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Factors associated with early failure of vascular access in acute-phase patients

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Abstract

Background: Acute-phase patients sometimes require hemodialysis therapy without vascular access (VA) present on admission. These patients require VA creation to continue hemodialysis after discharge. The risk of early VA failure in acute-phase conditions is considered high due to the unstable nature of the patients' condition. Hence, optimal timing of VA creation is not established.

Methods: This retrospective study included patients who had VA (arteriovenous fistula or graft) created between May 2010 and July 2016.

Results: During this study, 913 VA creations were performed among 804 patients. Of the included, 435 were acute-phase patients (275 men, 160 women). The average age was 67.4 ± 14.7 years. The causes of admission were exacerbation of renal failure (274 patients, 63.0 %), heart disease (61 patients, 14.0 %), infectious disease (30 patients, 6.9 %), and malignancy (15 patients, 3.4 %). Early VA failure occurred in 53 patients (12.2 %). There was no difference in causes of admission between patients with and without VA failure. Serum albumin level was significantly lower (2.7 \pm 0.8 g/dL vs. 3.0 \pm 0.6 g/dL, *P* < 0.01) in the early VA failure group than in the without early failure group. Albumin level was associated with early VA failure (odds ratio 0.4723, 95 % confidence interval 0.2744–0.8130, *P* < 0.01). Assessing only patients with arteriovenous fistula, the serum albumin level was significantly lower (2.6 \pm 0.7 g/dL vs. 3.1 \pm 0.6 g/dL, *P* < 0.01) in the early VA failure group than in the without early failure group.

Conclusions: When we perform VA creation in acute-phase patients, hypoalbuminemia is associated with the risk of early VA failure. The status of the patient is an important factor to consider when creating VA.

Keywords: Early failure, Hemodialysis, Vascular access

Background

Patients, especially those with chronic kidney disease, who are admitted to the hospital with acute-phase illness, such as cardiovascular disease, infectious disease, and stroke, sometimes complicate with acute kidney injury and transition into end-stage renal disease (ESRD), which requires dialysis therapy. Furthermore, ESRD patients sometimes complicate with acute-phase illness and are admitted to the hospital with vascular access (VA) occlusion as a result. As our hospital has an emergency unit, many patients, with various diseases, are referred to our hospital without usable VA. VA must be created to continue hemodialysis (HD). However, the patient state during the acute phase is

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unstable, as evidenced by symptoms such as unstable blood pressure, hypercoagulation, and intravascular volume depletion. Hence, the risk of early VA failure during the acute-phase condition is considered to be increased. Furthermore, patients with complications, such as cardiovascular and cerebrovascular diseases, often already demonstrate advanced atherosclerosis. Hence, the maturation of VA may be poor. Clinically, we decide the timing of VA creation by taking general condition, such as blood pressure, fluid volume, and presence of infection, into consideration. However, there is no established evidence showing what condition is optimal for VA creation. Some studies report that a small-diameter artery or vein is a disadvantage for VA maturation. Low volume of VA flow is also a reported disadvantage. However, regarding patients with VA placed during the acute phase,



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there is no information reported on optimal timing for VA maturation.

We herein assessed the factors of early VA failure in patients with VA placement during the acute phase.

Methods

Patients and data collection

This is a retrospective study. We included patients who had VA created between May 2010 and July 2016. Primary cause of admission, past history, physical examination, and laboratory data were collected from medical records. Blood pressure was defined as the reading immediately before VA creation. Laboratory data were defined as the most recent (within 1 week) prior to the first VA creation. Inclusion criteria consisted of the following: adult patient with VA creation performed, VA not available on admission, VA placed during hospitalization, hospitalization length of stay more than 3 days, and VA used at least once in our hospital. Because in our hospital the period of hospitalization for only VA creation is usually within 3 days, longer hospitalization means that there is other reason to continue hospitalization. Acute-phase illness means various ones which require admission other than VA creation. Exclusion criteria included patient death during hospitalization.

Vascular access creation

According to past reports, VA was created with vascular mapping by ultrasonography. An artery and a vein greater than 1.5 mm in diameter were used to create arteriovenous fistulas (AVF). If AVF creation was difficult, arteriovenous grafts (AVG) were created. An operating surgeon or instructor had more than 10 years of experience.

Definition of early vascular access failure

Early VA failure was defined as a case in which VA creation surgery was required two or more times during one hospitalization because first VA did not become usable.

Statistical analysis

Baseline characteristics were presented descriptively and were tested using Student's *t* test or χ^2 test. Logistic regression analysis and receiver operative characteristic (ROC) curve were used to evaluate early VA failure after acute-phase hospitalization. *P* values <0.05 were considered statistically significant.

Results

Baseline characteristics

During the period of this study, 913 VA creations in 804 patients were performed. Of them, 452 patients had VA creations performed during acute-phase condition. Of the 452 patients, 17 died before discharge. The remaining 435 patients (275 men and 160 women) were assessed. The average age was 67.4 ± 14.7 years. Table 1 depicts the

Table 1	Baseline	characteristics	of patients	receiving \	/A
placeme	ent $(n = 43)$	35)			

Parameter	
Age (years)	67.4 ± 14.7
Male/female	275/160
Diabetes (%)	46.0
Hypertension (%)	67.6
Atrial fibrillation (%)	9.2
Primary cause of admission	
Exacerbation of renal failure (%)	63.0
Heart disease (%)	14.0
Heart failure (%)	10.6
Coronary artery disease (%)	2.3
Infectious disease (%)	6.9
Malignancy (%)	3.4
Cephalopathy (%)	2.8
Cerebral infarction (%)	0.7
Intracranial hemorrhage (%)	0.9
Peripheral artery disease (%)	0.7
Aortic disease (%)	0.9
Others (%)	8.3
AVF (%)	76.1
Early failure (%)	12.2

VA vascular access, AVF arteriovenous fistula

baseline profile of all patients. The most frequent primary cause of admission was exacerbation of renal failure. Early VA failure occurred in 12.2 % of patients.

Characteristics of patients with and without early failure of vascular access

Table 2 is a comparison of patients with and without early VA failure. There was no significant difference between the patients with and without VA failure in age, past history, primary cause of admission, medication, or cardiac function. However, the percentage of male was significantly lower in the early VA failure group. Further, diastolic blood pressure (DBP) was significantly lower in the early VA failure group. Serum albumin level (ALB) was significantly lower and C-reactive protein (CRP) higher in the early VA failure group.

The impact of serum ALB levels on early VA failure

Table 2 displays the association between early VA failure and DBP, serum ALB, or CRP. Table 3 shows non-adjusted odds ratios after logistic regression analysis using early VA failure as the objective variable. Table 4 illustrates odds ratio adjusted by age, gender, past history of diabetes, DBP, serum ALB, creatinine (Cr), CRP, and AVF. Only the level of serum ALB showed significant association with early VA failure.

Table 2 Characteristics of patients with and without early VA failure

Parameter	Without failure (n = 382)	With failure $(n = 53)$	P value
Age (years)	66.9 ± 14.6	70.7 ± 15.6	0.0819
Male (%)	65.2	49.1	0.0225*
Diabetes (%)	45.0	52.8	0.2854
Hypertension (%)	68.3	62.3	0.3770
Atrial fibrillation (%)	8.3	15.1	0.1128
Primary cause of admission			
Exacerbation of CRF (%)	64.1	54.7	0.1832
Heart disease (%)	13.6	17.0	0.5081
Heart failure (%)	9.9	15.1	0.2535
Coronary artery disease (%)	2.4	1.9	0.8309
Infectious disease (%)	6.5	9.4	0.4366
Malignancy (%)	3.4	3.8	0.8898
Cephalopathy (%)	2.6	3.8	0.6302
Cerebral infarction (%)	0.5	1.9	0.2611
Intracranial hemorrhage (%)	1.0	0.0	0.4542
Peripheral artery disease (%)	0.5	1.9	0.2611
Aortic disease (%)	1.0	0.0	0.4542
Others (%)	8.1	9.4	0.7440
Warfarin (%)	9.7	11.3	0.7086
Antiplatelet agent (%)	31.2	32.1	0.8919
Statin (%)	32.2	30.2	0.7687
ACEi or ARB (%)	46.9	41.5	0.4642
Beta blocker (%)	34.0	34.0	0.9921
CCB (%)	60.0	60.4	0.9523
LVEF (%)	55.6 ± 12.9	56.5 ± 12.7	0.7022
SBP (mmHg)	138.6 ± 24.2	132.1 ± 23.7	0.0671
DBP (mmHg)	75.1 ± 16.2	69.1 ± 17.3	0.0119*
WBC (10 ³ /µL)	7.2 ± 3.2	8.0 ± 3.5	0.0870
Hb (g/dL)	9.8 ± 1.7	9.7 ± 1.9	0.6712
PLT (10 ⁴ /μL)	19.2 ± 7.8	19.7 ± 8.3	0.6834
TP (g/dL)	6.1 ± 0.9	5.9 ± 1.0	0.1570
ALB (g/dL)	3.0 ± 0.6	2.7 ± 0.8	0.0002**
BUN (mg/dL)	68.5 ± 28.7	63.0 ± 34.2	0.2035
Cr (mg/dL)	7.3 ± 3.0	6.4 ± 2.4	0.0414*
eGFR (mL/min/1.7 m ²)	7.3 ± 3.9	7.6 ± 3.6	0.6209
AST (IU/L)	23.2 ± 20.0	25.8 ± 24.9	0.3891
ALT (IU/L)	18.9 ± 21.3	17.7 ± 21.4	0.7076
CRP (mg/dL)	2.2 ± 3.3	3.2 ± 4.4	0.0390*
APTT	30.2 ± 9.7	31.2 ± 8.1	0.5918
PT-INR	1.16 ± 0.40	1.16 ± 0.20	0.9994
AVF (%)	77.5	66.0	0.0671

VA vascular access, CRF chronic renal failure, ACEi angiotensin-converting enzyme inhibitor, ARB angiotensin receptor blocker, CCB calcium channel blocker, LVEF left ventricular ejection fraction, SBP systolic blood pressure, DBP diastolic blood pressure, WBC white blood cell, Hb hemoglobin, PLT platelet, TP total protein, ALB albumin, BUN blood urea nitrogen, Cr creatinine, eGFR estimated glomerular filtration rate, AST aspartate aminotransferase, ALT alanine transaminase, CRP C-reactive protein, APTT activated partial thromboplastin time, PT-INR international normalized ratio of prothrombin time, AVF, arteriovenous fistula *P < 0.05; **P < 0.01

 Table 3 Odds ratio for early VA failure with evaluated parameters (non-adjusted)

Parameter	Odds ratio	95 % CI	P value		
DBP (mmHg)	0.9770	0.9593-0.9950	0.0124*		
ALB (g/dL)	0.4287	0.2709-0.6784	0.0003**		
Cr (mg/dL)	0.8929	0.8003-0.9961	0.0424*		
CRP (mg/dL)	1.0728	1.0017-1.1489	0.0447*		
AVF	0.5649	0.3048-1.0471	0.0697		

VA vascular access, CI confidence interval, DBP diastolic blood pressure, ALB albumin, Cr creatinine, CRP C-reactive protein, AVF arteriovenous fistula *P < 0.05; **P < 0.01

Receiver operative curve for early VA failure

The data in Tables 3 and 4 support the association between early VA failure and serum ALB, so a ROC curve was assessed to detect early VA failure. Figure 1 illustrates the ROC curve of serum ALB. From this finding, we considered serum ALB less than 2.82 g/dL to be the cutoff level to predict early VA failure.

Analyses for only AVF

Next, we assessed only patients with AVF because the characteristics of AVG failure may be different from the ones in AVF. We assessed for majority of our patients with AVF (n = 331). Table 5 is a comparison of patient-created AVF with and without early VA failure. There was no significant difference between the patients with and without VA failure in age, past history, primary cause of admission, medication, or cardiac function. However, the level of ALB was significantly lower and white blood cell count higher in the early VA failure group. Table 6 shows non-adjusted and Table 7 shows adjusted odds ratios using early VA failure as the objective variable. Table 7 illustrates odds ratio adjusted by age, gender, past history of diabetes, white blood cell count, and serum ALB. Only the level of serum ALB showed significant association with early VA failure in patients with AVF.

Discussion

In this study, we evaluated the association between early VA failure and serum ALB level in acute-phase illness

Table 4 Odds ratio for	early VA failure with evaluated
parameters (adjusted)	

Parameter	Odds ratio	95 % CI	P value	
DBP (mmHg)	0.9866	0.9668-1.0068	0.1924	
ALB (g/dL)	0.4723	0.2744-0.8130	0.0068**	
Cr (mg/dL)	1.0270	0.8977-1.1748	0.6980	
CRP (mg/dL)	1.0444	0.9639–1.1316	0.2883	
AVF	0.6260	0.3239-1.2097	0.1634	

Adjusted by age, gender, diabetes, DBP, ALB, Cr, CRP, and AVF VA vascular access, CI confidence interval, DBP diastolic blood pressure,

ALB albumin, Cr creatinine, CRP C-reactive protein, AVF arteriovenous fistula **P < 0.01

1

0.8

0.6

0.4

0.2

0

0

0.2

TPF

patients who were admitted to our hospital and required dialysis therapy. On the other hand, there was no relation between early VA failure and the type of acutephase illness. We opine that the more important point for VA creation is a stable condition, rather than cause of admission or type of medicine. In other words, to decide the timing of VA creation, it is more important to confirm that the patient's condition is stable.

0.4 0.6 0.8

FPF Fig. 1 The ROC curve for early vascular access failure using serum ALB levels in all patients. The AUC of ALB is 0.652 and the cutoff value is 2.82 g/dL. *ROC* receiver operative characteristic, *ALB* albumin, *AUC* area under the curve, *TPF* true positive fraction, *FPF* false positive fraction

AUC: 0.652 Cut off: 2.82

1

Past reports assessed early VA failure regardless of the presence of acute-phase illness. Despite better patient condition due to the absence of acute-phase illness, 20 to 60 % early VA failure was reported [1, 2]. The prevalence of early VA failure in our study was lower than that of the past reports despite worse patient condition.

In the previous reports, the diameter of the artery or vein is associated with the patency and maturation of VA [3–6]. In this study, the diameters of the artery and vein were not assessed; however, our hospital creates AVF when the diameters of the artery and vein are more than 1.5 to 2 mm with mapping by ultrasonography [7, 8]. As this study is from a single center, there seems to be little variability of the diameter of the artery and vein used for VA creation.

Previous reports suggested that the level of CRP, the presence of diabetes mellitus (DM), and hypertension (HT) are associated with early VA failure [1, 2, 9]. However, our results did not show significant association between early VA failure and DM or HT. As many elderly patients included in our study were already diagnosed with advanced atherosclerotic diseases, the effects of DM and HT were likely diminished. There have been no reports assessing appropriate timing of VA creation during acute-phase illness. Our study is considered to be extremely clinically useful and meaningful.

Table 5 Char	acteristics c	of patient	t-created	AVF	with	and	without
early VA failur	e						

Parameter	Without failure $(n = 296)$	With failure $(n = 35)$	P value
Age (years)	66.4 ± 15.0	67.8 ± 17.1	0.5903
Male (%)	68.2	57.1	0.1864
Diabetes (%)	45.6	48.6	0.7393
Hypertension (%)	70.6	71.4	0.9197
Atrial fibrillation (%)	8.5	11.4	0.5551
Primary cause of admission			
Exacerbation of CRF (%)	65.9	62.9	0.7221
Heart disease (%)	13.9	14.3	0.9440
Heart failure (%)	10.5	14.3	0.4933
Coronary artery disease (%)	2.0	0.0	0.3953
Infectious disease (%)	5.4	8.6	0.4464
Malignancy (%)	4.1	5.7	0.6444
Cephalopathy (%)	3.0	2.9	0.9522
Cerebral infarction (%)	0.7	2.9	0.1978
Intracranial hemorrhage (%)	1.0	0.0	0.5496
Peripheral artery disease (%)	0.7	2.9	0.1978
Aortic disease (%)	1.4	0.0	0.4890
Others (%)	5.7	2.9	0.4764
Warfarin (%)	10.5	11.4	0.8620
Antiplatelet agent (%)	27.0	22.9	0.5975
Statin (%)	32.4	22.9	0.2485
ACEi or ARB (%)	49.0	45.7	0.7142
Beta blocker (%)	33.1	25.7	0.3765
CCB (%)	63.5	71.4	0.3552
LVEF (%)	56.0 ± 12.5	56.8 ± 13.3	0.7316
SBP (mmHg)	138.9 ± 24.7	132.6 ± 23.4	0.1568
DBP (mmHg)	75.5 ± 16.6	71.1 ± 14.5	0.1309
WBC (10 ³ /µL)	7.2 ± 3.2	8.4 ± 3.6	0.0376*
Hb (g/dL)	9.7 ± 1.8	9.7 ± 1.7	0.8780
PLT (10 ⁴ /μL)	19.2 ± 8.1	21.2 ± 8.9	0.1666
TP (g/dL)	6.1 ± 0.9	5.8 ± 0.9	0.0540
ALB (g/dL)	3.1 ± 0.6	2.6 ± 0.7	0.0006**
BUN (mg/dL)	70.1 ± 29.2	60.2 ± 27.8	0.0578
Cr (mg/dL)	7.6 ± 3.0	6.9 ± 2.6	0.1933
eGFR (mL/min/1.7 m ²)	7.1 ± 3.8	7.4 ± 3.5	0.6445
AST (IU/L)	22.6 ± 20.3	21.9 ± 12.0	0.8438
ALT (IU/L)	18.6 ± 20.9	15.6 ± 15.9	0.4238
CRP (mg/dL)	2.3 ± 3.4	2.7 ± 4.6	0.5259
APTT	30.7 ± 14.2	28.7 ± 4.7	0.4961
PT-INR	1.17 ± 0.42	1.14 ± 0.25	0.6554

VA vascular access, CRF chronic renal failure, ACEi angiotensin-converting enzyme inhibitor, ARB angiotensin receptor blocker, CCB calcium channel blocker, LVEF left ventricular ejection fraction, SBP systolic blood pressure, DBP diastolic blood pressure, WBC white blood cell, Hb hemoglobin, PLT platelet, TP total protein, ALB albumin, BUN blood urea nitrogen, Cr creatinie, eGFR estimated glomerular filtration rate, AST aspartate aminotransferase, ALT Alanine transaminase, CRP C-reactive protein, APTT activated partial thromboplastin time, PT-INR international normalized ratio of prothrombin time *P < 0.05; **P < 0.01

Table 6 Odds ratio for early VA (AVF) failure with evaluated parameters (non-adjusted)

Parameter	Odds ratio	95 % CI	P value
WBC (10 ³ /µL)	1.0950	1.0024-1.1961	0.0441*
ALB (g/dL)	0.3849	0.2187-0.6772	0.0009**

VA vascular access, AVF arteriovenous fistula, CI confidence interval, WBC white blood cell, ALB albumin *P < 0.05; **P < 0.01

Hypoalbuminemia, which results in intravascular volume reduction, is considered to be a factor in occlusion of VA. There was a previous report which described that hypoalbuminemia was a cause of VA failure [10]. However, this report did not focus on the patients' state, different from our study which focused on acute-phase patients. There is another report which described that hyperinsulinism is a cause of VA failure [11]. However, this report did not focus on the patients' status, as well. Furthermore, inflammation may induce excessive coagulation of blood. Since hypoalbuminemia progresses during times of inflammation, it may also be considered an indication of inflammation. When hypoalbuminemia and/or inflammation are present, unphysiological blood flow, such as present in a shunt, seems likely to occlude before maturation. In that sense, adjusting the timing of VA creation to when the influence of the acute illness has faded might be effective in order to prevent early VA failure. However, when patients are complicated with dialysis catheter-related blood stream infections and require VA creation as soon as possible, a heparin infusion or supporting intravascular volume may be choices to prevent excessive coagulation.

This study has some limitations. First, this study is a single center study in Japan. Recently, the number of elderly patients in Japan initiated into dialysis therapy is increasing [12], and the vascular state of these patients is poor due to age or other complications. This result may be difficult to apply in other countries where a majority of patients initiated into dialysis therapy are younger. However, despite adverse patient conditions, our results were superior to other reports on early VA failure rate. In addition, although using a single facility is a limitation, the fact of less variation in operator competence may be a benefit.

Second, although we included acute-phase illness, we did not assess the severity of illness by using acute physiology

Table 7 Odds ratio for early VA (AVF) failure with evaluated parameters (adjusted)

Parameter	Odds ratio	95 % CI	P value
WBC (10 ³ /µL)	1.0798	0.9835-1.1855	0.1073
ALB (g/dL)	0.4198	0.2339–0.7533	0.0036**

Adjusted by age, gender, diabetes, WBC, and ALB

VA vascular access, AVF arteriovenous fistula, CI confidence interval, WBC white blood cell, ALB albumin **P < 0.01

and chronic health evaluation (APACHE) II scores [13] or sequential organ failure assessment (SOFA) scores [14]. Since not all the patients were admitted to an intensive care unit, this could affect the results.

Conclusions

When performing VA creation in acute-phase illness patients, hypoalbuminemia is associated with the risk of early VA failure. We must consider a factor in the serum ALB level when deciding the timing of VA creation.

Abbreviations

ALB: Albumin level; APACHE: Acute physiology and chronic health evaluation; AVF: Arteriovenous fistulas; AVG: Arteriovenous grafts; Cr: Creatinine; CRP: C-reactive protein; DBP: Diastolic blood pressure; DM: Diabetes mellitus; ESRD: End-stage renal disease; HD: Hemodialysis; HT: Hypertension; ROC: Receiver operative characteristic; SOFA: Sequential organ failure assessment; VA: Vascular access

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Availability of data and materials

Please contact the author for data requests.

Authors' contributions

AT designed this study, performed the statistical analysis, and wrote this manuscript. All authors participated in the medical care for the patients in this paper. All authors read and approved the final manuscript.

Competing interests

The authors declare that they have no competing interests.

Consent for publication

Not applicable.

Ethics approval

The study was approved by the Ethical Committee of the Institutional Review Board of the Japanese Red Cross Nagoya Daini Hospital (approval number 1110) and was conducted under the Declaration of Helsinki.

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