Original Article

Impact of initial blood flow on outcomes of vascular access in hemodialysis patients

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A B S T R A C T

Background: Direct access flow measurements are considered the most useful surveillance method for significant stenosis, and ultrasound dilution has become the most popular and validated technique. The goal of this study was to evaluate access flow (Qa) at the time of first cannulation and its relationship to the survival of vascular access in Korean hemodialysis patients.

Methods: We conducted a prospective observational study from May 2004 to June 2011. We enrolled 60 patients (36 men) who underwent the first access operation between January 2004 and December 2005 and were followed-up for surveillance.

Results: Maturation failure occurred in nine patients (15%). Mean time to first use was 1.8 ± 1.2 months after surgery. The patients were followed-up for a mean of 50.5 ± 25.9 months. There were 25 deaths and six kidney transplants in patients with a functioning access. The total percutaneous transluminal angioplasty incidence was 50 in 27 patients (0.14/access-year). The initial Qa was 757.5 ± 476.4 mL/minute. First cannulation time was not significantly correlated with initial Qa (r = 0.234, P = 0.075). A total of 22 of the 60 patients (36.7%) had an initial Qa < 500 mL/minute. Maturation failure, initial Qa < 500 mL/minute, and the use of antiplatelet agents were risk factors for poor primary patency. Diabetic status and use of a graft were risk factors for low cumulative patency.

Conclusion: An initial Qa < 500 mL/minute is a risk factor for poor primary patency, while an initial Qa < 500 mL/minute is not a risk factor for low cumulative patency or mortality.

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Introduction

Vascular access dysfunction in hemodialysis is associated with a significant increase in morbidity and cost. Access with a blood flow of 600–1000 mL/minute is necessary to allow sufficient removal of uremic toxins from a patient within a reasonable time [1]. Routine surveillance to detect stenosis is recommended to allow preemptive intervention before thrombotic occlusion. Because the physiologic effect of stenosis is

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decreased access blood flow (Qa), direct access flow measurements are considered the most useful surveillance method to detect stenosis, and ultrasound dilution has become the most popular and validated technique [2]. However, the outcomes and surveillance methods of hemodialysis access in Korean patients remain undefined. Our goal in this study was to evaluate Qa at the time of first cannulation and its relationship to outcomes of vascular access in Korean hemodialysis patients.

Methods

We conducted a prospective, observational study in a hospital hemodialysis center from May 2004 to June 2011. This study was approved by the Institutional Review Board of our Hospital (SCHBC-IRB-09-65). Patient criteria for enrollment in the study were as follows: (1) the first operation for arteriovenous fistula (AVF) or arteriovenous graft (AVG) was performed at our hospital between January 2004 and December 2005; (2) cannulation was started and hemodialysis was maintained for at least 1 month; (3) Qa was measured monthly; and (4) follow-up for access surveillance occurred at our hospital, even for patients transferred to and receiving hemodialysis elsewhere. The type of AVF or AVG was determined based on the preferences of two surgeons.

Cannulation of the AVF/AVG was attempted after a clinical assessment suggested that the access was sufficiently well developed to support hemodialysis after a minimum maturation period of 30 days. Qa was measured monthly using a Transonic hemodialysis monitor (Transonic Systems, Inc., Ithaca, NY, USA). All measurements were performed at a fixed dialyzer blood flow of 200–250 mL/minute within the first hour after the start of hemodialysis. Ultrafiltration was turned off during the actual blood flow measurement. Patients in whom the AVF Qa decreased to <500 mL/minute or dropped by more than 25%, or those in whom the AVG Qa decreased to <600 mL/minute or dropped by more than 25%, were sent for fistulography.

We defined first cannulation time as the time from the access surgery to first cannulation. We considered the inability to use an AVF/AVG beyond 30 days after surgery to be a maturation failure. When maturation failure of an AVF/AVG was suspected, the patient was referred to the surgeons who made the access. Because surgeons rather than intervention radiologists performed the percutaneous transluminal angioplasty (PTA) in contrast to the practice in most other hospitals, the surgeons decided whether PTA or a revision operation was more appropriate. PTA was performed using standard techniques. An access stenosis was considered hemodynamically relevant when it averaged >50% of the luminal diameter. A balloon catheter was inflated in the stenotic lesion, and patency was visualized thereafter by additional fistulography. Residual stenosis of <30% of the luminal diameter was considered procedural success. The initial Qa was measured between the first and third cannulation of AVF/AVG. If maturation failure of an AVF/AVG was suspected, then the initial Qa was measured after intervention. Primary patency was defined as the time elapsed from access surgery to the time of any intervention. Cumulative (secondary) patency was defined as the time from access surgery to complete failure of the fistula or graft.

Data are presented as means ± standard deviation, with 95% confidence intervals (CIs) where appropriate. The Chi-square and Fisher’s exact tests were used to compare dichotomous variables. Normally distributed continuous variables were compared using Student’s t-test. Variables influencing access patency and patient survival were evaluated by Cox regression analysis. Values of P < 0.05 were considered to indicate statistical significance. All statistical analyses were performed using SPSS version 14.0 (SPSS, Inc., Chicago, IL, USA).

Results

Patient characteristics

Table 1 lists the characteristics of the 60 participants enrolled in this study. The mean patient age was 54.9 ± 15.6 years, and 78% of the patients had hypertension. The numbers of male and female patients were 36 and 24, respectively. The most common cause of end-stage renal disease was diabetes mellitus (DM, 45%). The access characteristics are shown in Table 2. Proportions of native and left access were higher than those of graft and right access. Radiocephalic AVF was the most common access type.

Maturation failure

Mean time to first use of the AVF/AVG was 1.8 ± 1.2 (range, 1–6) months after access surgery. Maturation failure occurred in nine patients (15%), four of who had received AVG. Three patients underwent revision operations. Another six AVF/AVG patients demonstrated stenosis upon fistulography but had functional access after PTA at 1.8 ± 0.7 months. The initial mean Qa of this group was 700 ± 230 mL/minute. Three of the six patients lost access patency again at 3, 24, or 27 months after the initial surgery. Two of these three patients underwent an additional procedure.

Table 1. Clinical characteristics of the study patients (n = 60)

| Clinical characteristic | Number (%) |
|-------------------------|------------|
| Age (y)                 | 54.9 ± 15.6|
| Sex, M:F (no.)          | 36:24      |
| Height (cm)             | 163.3 ± 8.7|
| Weight (kg)             | 58.4 ± 11.9|
| Cause of end-stage renal disease | 27 (45.0) |
| Diabetes mellitus       | 14 (23.3)  |
| Glomerulonephritis      | 1 (1.7)    |
| Unknown                 | 15 (25.0)  |
| Others                  | 3 (5.0)    |
| Diabetes mellitus       | 30 (50)    |
| Hypertension            | 47 (78.3)  |
| Anticoagulation agents  | 39 (65.0)  |

Table 2. The characteristics of arteriovenous fistulae

| Characteristic           | Number (%) |
|-------------------------|------------|
| Access type             |            |
| Native                  | 48 (81.4)  |
| Graft                   | 12 (18.6)  |
| Access position         |            |
| Left                    | 55 (91.7)  |
| Right                   | 5 (8.3)    |
| Access vessel           |            |
| Radiocephalic           | 47 (80.0)  |
| Brachiocephalic         | 1 (1.7)    |
| Upper graft             | 1 (1.7)    |
| Forearm graft           | 11 (16.6)  |
Follow-up

Patients were followed-up for a mean of 50.5 ± 25.9 months (range, 1–89 months), for a total of 3,029 patient-months. There were 25 deaths and six kidney transplants in patients with a functioning access. The total PTA incidence was 50 in 27 patients (1.65 per 100 patient-months or 0.14/access-year). The primary patency rates of AVF at 12, 24, and 36 months were 80.0%, 57.3%, and 42.8%, respectively. The primary patency rates for AVG at 12, 24, and 36 months were 46.9%, 37.5%, and 18.8%, respectively. There was no statistically significant difference in primary patency rates between AVF and AVG (P = 0.184). The cumulative patency rate of AVF at 12 and 24 months were 89.9% and 86.6%, respectively, whereas those of AVG at 12 and 24 months were 55.6% and 27.4%, respectively. The cumulative patency rate of AVF was superior to those of AVG (P = 0.000). Patient survival rates at 12, 24, and 36 months were 83%, 68.8%, and 62.5%, respectively.

Initial Qa

The initial Qa was 757.5 ± 476.4 (range, 120–2930) mL/minute at 1.8 ± 1.2 (range, 1–6) months. Known variables, including patient age, sex, DM, hypertension, antiplatelet agents, and access type, did not influence the initial Qa. First cannulation time was not significantly correlated with initial Qa (r = 0.234, P = 0.075). Twenty-two of 60 patients (36.7%) had an initial Qa < 500 mL/minute.

Prognostic factors for access patency and patient survival

Univariate and multivariate Cox regression models revealed predictors for access patency and survival. Patients treated with antiplatelet agents had five times higher risk than other patients for losing access patency. Maturation failure and an initial Qa < 500 mL/minute were risk factors for poor primary patency (Table 3, Fig. 1). Diabetic status and use of a graft were risk factors for low cumulative patency (Table 4). An initial Qa < 500 mL/minute was not a risk factor for low cumulative patency (Table 4, Fig. 2) or mortality (Table 5, Fig. 3).

Discussion

The National Kidney Foundation’s Kidney Disease Outcomes Quality Initiative (K/DOQI) guidelines recommend routine surveillance for hemodynamically significant stenosis in AVGs and AVFs because prophylactic stenosis correction improves access patency rates [1]. However, this approach has been criticized as being premature, given the several unresolved issues surrounding the predictive accuracy of the monitoring tools. The full risks, benefits, and costs of surveillance programs remain unclear, as does the optimal timing of corrective intervention; there are few methodologically adequate studies that have addressed these issues [2]. Most studies to diagnose stenosis and predict thrombosis in AVF have been biased by small sample sizes and the reporting of cumulative data for AVFs and AVGs, and these studies have proposed a wide variety of diagnostic criteria [3–6]. We introduced Qa measurements and initiated surveillance using Transonic hemodialysis monitoring in 2004 [7]. Only a few authors have reported access outcomes, including patency rates and maturation failure rates, in Korean patients, and these have been determined using a variety of methods [8–12]. Therefore, we evaluated initial flow, surveillance, and survival of hemodialysis access in Korean patients.

In our study, the mean time to first cannulation was 1.8 ± 1.2 (range, 1–6) months. However, 25 of the 60 patients (41.7%) were not assessed at this first time point (data not shown). Contrary to our expectations, the initial Qa did not differ based on patient age, sex, DM, hypertension, anti-platelet agents, or use of a graft. Only the first cannulation time influenced the initial Qa, despite not significantly (r = 0.234,

![Figure 1. Primary access patency in patients with an initial Qa > 500 mL/minute and those with an initial Qa < 500 mL/minute (N=60).](image-url)

Table 3. Predictors of primary access patency by univariate and multivariate cox analysis

| Parameter                  | Univariate analysis |          |          |          | Multivariate analysis |          |          |
|----------------------------|---------------------|----------|----------|----------|-----------------------|----------|----------|
|                            | Relative risk       | 95% CI   | P        | Relative risk | 95% CI | P          | Relative risk | 95% CI | P |
| Age (y)                    | 1.007               | 0.987–1.028 | 0.498    | 1.007 | 0.984–1.030 | 0.559 |
| Male sex                   | 0.790               | 0.393–1.591 | 0.510    | 1.150 | 0.482–2.744 | 0.752 |
| DM                         | 0.893               | 0.446–1.789 | 0.749    | 0.715 | 0.309–1.653 | 0.433 |
| HTN                        | 1.284               | 0.554–2.973 | 0.560    | 0.536 | 0.194–1.483 | 0.230 |
| AntiPLT                    | 1.914               | 0.857–4.272 | 0.113    | 5.677 | 1.841–17.502 | 0.003 |
| Maturation failure         | 5.641               | 2.555–12.454 | 0.000    | 14.662 | 4.505–47.719 | 0.000 |
| Graft                      | 1.719               | 0.765–3.859 | 0.189    | 2.041 | 0.703–5.924 | 0.189 |
| First cannulation time     | 0.938               | 0.708–1.242 | 0.655    | 1.012 | 0.743–1.376 | 0.942 |
| Initial Qa < 500 mL/min    | 2.042               | 1.013–4.119 | 0.046    | 2.784 | 1.091–7.100 | 0.032 |

AntiPLT, antiplatelet agent; CI, confidence interval; DM, diabetes mellitus; HTN, hypertension; Qa, access flow.
In addition, the results shown in Table 5 and Fig. 3 indicate that an initial Qa was associated with new vascular access events [14]. Although the Qa was not influenced by patient age, systolic blood pressure, overweight status, or diabetic status, in contrast to previous Korean reports. Many previous studies have reported more vascular complications in women [18–20]. In addition, the presence of DM and hypertension did not influence primary patency. Tonelli and colleagues [13] and Miller and coauthors [21] found no effect of gender. Dixon and others [18] suggested that only the type of access and the surgeon were the risk factors, and that age, sex, race, DM, and hypertension did not influence primary access patency.

Table 4. Predictors of secondary access patency by univariate and multivariate Cox analysis

| Parameter                  | Univariate analysis | Multivariate analysis |
|----------------------------|---------------------|-----------------------|
|                           | Relative risk       | 95% CI                | P        | Relative risk       | 95% CI                | P        |
| Age (y)                   | 1.012               | 0.980–1.044           | 0.483    | 1.024               | 0.985–1.065           | 0.251    |
| Male sex                  | 0.255               | 0.088–0.779           | 0.012    | 2.219               | 0.554–8.885           | 0.210    |
| DM                        | 3.287               | 1.048–10.309          | 0.041    | 13.734              | 2.265–83.273          | 0.004    |
| HTN                       | 0.663               | 0.187–2.355           | 0.525    | 1.152               | 0.245–5.413           | 0.858    |
| AntiPLT                   | 1.134               | 0.387–3.323           | 0.819    | 2.0273              | 0.480–8.564           | 0.336    |
| Maturation failure        | 2.896               | 0.918–9.139           | 0.070    | 1.643               | 0.217–12.474          | 0.631    |
| Graft                     | 5.442               | 1.852–15.995          | 0.002    | 5.584               | 1.186–26.288          | 0.030    |
| PTA                       | 1.233               | 0.923–1.648           | 0.156    | 1.405               | 0.491–5.628           | 0.223    |
| First cannulation time    | 0.868               | 0.574–1.313           | 0.502    | 0.730               | 0.434–1.228           | 0.236    |
| Initial Qa < 500 mL/min   | 1.565               | 0.579–4.231           | 0.377    | 1.152               | 0.245–5.413           | 0.858    |

AntiPLT, anti-platelet agent; DM, diabetes mellitus; HTN, hypertension; PTA, percutaneous transluminal angioplasty; Qa, access flow.

Figure 2. Secondary access patency in patients with an initial Qa > 500 mL/minute and those with an initial Qa < 500 mL/minute (N = 60).

P = 0.075). Although the Qa was < 500 mL/minute in 36.7% of 60 patients, there was no difference in the AVF/AVG ratio among patients with a Qa < 500 mL/minute or among those with a Qa ≥ 500 mL/minute. These results are largely consistent with the report of Tonelli and colleagues [13]. These authors showed that Qa was not influenced by patient age, vessel diameter may explain the poorer outcomes of fistulae in women [18–20]. In addition, the presence of DM and hypertension did not influence primary patency. Tonelli and colleagues [13] and Miller and coauthors [21] found no effect of gender. Dixon and others [18] suggested that only the type of access and the surgeon were the risk factors, and that age, sex, race, DM, and hypertension did not influence primary access patency.

The maturation failure rate of AVFs was less than that of AVGs (10.4 vs. 33.3%, respectively), but the difference was not significant (P = 0.069). The AVF maturation failure rate in our study differed from the previously reported primary failure rates of 20%–50% [15]. The AVF/AVG ratio in our study is consistent with that reported by Jung and colleagues [11]. They reported a primary failure rate of 13.2%, which was similar between 142 patients with AVF and 40 patients with AVG. The total number of PTA s with AVF was approximately twofold the number of PTA s with AVF (1.3 ± 2.0 vs. 0.7 ± 1.0, P = 0.127). Therefore, graft use is a risk factor that affects cumulative patency (Table 4). These results are consistent with the recent report of Lee and colleagues [17].
Table 5. Predictors of decreased patient survival by univariate and multivariate cox analysis

| Parameter                  | Univariate analysis | Multivariate analysis |
|----------------------------|---------------------|-----------------------|
|                            | Relative risk | 95% CI      |  P     | Relative risk | 95% CI |  P     |
| Age (y)                    | 1.033     | 1.004–1.033  | 0.027  | 1.031     | 0.996–1.066  | 0.083  |
| Male sex                   | 1.650     | 0.671–4.057  | 0.275  | 1.507     | 0.552–4.110  | 0.424  |
| DM                         | 1.983     | 0.831–4.730  | 0.123  | 2.316     | 0.869–6.173  | 0.093  |
| HTN                        | 0.906     | 0.333–2.462  | 0.847  | 0.613     | 0.205–1.830  | 0.380  |
| AntiPLT                    | 1.411     | 0.552–3.608  | 0.522  | 0.918     | 0.311–2.706  | 0.876  |
| Maturation failure         | 1.281     | 0.433–3.787  | 0.957  | 2.723     | 0.707–10.491 | 0.145  |
| Graft                      | 0.786     | 0.265–2.327  | 0.663  | 1.192     | 0.309–4.590  | 0.799  |
| PTA                        | 0.975     | 0.727–1.339  | 0.932  | 0.763     | 0.501–1.163  | 0.209  |
| First cannulation time     | 0.862     | 0.582–1.276  | 0.458  | 0.930     | 0.585–1.477  | 0.758  |
| Initial Qa < 500 ml/min    | 1.479     | 0.639–3.425  | 0.361  | 2.827     | 0.972–8.223  | 0.056  |

AntiPLT, antiplatelet agent; DM, diabetes mellitus; HTN, hypertension; PTA, percutaneous transluminal angioplasty; Qa, access flow.

Conflict of interest

None declared.

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Figure 3. Survival in patients with an initial Qa > 500 mL/minute and those with an initial Qa < 500 mL/minute.

Tonelli and others [22] monitored access flow in a total of 303 patients with native AVF and previous angioplasty: of 69 patients (23%) with stenosis, 53 underwent angioplasty, and 19 patients had recurrent positive evaluations and underwent repeated fistulography. In our study, 27 patients (38.0%) underwent angioplasty and 12 (44.4%) of those patients underwent repeated angioplasty. However, these studies are not directly comparable, because Tonelli and colleagues [23] used Canadian guidelines, which, in patients with AVFs, calls for angiography when fistula flow decreases to < 500 mL/minute or drops > 20% from baseline and in patients with AVGs, calls for angiography when blood flow decreases to < 650 mL/minute or there is a drop of > 20% from baseline. We used a modified version of the K/DOQI and Canadian guidelines.

Our study has several limitations, including the small number of patients overall (selection bias) and the lack of randomization. It also did not perform preoperative mapping of vessels. Because there is no standardized description for access and PTA results in Korea, these outcomes may not definitively reflect patency rates and access survival. Nevertheless, this prospective study provided data on hemodialysis access in Korean patients.

In conclusion, an initial Qa < 500 mL/minute is a risk factor for poor primary patency, while an initial Qa < 500 mL/minute is not a risk factor for low cumulative patency or mortality.
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