Original Article

Serum endothelial injury markers in hemodialysis patients with arteriovenous fistula stenosis

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ABSTRACT

Background：In hemodialysis patients, failure of arteriovenous fistula（AVF）is a serious problem. AVF stenosis is dominant cause of vascular access failure. We hypothesized that vascular endothelial damage may be involved in arteriovenous fistula（AVF）stenosis.

Methods：A cross-sectional observational survey was performed in 122 patients receiving maintenance hemodialysis in January - April 2004. Serum levels of adiponectin, adhesion molecules（intercellular adhesion molecule-1；ICAM-1 and vascular cell adhesion molecule-1；VCAM-1）, and endothelial injury markers（CD146 and thrombomodulin）were compared between 46 patients with AVF stenosis and 76 patients without AVF stenosis to determine factors associated with AVF stenosis.

Results：The serum adiponectin level was significantly lower in patients with AVF stenosis compared to those without AVF stenosis. Similarly, the serum levels of ICAM-1 and thrombomodulin were significantly lower in patients with AVF stenosis, whereas the serum level of VCAM-1 was significantly higher in patients with AVF stenosis. There were no significant differences in other parameters between the two groups. Logistic regression analysis with the presence or absence of AVF stenosis as the dependent variable showed that administration of an antihypertensive drug, VCAM-1, ICAM-1 and thrombomodulin were significantly associated with the presence of AVF stenosis in hemodialysis patients.

Conclusion：The significant associations of administration of an antihypertensive drug, VCAM-1, ICAM-1 and thrombomodulin with AVF stenosis suggest that endothelial injury may play a critical role in this condition.

（Key words：adhesion molecule, arteriovenous fistula stenosis, endothelial injury, hemodialysis）

INTRODUCTION

Vascular access failure is the dominant cause of morbidity and a major cost in care for patients on hemodialysis[1]. A native arteriovenous fistula（AVF）remains the preferred route for primary vascular access in hemodialysis patients because of its superior patency and lower complication rates compared to a prosthetic graft. The most frequent complications of AVF are stenosis of the anastomosis, draining vein or central vein, and subsequent thrombosis in the outflow vein[2]. Interventional therapy such as percutaneous transluminal angioplasty（PTA）remains the standard treatment for salvage of stenosis, but the long-term patency rate after interventional therapy is unsatisfactory[3]. Reduction of the rate of AVF complications requires improved understanding of the vascular pathology of thrombosed or stenotic AVFs.

Adiponectin is an adipose tissue-derived cytokine that was first identified in a human adipose tissue cDNA library[4]. Clinically, serum adiponectin levels are reduced in various pathological states, including obesity, diabetes mellitus and ischemic heart disease[5, 6]. Hypoadiponectinemia increases the prevalence of ischemic heart disease by 2-fold[7], which suggests that adiponectin might act as a protective factor against atherosclerosis. Serum adiponectin levels are also lower in hemodialysis patients with cardiovascular events compared to those without cardiovascular events[8]. Experimental data suggest that adiponectin inhibits endothelial expression of

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adhesion molecules, including vascular cell adhesion molecule (VCAM-I), intercellular adhesion molecule (ICAM-I) and E-selectin, which is triggered by inflammatory cytokines such as TNF α[9]. Thus, adiponectin may serve as a regulator of endothelial adhesion molecules. Malyszko et al.[10] also found a relationship between serum levels of adiponectin and CD146, a marker of endothelial cell injury, and suggested that CD146 might mitigate endothelial cell damage and cardiovascular risk.

It is well known that inflammation plays an important role in the development of various atherosclerotic vascular diseases in the general population, and thrombotic events in the human coronary artery have been associated with inflammation of affected vessels[11]. In uremic patients, inflammation also plays an important role in development of atherosclerotic vascular diseases[12]. We previously reported significant changes in serum adiponectin, adhesion molecules, and endothelial cell injury markers in ESRD patients with peripheral artery disease (PAD)[13]. AVFs are arteriovenous anastomoses and AVF stenosis mainly occurs at the venous limb or juxta-anastomotic region of the AVF. Therefore, we hypothesized that inflammation similar to that in arteries might be involved in stenotic AVFs, which is venous disease. Changes in serum adiponectin, adhesion molecules (VCAM-I and ICAM-I) and endothelial cell injury markers (CD146 and thrombomodulin) in AVF stenosis in hemodialysis patients have not been examined in detail. In the present study, we measured the serum levels of these molecules in patients on maintenance hemodialysis with and without AVF stenosis. The goal of this study was to determine clinical and laboratory correlates of AVF stenosis in hemodialysis patients.

METHODS

Subjects

This study was performed in Kotouda-Jin Clinic in January-April 2004. The subjects were 122 hemodialysis patients (90 men, 32 women) with a mean age of 60.9 ± 11.0 (mean ± SD) years old (range : 35 to 85 years old) (Table 1). The median duration of hemodialysis was 60 months (range : 2 to 355 months). Patients with active infection, autoimmune disease, liver dysfunction, or malignancies were excluded from the study. Sixty-four patients were being treated with antihypertensive drugs (angiotensin-converting enzyme inhibitors, β-blockers or calcium channel blockers) at the time of the study. Thirty-two patients were being treated with antiplatelet drugs. The causes of renal failure included diabetic nephropathy in 58 cases, glomerulonephritis in 28, nephrosclerosis in 23, polycystic kidney disease in 7, and unknown in 6 cases. All patients had native radiocephalic AV fistulas : on the right arm in 14 cases and on the left arm in 108 cases. All 46 patients with AVF stenosis were treated with interventional therapy in Kotoda-Jin Clinic during January-April 2004. The presence of AVF stenosis was confirmed by duplex ultrasound and angiography with identification of 50% or more stenosis. The number of past AV fistula stenoses for which interventional therapy was needed for salvage of stenosis was recorded for each treated patient. Eighteen patients had no previous episode of AVF stenosis ; 18 had one previous episode ; and 10 had two or more previous episodes. The data for the 46 patients (27 men, 19 women) with AVF stenosis were compared with those for the 76 patients (63 men, 13 women) without AVF stenosis. Informed consent for participation in the study was obtained from all patients.

Table 1. Clinical data for hemodialysis patients with and without arteriovenous fistula (AVF) stenosis

	Patients without AVF stenosis	Patients with AVF stenosis	P-value
N	76	46	
Sex(Male/Female)	63 / 13	27 / 19	0.15
Age (years)	61.9 ± 10.6	59.3±11.6	0.19
Duration of HD (month)	60 (10, 355)	60 (2, 343)	0.29
BMI	22.2 ± 2.7	22.4 ± 3.0	0.64
Diabetes mellitus (+/-)	37 / 39	21 / 25	0.85
LDL cholesterol (mg/dl)	101.1 ± 25.9	92.5 ± 29.4	0.10
HDL cholesterol(mg/dl)	44.2 ± 12.9	40.5 ± 13.2	0.13
Triglyceride (mg/dl)	123.2 ± 46.6	108.5 ± 50.4	0.09
Hemoglobin (g/dl)	10.2 ± 1.2	10.0 ± 1.0	0.48
Albumin (g/dl)	3.78 ± 0.47	3.82 ± 0.34	0.62
Kt/V	1.25 ± 0.20	1.32 ± 0.28	0.19
PCR	0.85 ± 0.11	0.86 ± 0.16	0.99
%CGR	101.1 ± 19.3	97.4 ± 27.7	0.42
Adiponectin (μg/ml)	10.3 (1.3, 50.8)	6.8 (0.6, 33.8)	0.003
CD146 (ng/ml)	579.2 ± 165.2	574.6 ± 155.0	0.88
Thrombomodulin (ng/ml)	56.8 ± 20.1	44.3 ± 18.4	0.001
VCAM-1 (ng/ml)	2220.9 ± 1341.3	4224.5 ± 1631.5	<0.001
ICAM-1 (ng/ml)	303.8 (18.7, 1014.8)	190.3 (18.7, 1213.9)	0.002
Medications			
Antihypertensive drug (+/-)	37/39	27 /19	0.35
Antiplatelet drug (+/-)	20/53	12/34	0.84

HD, hemodialysis; BMI, body mass index; PCR, protein catabolic rate ; %CGR, %creatinine generation rate.

Laboratory measurements

Blood samples were collected from the AVF immediately before the beginning of a routine 4-hour HD session for performance of routine blood tests in patients without AVF stenosis in April 2004. In patients with AVF stenosis, blood samples were collected from the AVF immediately before the beginning of interventional therapy in January-April 2004. Blood was collected in tubes and centrifuged at 3,000 rpm for 15 min at 4℃. The supernatants were decanted and frozen at –80 ℃ until analyses. We determined serum levels of adiponectin, ICAM-I, VCAM-I, CD146 and thrombomodulin. Serum adiponectin was measured by ELISA using an Adiponectin ELISA kit (Otsuka Pharmaceutical Co., Osaka, Japan). Serum levels of adhesion molecules (ICAM-I and VCAM-I) were measured by ELISA using kits from R&D Systems (Quantikine, Abingdon, UK). Mean serum levels of ICAM-I and VCAM-I of 230.3 ± 47.4 ng/ml and 550 ± 45 ng/ml, respectively, were determined by R&D Systems using these ELISAs in 50 healthy adults. Markers of endothelial cell injury (CD146 and thrombomodulin) were assayed using ELISA kits purchased from Biocytex (Cy-Quant™ ELISA, Marseille, France) and American Diagnostica (Greenwich, CT, U.S.A.), respectively. A mean serum CD146 level of 273

± 70 ng/ml was determined by Biocytex in 61 healthy adults and a mean serum thrombomodulin level of 4.46 ± 1.36 ng/ml was determined by American Diagnostica in 55 healthy adults. Other parameters were measured by standard laboratory methods. We calculated Kt/V based on dialyzer clearance of urea, using the prescribed blood and dialysate flow (K), treatment time (t), and anthropometric volume (V) in the formula of Daugirdas.

Statistical analyses

Values are shown as the mean ± SD for normally distributed data and as the median (minimum, maximum) for non-normal distributions, unless otherwise noted. Comparisons between groups with or without AVF stenosis were analyzed by unpaired t-test for normally distributed data, by Wilcoxon rank sum test for non-normal distributions, and by x^2 test for nominal variables (Tables 1 and 2). Logistic regression analysis was performed to examine the relationships of demographic, clinical and laboratory variables with the presence of AVF stenosis. VCAM-1, thrombomodulin, ICAM-1, male patients, administration of an antihypertensive drug, and adiponectin were included in logistic regression analysis (Table 3). All analyses were conducted using JMP ver. 8 (SAS Institute, Cary, NC, USA) software. $P<0.05$ was considered to be significant.

Table 2. Clinical data in patients with AVF stenosis based on episode frequency

	First episode	Plural episodes	P-value
N	18	28	
Sex(Male/Female)	9 / 9	18 / 10	0.37
Age (years)	56.3 ± 10.4	61.2 ± 12.1	0.16
Duration of HD (month)	54 (3, 300)	60 (2, 343)	0.99
BMI	22.9 ± 2.8	22.1 ± 3.1	0.35
Diabetes mellitus (+/-)	7 / 11	14 / 14	0.55
LDL cholesterol (mg/dl)	90.4 ± 27.6	93.8 ± 29.8	0.70
HDL cholesterol(mg/dl)	41.4 ± 15.2	39.9 ± 12.0	0.71
Triglyceride (mg/dl)	104.7 ± 35.1	114.0 ± 59.7	0.55
Hemoglobin (g/dl)	10.1 ± 1.1	9.9 ± 1.0	0.77
Albumin (g/dl)	3.84 ± 0.30	3.81 ± 0.36	0.76
Kt/V	1.22 ± 0.29	1.38 ± 0.26	0.06
PCR	0.82 ± 0.19	0.88 ± 0.14	0.25
%CGR	99.6 ± 29.8	95.9 ± 26.6	0.67
Adiponectin (μg/ml)	7.8 (2.2, 31.8)	6.1 (0.6, 33.8)	0.14
CD146 (ng/ml)	558.1 ± 159.5	585.2 ± 154.0	0.59
Thrombomodulin (ng/ml)	48.1 ± 18.8	41.9 ± 18.1	0.26
VCAM-1 (ng/ml)	4202.1 ± 1807.9	4238.9 ± 1542.0	0.94
ICAM-1 (ng/ml)	123.7 (18.7, 856.9)	243.9 (26.9, 1213.9)	0.07
Medications			
Antihypertensive drug (+/-)	10 / 8	17 / 11	0.77
Antiplatelet drug (+/-)	2 / 16	10 / 18	0.09

Table 3. Multiple logistic regression analysis for the presence of AVF stenosis in hemodialysis patients

	Odds Ratio	95% Confidence Interval	P-value
Male patient	0.315		0.052
Administration of an antihypertensive drug	3.225		0.047
Adiponectin (μg/ml)	0.947	0.871 - 1.019	0.168
Thrombomodulin (ng/ml	0.957	0.926 - 0.985	0.005
VCAM-1 (μg/ml)	2.766	1.944 - 4.265	<0.001
ICAM-1 (μg/ml)	0.045	0.926 - 0.985	0.032

RESULTS

The clinical profiles of the patients with / without AVF stenosis are shown in Table 1. There were no significant differences in sex, age, duration of HD, BMI, LDL, HDL, triglyceride, hemoglobin, albumin, Kt/V, protein catabolic rate (PCR) and creatinine generation rate (%CGR) between patients with and without AVF stenosis. The mean serum adiponectin level in patients with AVF stenosis was significantly lower than that in patients without AVF stenosis (6.8 (0.6, 33.8) vs. 10.3 (1.3, 50.8) μg/ml, $P<0.01$). Serum ICAM-1 and thrombomodulin were significantly lower and serum VCAM-1 was significantly higher in patients with AVF stenosis. There was no significant difference in serum CD146 between patients with and without AVF stenosis.

Of the 46 patients with AVF stenosis, 18 patients had first episode of AVF stenosis and 28 had plural episodes. Data for these sub-groups of patients are shown in Table 2. There were no significant differences in any measured parameters between patients with first and plural episodes.

To identify risk factors for AVF stenosis, multiple logistic regression analysis was performed with VCAM-1, thrombomodulin, ICAM-1, male patients, administration of an antihypertensive drug, and adiponectin as independent variables and the presence or absence of AVF stenosis as the dependent variable. In this analysis, administration of an antihypertensive drug, thrombomodulin, VCAM-1 and ICAM-1 were significantly associated with a risk of AVF stenosis in hemodialysis patients (Table 3).

DISCUSSION

Many factors have been associated with shorter survival of vascular access, including older age, black ethnicity, synthetic AV graft, small vein size, diabetes mellitus, erythropoietin therapy, increased haematocrit, reduction of fistula flow, hypoalbuminemia, increased lipoprotein, and the presence of anti-phospholipid antibody[14, 15]. Identification of cellular processes and proteins involved in AVF stenosis is also increasingly common. In this study, there were no significant differences in routine serum parameters between patients with and without AVF stenosis. However, there were significant differences in serum adiponectin, thrombomodulin, ICAM-1, and VCAM-1, which suggest that these molecules might be involved in the development of AVF stenosis.

Neointimal hyperplasia occurring at the venous limb or juxta-anastomotic region of the AVF is a fundamental mechanism contributing to AVF stenosis[16]. Neointimal hyperplasia progressively encroaches upon the vascular lumen, diminishes blood flow, and promotes thrombus formation secondary. While the basis of neointimal hyperplasia is uncertain, essential features of this lesion include proliferation and migration of smooth muscle cells and the phenotypic switch of smooth muscle cells from a contractile to a proliferative and synthetic phenotype[17]. In this study, there

were no significant differences in serum adiponectin, ICAM-1, VCAM-1 and thrombomodulin among hemodialysis patients with AVF stenosis sub-grouped based on episode frequency. These results indicate that changes of these inflammatory markers in AVF stenosis may represent a common process of damage regardless of episode frequency.

Inflammatory mediators play a key role in the pathogenesis of atherosclerosis. Early atherosclerotic development involves attraction and adherence of macrophages and lymphocytes to, and subsequent transmigration through, the vascular endothelium[18]. Adhesion molecules（E-selectin, ICAM-I and VCAM-I）are sequentially induced in endothelial cells within a few hours by inflammatory mediators such as interleukin-1（IL-1）, tumor necrosis factor-α（TNF-α）, and interferon-γ（IFN-γ）[19,20]. ICAM-1 and VCAM-1 are thought to regulate the adherence and subsequent transmigration of leukocytes across the vascular endothelium[21]. Serum levels of ICAM-1 and VCAM-1 have reported to be associated with inflammation, malnutrition, and death in patients with chronic kidney disease[22]. However, elevation in serum VCAM-1 and decrease of ICAM-1 were seen in patients with AVF stenosis in our study. The reason for the different effects on serum VCAM-1 and ICAM-1 is unclear. Both macrophages and endothelial cells produce ICAM-1 in response to inflammatory cytokines such as IL-1, TNF and IFN-γ, whereas VCAM-1 is mainly restricted to endothelial cells[23]. Moreover, expression of VCAM-1, but not of ICAM-1, has been shown to precede macrophage and T-lymphocyte recruitment to atheromatous plaques[24]. In the rabbit aorta after balloon injury, VCAM-1 shows strong endothelial expression but only weak immunostaining in neointimal smooth muscle cells, whereas ICAM-1 shows marked expression in neointimal smooth muscle cells[25]. Chang et al. recently found that thrombosis in AVFs is characterized by infiltration of abundant macrophages in the vascular wall and accompanied by increased expression of VCAM-1, IL-6 and TNF-α[26]. Taken together with the findings in Tanaka et al.[25], elevation of serum VCAM-1 may be a more sensitive reflection of endothelial injury in AVF stenosis, compared to the ICAM-1 level. In the general population, a high concentration of thrombomodulin may be associated with decreased risk of coronary heart disease[27], and thrombomodulin concentrations serve as a useful marker for endothelial cell damage. Lower thrombomodulin concentration may play an important role in progression of coronary heart disease[28]. The significant associations of administration of an antihypertensive drug, VCAM-1, ICAM-1 and thrombomodulin with AVF stenosis in logistic analysis suggest that endothelial injury may be involved in AVF stenosis.

In summary, elevation in serum VCAM-1 levels and decrease of serum ICAM-1 and thrombomodulin were found in hemodialysis patients with AVF stenosis and this may reflect endothelial injury in AVF stenosis. The significant association of administration of anti-hypertensive drug, VCAM-1, ICAM-1 and thrombomodulin with AVF stenosis suggests that vascular inflammation may play a critical role in AVF stenosis. Measurement of serum VCAM-1, ICAM-1, and thrombomodulin may be useful for prediction of native AVF stenosis in hemodialysis patients. However, our study is limited due to its cross-sectional nature. The association between endothelial injury marker, adhesion molecules and AVF stenosis requires confirmation in prospective studies based on outcome measures such as mortality and incidence of AVF stenosis.

REFERENCES

1. Feldman HI, Kobrin S and Wasserstein A. Hemodialysis vascular access morbidity. *J Am Soc Nephrol* 1996；7：523-535.
2. Schwab SJ, Besarab A, Beathard G et al. National Kidney Foundation DOQI Clinical Practice Guidelines for Hemodialysis Vascular Access Working Group. *Am J Kidney Dis* 1997；30（Suppl 3）：S154-S196.
3. Turmel-Rodrigues L, Pengloan J, Rodrigue H et al. Treatment of failed native arteriovenous fistulae for hemodialysis by interventional radiology. *Kidney Int* 2000；57：1124-1140.
4. Scherer P, Williams S, Fogliano M et al. A novel serum protein similar to C1q, produced exclusively in adipocytes. *J Biol Chem* 1995；270：26746-26749.
5. Hotta K, Funahashi T, Arita Y et al. Plasma concentrations of a novel, adipose-specific protein adiponectin, in type 2 diabetic patients. *Arterioscler Thromb Vasc Biol* 2000；20：1595-1599.
6. Kumada M, Kihara S, Sumitsuji S et al. Association of hypoadiponectinemia with coronary artery disease in men. *Arterioscler Thromb Vasc Biol* 2003；23：85-89.
7. Pichon T, Girman CJ, Hotamisligil GS et al. Plasma adiponectin levels and risk of myocardial infarction in men. *JAMA*2004；291：1730-1737.
8. Zoccali C, Mallamaci F, Tripepi G et al. Adiponectin, metabolic risk factors, and cardiovascular events among patients with end-stage renal disease. *J Am Soc Nephrol* 2002；13：134-141.
9. Ouchi N, Kihara S, Arita Y et al. Novel modulator for endothelial adhesion molecules：adipocyte-derived plasma protein adiponectin. *Circulation* 1999；100：2473-2476.
10. Malyszko J, Malyszko JS, Brzosko S et al. Adiponectin is related to CD146, a novel marker of endothelial cell activation/injury in chronic renal failure and peritoneally dialyzed patients. *J Clin Endocrinol Metab* 2004；89：4620-4627.
11. Libby P. The molecular bases of the acute coronary syndrome. *Circulation* 1995；99：1726-1732.
12. Stenvinkel P, Heimburger O, Paultre F et al. Strong association between malnutrition, inflammation, and

atherosclerosis in chronic renal failure. *Kidney Int* 1999；55：1899-1911.
13. Saito O, Saito T, Okuda K et al. Serum adiponectin and markers of endothelial injury in hemodialysis patients with arteriosclerosis obliterans（ASO）. *Clin Exp Nephrol* 2008；12：58-64.
14. Churchill DN, Taylor DW, Cook RJ et al. Canadian Hemodialysis Morbidity Study. *Am J Kidney Dis* 1992；19：214-234.
15. Windus DW. The effect of comorbid conditions on hemodialysis access patency. *Adv Renal Replac Ther* 1994；1：148-154.
16. Kanwar YS. Functional duality of progenitor cells influxing into arterio-venous fistula during its neoangiogenesis. *Am J Physiol Renal Physiol* 2007；293：F468-F469.
17. Roy-Chaudhury P, Spergel LM, Besarab A et al. Biology of arteriovenous fistula failure. *J Nephrol* 2007；20：150-163.
18. Libby P. inflammation in atherosclerosis. *Nature* 2002；420：868-874.
19. Dustin ML, R Rothlein, AK Bhan et al. Induction by IL-1 and interferon-gamma：tissue distribution, biochemistry, and function of a natural adherence molecule（ICAM-I）. *J Immunol* 1986；137：245-254.
20. Prober JS, MA Gimbrone, LA Lapierre et al. Overlapping patterns of activation of human endothelial cells by interleukin 1, tumor necrosis factor and immune interferon. *J Immunol* 1986；137：1893-1896.
21. Adams DH and Shaw S. Leucocyte-endothelial interactions and regulation of leucocyte migration. *Lancet* 1994；343：831-836.
22. Stenvinkel P, Lindholm B, Heimburger M et al. Elevated serum levels of soluble adhesion molecule predict death in pre-dialysis patients：Association with malnutrition, inflammation, and cardiovascular disease. *Nephrol Dial Transplant* 2000；15：1624-1630.
23. Davis MJ, Gordon JL, Gearing AJ et al. The expression of the adhesion molecules ICAM-1, VCAM-1, PECAM, and E-selectin in human atherosclerosis. *J Pathol* 1993；171：223-229.
24. Sakai A, Kume N, Nishi E et al. P-selectin and vascular cell adhesion molecule-1 are focally expressed in aortas of hypercholesterolemic rabbits before intimal accumulation of macrophages and T lymphocytes. *Arterioscler Thromb Vasc Biol* 1997；17：310-316.
25. Tanaka H, Suzuki A, Schwartz D, et al. Activation of smooth muscle and endothelial cell following ballon injury. *Ann NY Acad Sci* 1995；748：526-529.
26. Chang CJ, Ko YS, Ko PJ et al. Thrombosed arteriovenous fistula for hemodialysis access is characterized by a marked inflammatory activity. *Kidney Int* 2005；68：1312-1319.
27. Salomaa V, Matei C, Aleksic N et al. Soluble thrombomodulin as a predictor of incident coronary heart disease and symptomless carotid artery atherosclerosis in the Atherosclerosis Risk in Communities（ARIC）study：a case-cohort study. *Lancet* 1999；353：1729-1734.
28. Wu KK. Soluble thrombomodulin and coronary heart disease. *Curr Opin Lipidol* 2003；14：373-375.

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動静脈シャント狭窄を有する透析患者における血中血管内皮細胞障害マーカー濃度の検討

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要　約

【目的】透析患者ではバスキュラーアクセス機能不全は予後に影響を及ぼす重大な問題である。今回 動静脈シャント狭窄（AVF stenosis）と adiponectin・接着因子について検討し，AVF stenosis に特異的な因子を検討した。
【方法】維持期血液透析患者122名を対象に AVF stenosis 既往を有する群46名と有さない群76名に分け，横断研究にて検討した。パラメーターとして血中 adiponectin, vascular cell adhesion molecule（VCAM-1), intercellular adhesion molecule- 1（ICAM-1), Thrombomodulin, CD146濃度を測定した。
【結果】AVF stenosis 保有群では adiponectin 濃度は非保有群に比して有意に低値だった。血中 ICAM-1, thrombomodulin 濃度は保有群では有意に低値であり，VCAM-1濃度は逆に高値を示した。ロジステック回帰分析では降圧剤の内服者，VCAM-1, ICAM-1, Thrombomodulin が AVF stenosis の説明因子として挙げられた。
【考察】降圧剤の内服者，VCAM-1, ICAM-1, Thrombomodulin が AVF stenosis の説明因子として挙げられ，血管内皮障害が AVF stenosis に関与していることが示唆された。

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