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Prevalence and Risk Factors of AV Fistula Stenosis on patient with CKD

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ABSTRACT

Aim: AV fistula obstruction has become one of the main vascular access complications in patients undergoing haemodialysis. This complications have significant impacts on the morbidity and mortality of dialysis patients while also leading to higher medical costs. Clinical monitoring has been routinely used for early detection of AV fistula stenosis and obstruction, however screening with Doppler ultrasound is still not a routine recommendation. This study aims to know prevalence and risk factors of AV Fistula obstruction detected by Duplex ultrasound examination.

Methods: This study was a hospital-based descriptive analytic study with cross sectional design conducted at the haemodialysis center of National General Hospital Dr. Sardjito, Yogyakarta, Indonesia. Patient demographic and clinical risk factor were recorded using direct interview. AV fistula obstruction were assessed using Duplex ultrasound by professional sonographer.

Results: Seventy four (74) patients are using AV fistula as entry access for hemodialysis in RSUP dr. Sardjito. It is consist of 39 male (53%) and 35 Female (47%). The mean age of patients is 50 years old. Surveillance using Doppler ultrasound found 20 patients (27%) have stenotic AV Fistula. Smoking habits (OR 5.37, 95% CI, 1.760 - 16.431, p=0.002) and diabetes mellitus (OR 5.00, 95% CI, 1.631 – 15.503, p=0.004) increase risk for having stenotic AV fistula. Only 4 patient (20%) of all 20 patient with stenotic AV fistula were symptomatic, and needed for further vascular intervention.

Conclusion: Prevalence of AV fistula obstruction detected by Doppler ultrasound was 27% of all AV fistula patient with only 5% had symptomatic AV fistula failure. Smoking habits and diabetes mellitus are important risk factor for AV fistula obstruction. Asymptomatic AV fistula obstruction often goes undetected by clinical monitoring that can increase of risk of symptomatic AV fistula obstruction in the future. The further study is needed to determine level recommendation of routine AV fistula surveillance with Doppler Ultrasound.

INTISARI

Tujuan: Obstruksi fistula AV adalah salah satu komplikasi akses vaskular utama pada pasien yang menjalani hemodialisis. Komplikasi ini memiliki dampak yang signifikan terhadap morbiditas dan mortalitas pasien hemodialisis sehingga menyebabkan biaya medis yang lebih tinggi. Pemantauan klinis telah rutin digunakan untuk deteksi dini obstruksi fistula AV, namun skrining dengan USG dupleks masih belum menjadi rekomendasi rutin. Penelitian ini bertujuan untuk mengetahui prevalensi dan faktor risiko obstruksi AV Fistula yang dideteksi pada pemeriksaan USG dupleks. **Metode:** Penelitian ini merupakan penelitian deskriptif analitik berbasis rumah sakit dengan desain potong lintang yang dilakukan di Pusat Hemodialisa Rumah Sakit Umum Daerah Dr. Sardjito Yogyakarta, Indonesia. Profil demografis pasien dan faktor risiko klinis dicatat menggunakan wawancara langsung. Obstruksi AV fistula dinilai menggunakan ultrasound dupleks oleh sonografer berkompetensi.

Hasil: Tujuh puluh empat (74) pasien menggunakan AV fistula sebagai akses vaskular untuk hemodialisis di RSUP dr. Sardjito. Subjek terdiri dari 39 lakilaki (53%) dan 35 perempuan (47%). Usia rata-rata pasien adalah 50 tahun. Surveilans menggunakan USG Doppler menemukan 20 pasien (27%) memiliki obstruksi fistula AV. Merokok (OR 5.37, 95% CI, 1.760 - 16.431, p=0.002) and diabetes mellitus (OR 5.00, 95% CI, 1.631 – 15.503, p=0.004) meningkatkan risiko terjadinya obstruksi fistula AV. Hanya 4 pasien (20%) dari 20 pasien dengan obstruksi fistula AV yang menunjukkan gejala simtomatis sehingga membutuhkan intervensi vaskular lebih lanjut.

Kesimpulan: Prevalensi obstruksi AV fistula yang terdeteksi oleh USG dupleks adalah sekitar 27% dari semua pasien dengan fistula AV meskipun hanya 5% yang menunjukkan gejala. Merokok dan diabetes mellitus adalah faktor resiko penting terjadinya obstruksi AV fistula. Obstruksi AV fistula asimtomatik sering tidak terdeteksi oleh pemantauan klinis dan dapat berujung pada risiko obstruksi fistula AV simtomatik di masa depan. Perlu dilakukan penelitian lebih lanjut untuk menentukan tingkat rekomendasi surveilans rutin AV fistula dengan Doppler Ultrasound.

Introduction

Chronic kidney disease (CKD) is a global health problem with high economic burden and become independent risk factor for the incidence of cardiovascular disease (CVD). All stages of CKD are associated with the increased risk of cardiovascular morbidity, mortality, and decreased quality of life (Hill et al., 2016). In 2013, the prevalence of CKD globally was around 8-16% of total population (Jha et al., 2013). In 2018, the prevalence of CKD in Indonesia was 3.8% of total population with the age group 65-74 years having the highest prevalence (Riskesdas, 2018). Chronic kidney disease will eventually progress to end-stage renal disease so that requiring renal replacement therapy (Schroeder et al., 2017). Hemodialysis is the most frequently used method of renal replacement therapy, accounting for 95% of total renal replacement therapy (IRR, 2016). AV fistula was used in 92% of total hemodialysis (Pisoni et al., 2015).

AV fistulas obstruction consisting of stenosis (14% - 42%) and thrombosis (17% - 25%) are still the main problem. The complications associated with vascular access will increase morbidity, reduce the patient's quality of life, and increase treatment costs (Ren et al., 2018) (MacRae *et al.*, 2016) (Stolic R, 2013). In addition, stenosis and thrombosis will affect the patency rate of the AV Fistula. (Kazemzadeh *et al.*, 2012). This poor patency will prevent adequate hemodialysis from being achieved, resulting in increased morbidity and mortality by 51% and 18.2%, respectively. Therefore, frequent AV fistula monitoring is recommended by *Kidney Disease Outcomes Quality Initiative* (KDOQI) once a month (KDOQI, 2018).

The results of the diagnostic study by Asif et al (2007) which compared physical examination with angiography in detecting stenosis in arterio-venous fistulas showed that the sensitivity and specificity for outflow and inflow stenosis were 92%, 86%, 85 and 71%, respectively. Meanwhile, he results of a study by Maldonado-Cárceles *et al.*, (2017) which compared the accuracy of physical examination compared to ultrasonography on AV fistulas showed that the sensitivity and specificity were 82% and 67%.

KDOQI (2018) has not recommended Doppler ultrasonography (DUS) in a routine examinations for AV fistula obstruction. However, DUS is a highly accurate method of detecting stenotic artery lesions (sensitivity and specificity: 91% and 100%, respectively, for the subclavian artery; 93% and 100% for arteries in the upper arm; 89 and 99% for the arm. below), obstructive artery lesions (sensitivity and specificity 90% and 99%) (Zamboli *et al.*, 2014).

Methods

This study was a hospital-based descriptive analytic study with cross sectional design conducted at the haemodialysis Centre of National General Hospital Dr. Sardjito, Yogyakarta, Indonesia. All patients with AV Fistula undergoing routine haemodialysis in the Dr. Sardjito Hospital from February 2021 to April 2021, who meet the inclusion criteria will be subjects in this study. The inclusion criteria of this study were 1) Patients who have been diagnosed with end-stage chronic kidney disease undergoing routine hemodialysis 2) Patients who have been using AV Fistula at least for 2 months.

Patient demographic and clinical risk factor were recorded using direct interview. AV fistula obstruction were assessed using Doppler ultrasound by competent sonographer if any significant stenosis or thrombosis. The peak systolic velocity greater than 500 cm/s in Doppler ultrasound is used to determine the existence of significant stenosis.

Statistical analysis was performed with IBM SPSS Statistics 23 software. Categorical variables were displayed as frequencies and percentages. Continuous variables with normal data distribution were shown as mean ± standard deviation (SD), while variables without normal distribution were shown as median (minimum-maximum). Analysis of normality was performed using the Kolmogorov–Smirnov test. A chi-square test was used to compare categorical variables. To identify independent predictors of AV stenosis, logistic regression analysis was performed by entering parameters that had a value of p <0.25.

Results

There were 101 patients found to be undergoing routine haemodialysis at Dr. Sardjito Hospital in the period from October 2020 to April 2021. This study found about 74 patients were currently using AV Fistula for at least 2 months as entry access for haemodialysis. It was consist of 39 male (53%) and 35 Female (47%). The mean age of patients was 50 years old (21-85 years). The most common comorbidity found in patient undergoing routine haemodialysis using AV fistula was hypertension (81,1%), followed by smoking (28,4%), diabetes mellitus (26,7%), obesity (25,7%) heart disease (11,0%) and history of stroke (6,6%).

Surveillance using Doppler ultrasound found 54 patients (73%) have patent AV fistula and 20 patients (27%) with stenotic AV Fistula. Demographic and baseline characteristic of patent AV fistula group and stenotic AV fistula group are presented in (Table 1). We analysed association between several risk factors and incidence of stenotic AV fistula. We found that smoking habits (p=0.002) and diabetes (p=0.004) mellitus are associated with incidence of stenotic AV fistula whereas hypertension (p=0.600), obesity (p=0.382), history of stroke (p=0.499) and history of heart disease (p=480) exhibited nonsignificant result.

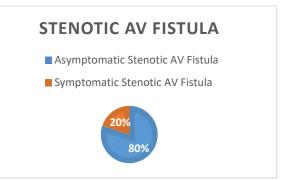
Logistic regression analysis was performed on to identify independent predictors for stenotic AV fistula and found that smoking habits and diabetes mellitus increase risk for having stenotic AV fistula (Smoking; OR 5.37, 95% CI, 1.760 - 16.431) (Diabetes Mellitus; OR 5.00, 95% CI, 1.631 – 15.503)

From 20 patients with stenotic AV Fistula detected by Doppler ultrasound, 16 patients (80%) were asymptomatic, and only 4 patients (20%) were symptomatic (Figure 1). Symptomatic patients complain that they feel frequent pain and have prominent edema on arm with AV fistula. Symptomatic patients also needed further vascular intervention because vascular access difficulties during haemodialysis **Table 1.** Demographic and Clinical Risk Factor of Patients with AV

 Fistula

Fistula			
Variables	Patent AV Fistula	Stenotic AV Fistul	р
	(n=54)	(n=20)	
Age (years)	51 (26-85)	48 (21-65)	
(mean/min-max)			
Sex (n, %)			
Male	29 (53.7%)	10 (50%)	
Female	25 (46.3%)	10 (50%)	
Systolic	141.51 <u>+</u> 21.51	151.25 <u>+</u> 16.83	
Blood Pressure			
(mean <u>+</u> SD)			
BMI	22.53 <u>+</u> 3.56	23.72 <u>+</u> 4.73	
(mean <u>+</u> SD) (Kg/m ²)			
Risk Factor			
Hypertension, n (%)			0.600
Yes	43 (79.6%)	17 (85.0%)	
No	11 (20.4%)	3 (15.0%)	
Smoking, n (%)			0.002
Yes	10 (18.5%)	11 (55.0%)	
No	44 (81.5%)	9 (45.0%)	
Diabetes Mellitus,			0.004
(%)			
Yes	9 (16.7%)	10 (50.0%)	
No	45 (83.3%)	10 (50.0%	
Obesity, n (%)			0.382
Yes	11 (20.4%)	6 (30.0%)	
No	43 (79.6%)	14 (70.0%)	
Heart disease, n (%)			0.480
Yes	5 (9.3%)	3 (15%)	
No	49 (90.7%)	17 (85%)	
Stroke, n (%)			0.499
Yes	3 (5.6%)	2 (10%)	
No	51 (94.4%)	18 (90.0%)	

Figure.1 Distribution of patient with AV Fistula Stenosis.



Vascular access is one of the main factors of successful haemodialysis practice. In this study, we are screening patient with chronic kidney disease that require routine hemodialysis in hemodialysis unit of RSUP dr. Sardjito from October 2020 until April 2021. We found that majority of patients that are doing routine hemodialysis are using AV Fistula as entry access which are 74 patient of 101 total patients (73%). Other method for hemodialysis entry access are by using *central venous catheter (CVC)* (25%) and synthetic arteriovenous graft (AVG) (2%). The Kidney Disease Outcomes Quality Initiative (KDOQI) guideline states that AV fistula is the most common vascular access and used by more than 65% of total patients receiving hemodialysis (KDOQI, 2006). Successful functional AVfistula can be used for a long time with low thrombosis and infection rates (Ravani et al., 2013).

We analysed association between several risk factors and incidence of stenotic AV fistula. We found that smoking habits (OR 5.37, 95% CI, 1.760 - 16.431, p=0.002) and diabetes mellitus (OR 5.00, 95% CI, 1.631 - 15.503, p=0.004) increase risk for appearance of stenotic AV fistula. A meta-analysis of the association between diabetic patients and AVF failure in dialysis revealed a statistically significantly higher rate of AVF failure in diabetic patients compared with nondiabetic patients. The pooled OR estimate for the AVF failure of diabetic patients was 1.682 (95% CI, 1.429–1.981, Test of OR = 1: z = 6.25, p < .001) (Yan et al., 2018). Tobacco smoking is a well-known risk factor for vascular disease and arteriosclerosis. Wetzig et al. (1985) first described the direct link to AVF failure and reported a significantly higher incidence of early and late fistula failure in patients who were cigarette smokers, findings that have since been confirmed by other studies (Smith *et al.*, 2012)

Our surveillance using USG Doppler found 20 patients (27%) using AV Fistula has AV Fistula stenosis. Other study compared the prevalence of HD access obstruction found stenosis 36/122 (29%) in AV grafts and 41/101 (40%) in AV fistulas. The cumulative incidence was 77/223 (35%) (Asif et al., 2007). KDOQI guidelines define significant stenosis of the vessel lumen as a reduction by more than 50%. The peak systolic velocity (PSV) in Doppler ultrasound can be used to determine the presence of stenosis. Values greater than 500 cm/s indicate the presence of stenosis. PSV of \geq 500 cm/s predicted a 50% or greater stenosis with a sensitivity of 89% (95% confidence interval 87-91) and PPV of 99% (99-100) (Wo et al., 2016). Symptomatic AV fistula stenosis is detected by the presence of signs and symptoms such as reduced quality of dialysis. difficulty to gain vascular access with puncture, prolonged bleeding after AVF puncture, pain in the area of the fistula or increased venous pressure. Prolonged stenosis can increase risk of thrombosis of AV fistula. It usually occurs near a stenosis in the area of anastomosis or fistula vein. The risk of thrombosis increases with the degree of stenosis. Thrombosis is a crucial cause of loss of function of an AVF (Stoic, 2013).

This study found only 4 patients (20%) of patient with AV Fistula stenosis exhibited symptoms. In this case, 80% of patients with AV fistula stenosis were undetected. This can lead to unpredictable AVF failure that can cause poor quality and ineffective haemodialysis which may worsen the patient's illness. Doppler ultrasound is important examination for early detection of AV fistula stenosis, thrombosis and failure.

There is study that found a significant reduction in the thrombosis rate in the AV fistula patient group (QA group) that measured quarterly using Doppler ultrasound (0.025 thrombosis/patient/year in the QA group vs. 0.086 thrombosis/patient/year in the control group [p = 0.007]). There was a significant improvement in the thrombosisfree patency rate (HR, 0.30; 95% CI, 0.11-0.82; p = 0.011) and in the secondary patency rate in the QA group (HR, 0.49; 95% CI, 0.26-0.93; p = 0.030), with no differences in the primary patency rate between the groups (HR, 0.98; 95% CI, 0.57-1.61; p = 0.935). There was greater need for a central venous catheter and more hospitalizations associated with vascular access in the control group (p = 0.034/p = 0.029). Total vascular access-related costs were higher in the control group (\notin 227.194 vs. \notin 133.807; p = 0.029) (Aragoncillo et al., 2017).

Conclusions

Prevalence of AV fistula obstruction detected by Doppler ultrasound was 27% of all AV fistula patient with only 5% had symptomatic AV fistula failure. Smoking and diabetes mellitus are strong risk factor for AV fistula obstruction. Asymptomatic AV fistula obstruction often goes undetected by clinical monitoring that can increase of risk of symptomatic AV fistula obstruction in the future. The further study is needed to determine level recommendation of routine AV fistula surveillance with Doppler Ultrasound.

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Disclosures and Ethics

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