การศึกษาย้อนหลังนี้เป็นโครงการศึกษาวิจัยพหุสถาบัน กลุ่มตัวอย่างเป็นผู้ป่วยที่ได้รับการฟอกเลือดด้วยเครื่องไตเทียม รวมระยะเวลา 55 เดือน (พฤศจิกายน พ.ศ. 2558 ถึงเดือนธันวาคม พ.ศ. 2563) เก็บบันทึกข้อมูลปัจจัยต่างๆ ที่ส่งผลต่ออัตราการเสียชีวิต ได้แก่ ข้อมูลผู้ป่วย และข้อมูลเกี่ยวกับการฟอกเลือด การวิเคราะห์ความสัมพันธ์ระหว่างชนิดของหลอดเลือดหรือเส้นฟอกเลือดกับอัตราการเสียชีวิตของผู้ป่วยใช้วิธีวิเคราะห์การถดถอยโลจิสติกส์และการวิเคราะห์ระยะปลอดเหตุการณ์

ผลการศึกษา: ผู้ป่วยทั้งหมด 196 คน เป็นผู้ป่วยที่ใช้หลอดเลือดจริงร้อยละ 46.94 หลอดเลือดเทียมร้อยละ 27.55 และเส้นฟอกเลือดร้อยละ 25.51 พบว่า มีอัตราการเสียชีวิตโดยรวมร้อยละ 29.1 ปัจจัยที่มีผลต่ออัตราการเสียชีวิตเมื่อเปรียบเทียบกับผู้ป่วยที่ใช้หลอดเลือดจริงคือ ผู้ป่วยที่ใช้เส้นฟอกเลือด (Adjusted OR, 3.18; 95% CI, 1.37 - 7.37; $P < .05$) ขณะที่ผู้ป่วยใช้หลอดเลือดเทียมมีอัตราการเสียชีวิตเพิ่มขึ้นอย่างไม่มีนัยสำคัญ (Adjusted OR, 2.29; 95% CI, 0.96 - 5.46; $P > .05$)

สรุป: การเริ่มต้นฟอกเลือดด้วยเส้นฟอกเลือด มีความสัมพันธ์กับการเพิ่มขึ้นของอัตราการเสียชีวิตที่ 55 เดือน เมื่อเทียบกับการใช้หลอดเลือดจริงในผู้ป่วยไทยที่ได้รับการฟอกเลือดด้วยเครื่องไตเทียม

คำสำคัญ: การฟอกเลือดด้วยเครื่องไตเทียม อัตราการเสียชีวิต เส้นฟอกเลือด ชนิดของหลอดเลือดสำหรับการฟอกเลือด

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