Endovascular management in immature arteriovenous fistula for hemodialysis

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Abstract
To evaluate the outcomes and prognostic factors of endovascular management in immature arteriovenous fistula (AVF) for hemodialysis.

From April 2007 to September 2017, 54 patients (male:female = 31:23, mean age 65.63 years, range 33–90 years) who underwent endovascular management for the salvage of immature AVF were retrospectively reviewed. Clinical data, procedural details, and results were evaluated. Primary and secondary patency rates and factors influencing the patency were also analyzed.

Technical and clinical success rates were 88.9% (48/54) and 85.2% (46/54), respectively. Mean primary and secondary patency was 42.10 (±8.85) and 91.5 (±14.77) months, respectively. Primary and secondary patency rates were 66% and 89% in 1 year, 66% and 78% in 2 years, and 51% and 78% in 3 years. In multivariate analysis, only brachiocephalic AVF and antegrade access procedures showed significantly shorter primary patency (HR 5.196; 95% CI (1.04–25.77); P = .044, HR 8.096; 95% CI (1.36–48.00); P = .021). There was no statistically significant factor associated with secondary patency in the multivariate study.

Endovascular management in immature AVF is safe and effective to make the AVF available. Brachiocephalic AVF and antegrade access procedures are the factors influencing the patency in multivariate analysis.

Abbreviations: AVF = arteriovenous fistula, AVG = arteriovenous graft, CIs = confidence intervals, HRs = hazard ratios, PTA = percutaneous transluminal angioplasty.

Keywords: arteriovenous fistula, endovascular management, percutaneous transluminal angioplasty, primary patency rate, secondary patency rate

1. Introduction
Maintaining adequate dialysis access is essential in patients receiving hemodialysis. Native arteriovenous fistula (AVF) is regarded as favorable vascular access than arteriovenous graft (AVG) or central venous catheter because of lower access failure rate and mortality.[1,2] Therefore, as many as a possible situation, AVF has been attempted as a first choice in patients receiving dialysis. However, maturation of AVF is still a major problem (up to 50%) in a large population[3–4] and salvage of maturation failure AVF is an important part of successful access acquisition.

To make these AVFs available, endovascular management, mostly percutaneous transluminal angioplasty (PTA) has been regarded as an effective technique.[5–7] Besides treating stenosis or occluded lesion with angioplasty, ligation or embolization for an accessory vein that hinders AVF growth is also considered.[5,8,9]
However, multiple procedures might be needed for a properly matured AVF and biological effect of PTA on vascular injury is not yet fully understood.[7–10,11]

The purpose of this study was to evaluate the outcomes of endovascular management in immature arteriovenous fistula (AVF) for hemodialysis and investigate the factors that may adversely affect the patency.

2. Materials and methods
This is the retrospective study and was approved by institutional review board.

2.1. Patients
From April 2007 to September 2017, 54 consecutive patients (31 men and 23 women; mean age 65.63 years, range 33–90 years) were included in this study. All patients had immature AVF and underwent the endovascular procedure for salvage of AVF. Written informed consents were obtained from all patients before the procedures were performed.

Forty patients were diagnosed with diabetes, 43 with hypertension, and concomitant vascular disease such as cerebral, coronary and mesenteric vascular disease was found in 25 patients.
There were 46 AVF in left arm and 8 in the right arm. Forty-two patients had radiocephalic AVFs and 12 patients had brachiocephalic AVFs. The mean time from fistula creation to PTA was 81.8 days (range 28–188 days). Less than 90% of stenosis degrees was found in 22 and complete occlusion in 15 patients. In case of multiple lesions, the most severe lesion was used as the stenosis degree measurement.

Lesion location was categorized as followings; artery, anastomosis, juxta-anastomosis vein, proximal draining vein, distal draining vein, cephalic arch, and central vein. However, for the statistical analysis, distal draining vein lesion was defined as upper arm vein, cephalic arch and central vein in radiocephalic AVF, and cephalic arch and central vein in brachiocephalic AVF.

The mean follow-up period was 24.62 months (range, 0.9–115.63 months). During the follow-up period, 72 procedures were performed (1.3 procedure per patient). Two patients were lost to follow-up.

Retrospective review and analysis were performed for the following aspects; clinical data including demographics, comorbidities, fistula details, procedural details, and clinical results. When PTA was not performed due to the failure of cross the stenosed or occluded lesion, it was regarded as a technical failure. Subsequent to the procedure, if AVF access failed at least once for dialysis, it regarded as a clinical failure.

### 2.2. Endovascular management

Ultrasound was performed before the PTA to evaluate the fistula. Based on the ultrasound finding, decisions on access direction and entry site were made. In most of the cases, entry site was in the forearm in radiocephalic AVF and upper arm in brachiocephalic AVF. Two patients were accessed by the brachial artery, one via a brachial artery and draining vein, and in one case access via internal jugular vein was made. In the remaining patients, draining vein was the access site. Fistulography was performed following the access in all patients. If thrombus was found on ultrasound, 7Fr. sheath (Hoffman Sheath; COOK, Inc., Bloomington, IN) or 5Fr. a guiding catheter (Envoy; Codman, Raynham, MA) was used to aspirate the thrombus. PTA was performed for narrowed or occluded lesion. Balloon size was selected based on the adjacent normal vessel. If large accessory draining vein was still visualized after the effective PTA, coil embolization was performed. The suture was done for sheath insertion site and patients were discharged after hemostasis was confirmed. Time of AVF use was determined by the clinician.

### 2.3. Outcome assessment and statistical analysis

Outcome and patency rates were defined according to the reporting standards of the Society of Cardiovascular and Interventional Radiology. Primary patency was defined as uninterrupted patency after intervention until the next access thrombosis or repeat intervention. Secondary patency was defined as patency achieved by all repeated endovascular interventions.

Kaplan–Meier method and the log-rank test were used for primary and secondary patency rates. Cox proportional-hazard regression models were used to calculate hazard ratios (HRs) with 95% confidence intervals (CIs) for AVF survival. A P value <0.05 was defined to be statistically significant. Statistical analyses were performed using SPSS version 15.0 for Windows (SPSS, Chicago, IL).

## 3. Results

Patients’ demographics and AVF characteristics are presented in Table 1.

Technological and clinical success rates were 88.9% (48/54) and 85.2% (46/54), respectively.

In 3 patients, aspiration thrombectomy was performed to remove thrombi; in none of the cases, thrombolitics were employed. Large accessory vein embolization using a coil that was thought to hinder the AVF growth was performed in 7 patients.

Mean primary and secondary patency was 42.10 (±8.85) and 91.5 (±14.77) months, respectively.

Primary and secondary patency rates were 66% and 89% in 1 year, 66% and 78% in 2 years, and 51% and 78% in 3 years.

Table 2 shows univariate statistics for primary and secondary patency. Right arm AVF showed significantly lower primary patency than left arm AVF (P = .029). Longer primary patency in radiocephalic AVF was revealed compared with brachiocephalic AVF (P = .003). The direction of PTA access also showed statistical significance for primary patency, especially in antegrade access only compared to either retrograde only access or bidirectional access (P = .003). AVF with distal draining vein PTA lesion revealed shorter primary patency (mean 7.54 vs 49.41 months, P = .001).

Multivariate statistics for primary patency is demonstrated in Table 3. Brachiocephalic AVF and antegrade access only PTA showed significantly shorter primary patency in multivariate analysis (HR 5.196; 95% CI 1.04–25.77); P = .044, HR 8.096; 95% CI 1.36–48.00; P = .021).

For secondary patency, right arm AVF and brachiocephalic AVF showed significantly low patency in univariate analysis (P = 0.048, P = 0.041). There was no statistical significant factor

### Table 1

| Patient demographics and baseline characteristic of AVF. | N (%) |
|---|---|
| Age | < 65 years | 22 (40.7) |
| | ≥ 65 years | 32 (59.3) |
| Sex | Male | 31 (57.4) |
| | Female | 23 (42.6) |
| Comorbidity | Diabetes | 40 (74.1) |
| | Hypertension | 43 (79.6) |
| | Concomitant vascular disease* | 25 (46.3) |
| AVF location | Right arm | 8 (14.8) |
| | Left arm | 46 (85.2) |
| AVF location | Radiocephalic | 42 (77.8) |
| | Brachiocephalic | 12 (22.2) |
| Degree of stenosis† | < 90% | 22 (40.8) |
| | 90 ≤ <100% | 17 (31.5) |
| | 100% | 15 (27.8) |
| Lesion location | Artery | 1 (1.1) |
| | Anastomosis | 5 (5.8) |
| | Juxta-anastomosis vein | 30 (34.9) |
| | Proximal draining vein | 33 (38.4) |
| | Distal draining vein | 12 (13.9) |
| | Cephalic arch | 2 (2.3) |
| | Central vein | 3 (3.5) |
| Access direction | Retrograde | 23 (42.6) |
| | Bi-directional | 20 (37.0) |
| | Antegrade only | 11 (20.4) |

* Including coronary, cerebral, and mesenteric vascular disease.
† Most severe lesion.
examined for appropriate maturation 4 to 6 weeks postoperatively, and if poor prognostic signs are evident, immediate referral should be needed to the surgeon or interventionalist for prompt evaluation and intervention.\[11\]

Causes of maturation failure are stenosis or occlusion in inflow and outflow vessel, aggressive neointimal hyperplasia, and lack or appropriate outward remodeling in histology.\[11\]

To solve this problem, several reports suggest mapping, vascular access counseling as well as surgical ligation or embolization of accessory vein and PTA.\[3,5,8\]

Overall primary and secondary patency rates were 66% and 89% in 1 year, 66% and 78% in 2 years, and 51% and 78% in 3 years in our study, which are comparable with other studies despite the existence of different background.\[6,11,16–18\]

Right arm AVF and brachiocephalic AVF showed relatively poor patency in our study. Although relatively small number of this condition, it statistical significance was evident in primary and secondary patency. Considering that the left arm radiocephalic AVF is usually the first choice of operation site in most of the patients, right arm and/or brachiocephalic AVF means that patients could not use a first choice vessel or already abandoned that access. However, the exact history of each patient was not obtained.

Ultrasound evaluation of AVF before the procedure is helpful to locate the stenosis or thrombus and identify the vessel

### Table 2

| Primary patency and secondary patency. | Mean primary patency, months | P value | Mean secondary patency, months | P value |
|----------------------------------------|-----------------------------|---------|-------------------------------|---------|
| Age                                    |                            |         |                               |         |
| < 65 years                             | 36.91 ± 3.4                | .137    | 31.88 ± 4.87                 | .35     |
| ≥ 65 years                             | 35.39 ± 8.93               | .03     | 101.14 ± 9.61                | .01     |
| Sex                                     |                            |         |                               |         |
| M                                      | 41.33 ± 13.44              | .795    | 38.38 ± 12.05                | .967    |
| F                                       | 34.62 ± 8.66               | .304    | 80.70 ± 18.96                | .683    |
| Diabetes                                |                            |         |                               |         |
| Present                                | 35.62 ± 8.92               | .0307   | 84.99 ± 11.22                | .683    |
| Absent                                 | 35.56 ± 5.96               | .410    | 41.10 ± 0                    | .01     |
| Hypertension                            |                            |         |                               |         |
| Present                                | 45.15 ± 10.03              | .951    | 83.08 ± 15.0                 | .860    |
| Absent                                 | 31.90 ± 6.16               | .02     | 87.96 ± 20.19                | .124    |
| Concomitant vascular disease            |                            |         |                               |         |
| Present                                | 44.50 ± 11.07              | .215    | 46.55 ± 12.43                | .124    |
| Absent                                 | 40.85 ± 6.18               | .106    | 108.10 ± 7.27                | .048    |
| AVF location                            |                            |         |                               |         |
| Right arm                              | 5.18 ± 1.96                | .20     | 7.21 ± 3.17                  | .048    |
| Left arm                               | 43.67 ± 9.24               | .003    | 82.58 ± 12.85                | .041    |
| AVF location                            |                            |         |                               |         |
| Radiocephalic                           | 50.04 ± 10.37              | .03     | 89.0 ± 13.22                 | .041    |
| Brachiocephalic                         | 6.74 ± 1.00                | .021    | 17.29 ± 2.32                 | .817    |
| Stenosis degree                         |                            |         |                               |         |
| < 90%                                   | 41.67 ± 11.56              | .483    | 58.64 ± 11.62                | .817    |
| 90% ≤ <100%                            | 27.10 ± 4.92               | .108    | 99.36 ± 14.84                | .741    |
| 100%                                    | 26.57 ± 4.57               | .02     | 32.72 ± 4.89                 | .058    |
| PTA access                              |                            |         |                               |         |
| Including retrograde                   | 45.66 ± 9.53               | .03     | 82.54 ± 13.03                | .741    |
| Antegrade only                         | 5.15 ± 0.50                | .03     | 33.18 ± 6.18                 | .058    |
| Distal draining vein lesion             |                            |         |                               |         |
| Absent                                 | 49.41 ± 10.36              | .001    | 89.14 ± 13.23                | .741    |
| Present                                | 7.54 ± 1.68                | .021    | 23.40 ± 5.86                 | .058    |

| Table 3                                  | Cox regression analysis for primary patency. |
|------------------------------------------|---------------------------------------------|
| Hazard ratio                             | 95% CI                                      | P value |
| Age ≥ 65 years                           | 2.563                                       | .048–13.42 | .265    |
| Right arm AVF                            | 1.259                                       | .018–8.46 | .813    |
| Brachiocephalic AVF                      | 5.195                                       | 1.04–25.77 | .044    |
| Antegrade access                         | 8.096                                       | 1.36–48.00 | .021    |
| Distal draining vein lesion              | 1.439                                       | 0.29–7.06 | .654    |

\[\text{CI} = \text{confidence interval.}

### Table 4

| Cox regression analysis for secondary patency. |
|-----------------------------------------------|
| Hazard ratio | 95% CI | P value |
| Age ≥ 65 years | 0.153 | 0.021–1.119 | .064 |
| Concomitant vascular disease                 | 2.476 | 0.211–29.128 | .471 |
| Right arm AVF                               | 7.231 | 0.410–127.550 | .177 |
| Brachiocephalic AVF                          | 4.444 | 0.320–60.040 | .261 |
| Distal draining vein lesion                  | 1.771 | 0.132–23.741 | .666 |

\[\text{Reference value is concomitant vascular disease present.}

\[\text{CI} = \text{confidence interval.}]

4. Discussion

Because of the relatively high failure rate of newly created vascular access\[1,4,11\] and importance of the fate AVF in dialysis patients, data about the endovascular salvaging AVF have been published with various results.\[6,11,13,14\] However, controversies still exist that an AVF matured by these assisted procedures may have more frequent intervention to maintain its patency and has decreased long-term patency.\[10,11\]

The Kidney Disease Outcomes and Quality Initiative (KDQI) guidelines suggest that all newly created fistulae must be associated with secondary patency in multivariate analysis (Table 4).

There were no major complications. However, multiple minor complications were reported; a controlled rupture in 10 cases, rupture and dissection in 1 case, hematoma in 1 case, dissection in 1 case, and puncture site delayed bleeding in 1 case.

Among the 8 patients with clinical failure, 6 underwent re-access. However, the exact history of each patient was not obtained.

The mean follow-up period in technical success patients was 24.62 months (range, 0.9–115.63 months). During the follow-up period, 45 patients still underwent hemodialysis either AVF or central catheter, 4 had kidney transplantation, and 3 died.
AVF patency in several studies,[5,17,21] but, no signifi-

However, despite these presumptions, concomitant vascular
antegrade access procedures were identi-

medication.

That presumes the poor underlying
vascular condition not related with the operation. Woods et al[11]
reported that a history of peripheral vascular disease was
associated with a higher risk of AV graft or fistula failure.
However, despite these presumptions, concomitant vascular
disease failed to show statistical significance related to patency
\(P=0.215\) for primary patency, \(P=0.124\) for secondary patency) in
our study.

Age has been described as an important factor influencing the
AVF patency in several studies,[5,17,21] but, no significance was
observed in our study. On the contrary, patients more than 65
years of age showed longer secondary patency, but this is not
concluded with statistical significance in our study.

Recently, a few other treatment methods have been reported
for immature AVF, such as stent graft placement or drug-eluting
balloon angioplasty,[22,23] however, they lack concrete evidence.
It is anticipated that future studies might reveal the results of the
novel techniques.

There are several limitations in our study. First, it was a
retrospective study and selection bias could not be avoided.
According to the surgeon’s decision, there is a high likelihood
that they have been selected as likely candidates for treatment.
Second, this study includes small number of patients and
their statistical results. Larger data and complicated data
processing techniques are needed.[24,25] Third, data regarding
current medication of each patient were not completely
obtained; therefore our study cannot postulate the effect of the
medication.

In conclusion, endovascular management in immature AVF is
safe and effective for making the AVF. Brachiocephalic AVF and
antegrade access procedures were identified as the factors
influencing the patency in multivariate analysis.

Author contributions

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