Survival Time of Vascular Access and Predictive Factors of Vascular Access Dysfunction in Chronic Hemodialysis Patients

การศึกษาระยะเวลาการทำงานของเส้นฟอกเลือดสำหรับการล้างไตด้วยเครื่องไตเทียม และ ปัจจัยทำนายการสูญเสียหน้าที่ของเส้นฟอกเลือดในผู้ป่วยที่ฟอกเลือดด้วยเครื่องไตเทียมแบบเรื้อรัง

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ABSTRACT

Hemodialysis (HD) Treatment is a method that is used to achieve the extracorporeal removal of waste products from the blood via vascular access (VA). Thus, a well – functional vascular access influence quality of life of HD patients. The aim of this study was to compare survival functional time of tunneled cuffed catheters (TCs), arteriovenous fistulas (AVFs), and arteriovenous grafts (AVGs) and determine clinical factors associated with loss of their primary functional patency. This was a retrospective study of end stage renal (ESRD) patients who receiving chronic HD in the Kidney Foundation of Thailand at the Priest hospital from 1 January 1997 to 31 December 2012. During the study period, 552 VAs were created in 399 patients. There were 463 (83.9%) patients with AVFs, 69 (12.5%) patients with AVGs and 20 (3.6%) patients with TCs. Median age of patients at initial vascular access creation was 38.6 years (range, 29.6 to 48.4 years). Median time of HD was 9.4 years (range, 5.6 to 12.9 years). Median primary functional patency for AVF was 61.1 months (95% CI, 21.1 - 119.0) longer than AVGs was 44.3 months (95% CI, 21.8 - 66.9), and TCs was 29.6 (95% CI, 12.6 - 46.6). Multivariable analysis in AVFs and AVGs found that patients with AVGs (HR 2.80 [95% CI, 1.67 – 4.68], P = <0.001), BMI $\geq$ 30 kg/m^2 (HR 2.54 [95% CI, 1.00 – 6.44], P = 0.049) and history of retained central venous catheter (CVC) more 90 days (HR 2.48 [95% CI, 1.10 - 5.59], P = 0.029) were associated with a higher risk of primary functional vascular dysfunction. Multivariable analysis in 3 types of VAs demonstrated that patients with AVGs (HR 3.04 [95% CI, 1.82 - 5.09], P = <0.001) and BMI $\geq$ 30 kg/m^2 (HR 2.57 [95% CI, 1.11 - 5.96], P = 0.028), similar to above results. Although, patients with TCs, presence of peripheral vascular disease PVD, and hypoalbuminemia (serum albumin < 3.5 g/dl) were not significantly differences in vascular access survival but, those were trend toward increased primary vascular dysfunction. Thus, chronic HD patients with AVFs, the reduction of retained CVC time and the maintenance of normal BMI should benefit for HD patients.

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บทคัดย่อ

การฟอกเลือดด้วยเครื่องไตเทียมต้องอาศัยวิธีการในการนำเลือดซึ่งมีของเสียของผู้ป่วยออกสู่วงจรภายนอกร่างกายผ่านเข้าออกที่หลอดเลือดทางเส้นฟอกเลือด (vascular access) ฉะนั้นการดูแลรักษาเส้นฟอกเลือดให้มีประสิทธิภาพจึงส่งผลต่อคุภาพชีวิตที่ดีของผู้ป่วย วัตถุประสงค์ของการศึกษานี้เพื่อเปรียบเทียบอายุการใช้งานของเส้นฟอกเลือดด้วยเครื่องไตเทียมชนิด tunneled cuffed catheter (TC), arteriovenous fistula (AVF), และ arteriovenous graft (AVG) และศึกษาปัจจัยทางคลินิกที่ทีผลกระทบต่อการสูญเสียหน้าที่ของเส้นฟอกเลือดทั้งสามแบบ การศึกษานี้เป็นแบบเก็บข้อมูลย้อนหลังของผู้ป่วยที่มีภาวะโรคไตระยะสุดท้ายที่ฟอกเลือดด้วยเครื่องไตเทียมเรื้อรังอยู่ที่มูลนิธิโรคไตแห่งประเทศไทย ณ โรงพยาบาลสงฆ์ระหว่างวันที่ 1 มกราคม พ.ศ. 2540 ถึง 31 มกราคม พ.ศ. 2555 โดยการศึกษานี้มีผู้ป่วยทั้งหมด 399 คน มีเส้นฟอกเลือดทั้งหมด 552 เส้นซึ่งแบ่งเป็น AVF 463 เส้น คิดเป็น 83.9 เปอร์เซ็นต์ AVG 69 เส้น คิดเป็น 12.5 เปอร์เซ็นต์ และเส้นฟอกเลือดชนิด TC จำนวน 20 เส้น คิดเป็น 3.6 เปอร์เซ็นต์ โดยเฉลี่ยแล้วผู้ป่วยมีอายุ 38.6 ปี และฟอกเลือดด้วยเครื่องไตเทียม 9.4 ปี อัตราการใช้งานของเส้นฟอกเลือดเฉลี่ยอยู่ที่ 61.1 เดือนในผู้ป่วยที่ใช้ AVF ซึ่งนานกว่าผู้ป่วยที่ใช้ AVG ซึ่งมีอัตราการใช้งานของเส้นฟอกเลือดเฉลี่ยอยู่ที่ 44.3 เดือน และ ผู้ป่วยที่ใช้ TC ซึ่งมีอัตราการใช้งานของเส้นฟอกเลือดเฉลี่ยอยู่ที่ 29.6 เดือน เมื่อทำการวิเคราะห์แบบหลายตัวแปรใน AVF และ AVG พบว่า ผู้ป่วยที่มี AVG ดัชนีมวลกายมากว่าหรือเท่ากับ 30 กก./ม.^{2} และมีประวัติการคาสาย CVC ไว้นานกว่า 90 วัน มีโอกาสเสี่ยงที่จะสูญเสียหน้าที่ของเส้นฟอกเลือดเป็น 2.80, 2.54 และ 2.48 เท่าของผู้ป่วยที่ใช้ AVF ดัชนีมวลกายปกติ และมีประวัติการคาสาย CVC ไว้น้อยกว่าหรือเท่ากับ 90 วัน ตามลลำดับ (P; <0.001, 0.049, 0.029 ตามลำดับ) เมื่อทำการวิเคราะห์แบบหลายตัวแปรใน AVF AVG และ TC พบว่า ผู้ป่วยที่มี AVG ดัชนีมวลกายมากว่าหรือเท่ากับ 30 กก./ม. มีโอกาสเสี่ยงที่จะสูญเสียหน้าที่ของเส้นฟอกเลือดเป็น 3.04 และ 2.57 เท่าของผู้ป่วยที่ใช้ AVF และ ดัชนีมวลกาย (P; <0.001, 0.028 ตามลำดับ) นอกจากนี้ยังพบว่า ผู้ป่วยที่ใช้ TC มีโรคหลอดเลือดส่วนปลาย และมีภาวะอัลบูมินต่ำ (น้อยกว่า 3.5 ก./ดล.) มีแนวโน้มที่จะมีโอกาสเสี่ยงที่ทำให้เส้นฟอกเลือดเสียหน้าที่ได้ ดังนั้น ผู้ป่วยที่ฟอกเลือดด้วยเครื่องไตเทียมแบบเรื้อรังที่ใช้ AVF ลดระยะเวลาการคาสาย CVC ไว้ และควบคุมน้ำหนักตัวให้คงที่น่าจะมีผลดีกับผู้ป่วยที่ฟอกเลือดด้วยเครื่องไตเทียม

คำสำคัญ: โรคไตระยะสุดท้าย, การฟอกเลือดด้วยเครื่องไตเทียม, เส้นฟอกเลือด

Key Words: End stage renal disease, Hemodialysis, Vascular access

Introduction

The prevalence of HD (hemodialysis) in Thailand increased from 2007 to 2008, with an estimated 26,438 pmp (patients per million populations) (The Nephrology Society of Thailand, 2010). A well-functioning vascular access (VA) is required necessary for HD patients. Vascular access complications can lead to increased morbidity, hospitalization, and costs (Bethesda, et al., 2010). These all lead to significantly reduce quality of life for patients with ESRD (end stage renal disease). Thus, long-term HD vascular access patency becomes a critical issue, VA care require close management by health care provider team composed of nephrologists, HD nurses, vascular surgeons, and interventionist radiologists. However, many studies have shown that vascular patency and many risk factors affect to reduce vascular patency, but there have been limited data for functional patency and clinical factors for long term vascular access are not clear.

Objective of the study

The aim of this study was to compare survival functional time of tunneled cuffed catheters (TCs), arteriovenous fistulae (AVFs), and arteriovenous grafts (AVGs) and determine clinical factors affecting their survival function.

Methodology

Samples

This was a retrospective study of 399 ESRD patients receiving chronic HD treatment (> 3 months) from 1 January 1997 to 31 December 2012. All data were collected in the Kidney Foundation of Thailand at the Priest Hospital. This study was approved by the ethical committee for human research, Faculty of Public Health, Mahidol University, and the Kidney foundation of Thailand. The data was collected from HD work sheets, patient applications forms, history of illness, and physician progress notes and hemodialysis order sheets. Baseline characteristic data included demographic data (e.g. age at enrolled, gender, body weight, height, hospital creating vascular access) and clinical data consisted of type of VAs, anatomical locations of VAs, comorbidities, medications used (such as ACEI or ARB, anti-platelet drugs), history of previous CVC, lab results (e.g. serum albumin, calcium, phosphate, parathyroid hormone [PTH], hematocrit [Hct]).

Definitions

Primary unassisted patency was defined as the interval time from access creation to the first failure without intervention (vascular access thrombosis) or, the time from vascular access creation to the time of any intervention needed to maintain patency (surgical revision, angioplasty, balloon, stent, or thrombolysis) or, reaching a censored event.

Cumulative patency was defined as the interval time from access creation to permanent failure (vascular access thrombosis) which included the time of failure with intervention (surgical revision, angioplasty, balloon, stent, or thrombolysis) or reaching a censored event.

Post – intervention primary patency was defined as the interval time from access intervention (surgical revision, angioplasty, balloon, stent, or thrombolysis) needed to improve function until the next access thrombosis or re-intervention or reaching a censored event.

Primary functional patency was defined as the interval time from the date of successful first use of the access for hemodialysis to the first failure

without intervention (vascular access thrombosis) or, the time from vascular access creation to the time of any intervention needed to maintain patency (surgical revision, angioplasty, balloon, stent, or thrombolysis) or, reaching a censored event.

Cumulative functional patency was defined as the interval time from date of successful first use of the access for hemodialysis to date of thrombosis which included the time of failure with intervention (surgical revision, angioplasty, balloon, stent, or thrombolysis) or reaching a censored event.

Statistical methods

Descriptive statistics were performed to describe baseline characteristics, which included the assessment for continuous variables, means and standard deviations, minimum and maximum values or median and interquartile ranges were used. For categorical variables, proportion and percentage were used.

The comparison of patient baseline characteristics that determined by Chi-square test for categorical variables and independent continuous variables were analyzed to compare median by Mann-Whitney test for 2 groups and Kruskal-Wallis test for more 2 groups.

Survival analysis was used to assess vascular patency. Log rank test was used for comparison. The significant level of statistical tests was set at $\alpha = 0.05$ (P - value < 0.05). The HR of loss of primary functional patency was performed. Cox' x regression was performed for multivariable analysis. The variables chosen for inclusion in the multivariable Cox' x regression were those found in the bivariate analyses to be significantly (P – value < 0.05) associated with loss of primary functional patency. However, the variables were not significantly but those were objective of this study were included in the multivariable analysis.

Results

Baseline characteristics during the study period, 552 VAs were created in 399 patients. There were 463 (83.9%) patients with AVFs, 69 (12.5%) patients with AVGs and 20 (3.6%) patients with TCs. Median age of patients at initiated vascular access creation was 38.6 years (range, 29.6 to 48.4 years). Median time HD of patients was 9.4 years (range, 5.6 to 12.9 years). The baseline characteristics of the patients were listed in Table 1.

Primary functional patency rates had shown in figure 1. Primary functional patency rates at 12, 24, and 60 months for AVFs were 90.3 %, 87.4 % and 79.4 %, respectively, for AVGs were 81.9 %, 58,4 %, 32.5 %, respectively and for TCs were 73.9 %, 51.7 % and 38.3 %, respectively.

Median primary functional patency for AVFs was 61.1 months (95% CI, 21.1 - 119.0) longer than AVGs was 44.3 months (95% CI, 21.8 - 66.9), and TCs was 29.6 (95% CI, 12.6 - 46.6)

Considering only AVFs and AVGs, the HR of VA dysfunction by multivariable Cox' x regression analysis was 2.80 times (95% CI, 1.69 - 4.68) with patients with AVGs higher than patients with AVFs (P = <0.001). Moreover, patient had BMI $\geq$ 30 kg/m^2 (HR 2.54 [95% CI, 1.01 - 6.44], P = 0.049) and history of retained central venous catheter (CVC) more 90 days (HR 2.48 [95% CI, 1.10 - 5.59], P = 0.029) were the risk factors to predict primary functional vascular dysfunction.

Table 3, All 3 type VAs were analyzed. There found that patients with AVGs and had BMI $\geq$ 30 kg/m^2 were the risk factors for loss of primary

functional patency (HR 3.04 [95% CI, 1.82 - 5.02], P = <0.001 and HR 2.57 [95% CI, 1.11 - 5.92], P = 0.028, respectively).

However, patients with TCs, presence of PVD, Hct <30 and >36 %, hypoalbuminemia (serum albumin < 3.5 g/dl) were not significantly but those had trend toward to predict VA dysfunction.

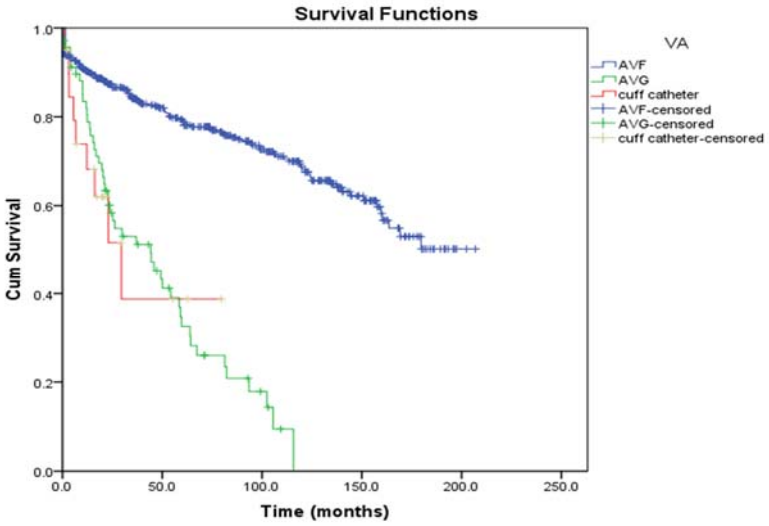

Figure 1 Primary functional patency of VA

Table 1 Baseline characteristics of HD patients by type of vascular access

Variables	AVF n (%)	AVGs n(%)	TC n(%)	All VA n(%)	P-value
Female gender	213(76.1)	51(18.2)	16(2.9)	280(50.7)	<0.001[a]
Comorbidities					
Diabetes	39(75.0)	11(21.2)	2(3.8)	52(9.4)	0.136[a]
Hypertension	405(86.5)	52(11.1)	11(2.4)	468(84.8)	<0.001[a]
CAD	22(84.6)	4(15.4)	0(0)	26(4.7)	0.557[a]
CVD	11(68.8)	2(12.5)	3(18.8)	16(2.9)	0.004[a]
PVD	1(25.0)	3(75.0)	0(0)	4(0.7)	0.001[a]
Type of Hospital					0.795[a]
Private	98(82.4)	17(14.3)	4(3.4)	119(21.6)	
Government	365(84.3)	52(12.0)	16(3.7)	442(78.4)	
Anatomical location					0.632[a]
Upper arm	132(86.3)	21(13.7)		153(28.9)	
Fore arm	331(87.8)	46(12.2)		377(71.1)	

Table 1 Baseline characteristics of HD patients by type of vascular access (Cont.)

Variables	AVF	AVGs	TC	All VA	P-value
	n (%)	n(%)	n(%)	n(%)	
Medications use					
ACEI or ARB use	40(87.0)	6(13.0)	0(0)	46(8.3)	0.389[a]
Anti-platelet agents use	23(79.3)	3(10.3)	3(10.3)	29(5.3)	0.143[a]
Time to first cannulate (days), n= 386, 58 (median [IQR; Q1-Q3])	90(61.0-92.0)	61(32.5-145.5)	87(61-92)	<0.001[b]	
Serum albumin (mg/dl) n=295, 45, 16 (median [IQR; Q1-Q3])	3.9(3.5-4.2)	3.9(3.6-4.2)	4.0(3.6-4.4)	3.9(3.5-4.2)	0.768[c]
Hematocrit (%) n=376, 54, 17 (median [IQR; Q1-Q3])	24(20-29)	27(22.8-31.2)	30(22.2-32.3)	24.2(20.1-30.3)	0.004[c]
Serum calcium (mg/dl) n= 347, 53, 18 (median [IQR; Q1-Q3])	9(8.0-9.8)	9.5(8.1-10.0)	9.6(8.6-10.2)	9(8.1-9.8)	0.135[c]
Serum phosphate (mg/dl) n= 343, 53, 18 (median [IQR; Q1-Q3])	5.9(4.3-7.3)	5.2(3.9-7.2)	4.4(3.5-5.6)	5.6(4.2-7.1)	0.010[c]
Ca×P (mg^2/dl^2) n= 342, 53, 18 (median [IQR; Q1-Q3])	50.0(39.2-64.0)	48.4(34.7-67.1)	37.6(32.1-57.7)	49.3(37.4-63.9)	0.074[c]
PTH (mg/dl) n= 94, 23, 7 (median [IQR; Q1-Q3])	191.1(67.5-447.5)	142.1(83.0-474.0)	360(129.5-911.1)	180.9(78.4-465.5)	0.503[c]

[a]P value base on χ^2 test, [b]P value base on Mann-Whitney U test, [c]P base on Kruskal-Wallis Test

AVF , arteriovenous fistula; AVG ,arteriovenous graft; TC, tunneled cuff catheter; VA ,vascular access ; CVC , temporary central venous catheter; CAD ,coronary artery disease;

CVD ,cerebrovascular disease; PVD, peripheral vascular disease; PTH ,parathyroid hormone; ACEI, angiotensin-converting enzyme inhibitor; ARB, angiotensin receptor blocker

Table 2 Adjust HR of primary functional patency loss in patients with AVF, and AVG

Variables		adjusted HR (95% CI)	P-value
Type of VA			
	AVF	1	
	AVG	2.80 (1.69-4.68)	<0.001[a]
PVD	absence	1	
	presence	1.64 (0.20-13.67)	0.649[a]

Table 2 Adjust HR of primary functional patency loss in patients with AVF, and AVG (Cont.)

Variables	adjusted HR (95% CI)	P-value
BMI (kg/m²)		
<18.5	1.06 (0.66-1.71)	0.811 [a]
18.5-24.9	1	
25-29.9	1.01 (0.39-2.60)	0.982 [a]
≥30	2.54 (1.01-6.44)	0.049 [a]
Hematocrit (%)		
<30	1.44 (0.84-2.47)	0.190 [a]
30-36	1	
>36	1.25 (0.49-3.21)	0.885[a]
Serum albumin (g/dl)		
<3.5	1.46 (0.81-2.45)	0.228 [a]
≥3.5	1	
Duration of CVC (days)		
≤ 90	1	
>90	2.49 (1.10-5.59)	0.029 [a]

[a]P after adjusted for age, gender, hypertension, serum calcium.

AVF, arteriovenous fistula; AVG, arteriovenous graft; VA, vascular access; CVC, central venous catheter; PVD, peripheral vascular disease

Table 3 Adjust HR of primary functional patency loss in patients with TC, AVF, and AVG

Variables	adjusted HR (95% CI)	P-value
Type of VA		
AVF	1	
AVG	3.04 (1.82-5.09)	<0.001[a]
TC	1.38 (0.53-3.59)	0.515 [a]
PVD absence	1	
presence	1.62 (0.20-13.29)	0.654[a]
BMI (kg/m²)		
<18.5	1.16 (0.73-1.86)	0.532 [a]
18.5-24.9	1	
25-29.9	1.00 (0.39-2.57)	1.000 [a]
≥30	2.57 (1.12-5.96)	0.028 [a]

Table 3 Adjust HR of primary functional patency loss in patients with TC, AVF, and AVG (Cont.)

Variables	adjusted HR (95% CI)	P-value
Hematocrit (%)		
<30	1.31 (0.78-2.01)	0.304 [a]
30-36	1	
>36	1.41 (0.59-3.65)	0.439 [a]
Serum albumin (g/dl)		
<3.5	1.52 (0.89-2.60)	0.128 [a]
≥3.5	1	

[a]P after adjusted for age, gender, , hypertension, serum calcium

AVF, arteriovenous fistula; AVG, arteriovenous graft; TC, tunneled cuffed catheter; VA, vascular accesses; PVD, peripheral vascular disease

Discussion and conclusion

These study retrospective analyzed 399 patients with 522 VAs to determine clinical factors for loss of primary functional patency after first used. In this study, the majority of patients initiated permanent vascular access placements were AVF (83.9%) that corresponding with the K/DOQI Clinical Practice Guideline for Vascular Access, update 2006, promoted the implementation of the Fistula First. The results demonstrated that AVFs had a better primary functional patency than AVGs and TCs, similar to previous reports (Bradley S.Dixon LN, et al., 2002; Suwanruangsri Veera, et al., 2008; Hemmati Hossein, et al., 2011).

Obesity is defined as BMI $\geq$ 30 kg/m^2 (World Health Organization [WHO], 2012). The creation and maintenance of permanent hemodialysis access, particularly AVFs, are generally considered more difficult in the obese patients because of the increased risk of perioperative complications, as well as a decreased maturation rate (Troy J, et al., 2007; Robert J. Feezor, et al., 2011). The National Kidney Foundation (K/DOQI), 2006 guidelines use the "rule of 6s" (i.e., 6 mm diameter vein, 6 mm. depth from skin, 600 mL/min) as their criteria for initiating access cannulation. Although the AVF may dilate sufficiently to satisfy the diameter criteria, it often needs to be elevated or superficialized to facilitate repeated cannulation and effective dialysis but the depth of superficial veins in obese patients may be too deep for cannulation the access. The result demonstrated that BMI $\geq$ 30 kg/m^2 was a significant factor in predicting primary functional vascular dysfunction, similar to report of Kats et al (2007).

Prior temporary catheters are known to cause central vascular stenosis. The interaction of different factors including the presence of CVC within the vessel, turbulence of the blood flow, endothelial injury, uremic milieu and inflammatory response play an essential role in development of central venous stenosis (CVS) (K/DOQI, 2006). An association of patient who receiving HD via CVC with a risk for vascular failure had been reported in many studies (Rayner Hugh C, et al., 2003; Ivan D, et al., 2009; Schinstoch Carrie A, et al., 2011). Moreover, Ghisliane Medkouri RA, et al. (2006)

reported that the number of prior temporary catheters used was related to an increased risk of thrombosis, but there had a little data for duration of prior temporary catheters used. This study demonstrated that long-term of prior CVC used duration (> 90 days) influenced to loss of primary functional patency.

Among patients with PVD, those receiving AVG were likely the greatest because of those with PVD are likely to be poor small vessels and inadequate collateralization (Wilson SE., et al., 2010). However, our study remains a small group of data on baseline patients having presence of PVD. Presence of PVD was not significantly related to primary vascular access patency; however, patients having presence of PVD was trend toward for vascular access dysfunction.

In conclusion, this study showed that HD patients should benefit from normal BMI maintenance and reduction of duration of CVC used.

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