The Natural History of Arteriovenous Access and Risk Factors Associated With Access Thrombosis After Successful Kidney Transplantation

M.H. Kim, K.M. Park, J.K. Hwang, S.C. Park, I.S. Moon, and J.I. Kim

ABSTRACT

Introduction. The purpose of this study was to determine the natural history of arteriovenous (AV) access after successful kidney transplantation (KT) and to identify the risk factors of spontaneous access closure in kidney transplant recipients.

Methods. We performed a retrospective review of 115 patients who underwent KT with functioning access from June 2010 to July 2012. AV access patency was checked and recorded daily during the hospital stay and at every visit to the outpatient clinic. Patients were divided into 2 groups according to the patency of access, and risk factors of access thrombosis were assessed. Access patency was followed up until patency was lost or the study was closed.

Results. At the end of follow-up, 18 (15.7%) AV accesses had spontaneously closed. Mean time to closure was 119 ± 163 days, and 12 of 18 were closed within 90 days after KT. AV access spontaneously closed in 8.5% of male patients, compared with 27.3% of female patients (\(P = .007\)), 12.2% of cases with native access compared with 35.3% of cases with artificial access (\(P = .016\)), and 11.3% of cases with wrist access compared with 25.7% of cases with elbow access (\(P = .049\)). Spontaneously closed AV accesses tended to have a lower mean access flow compared with functioning accesses (\(P = .019\)). On multivariate analysis, female sex and AV access flow volume affected spontaneous AV access closure (odds ratio 4.749, 95% confidence interval 1.919–35.383, \(P = .008\); odds ratio 0.998, 95% confidence interval 0.996–0.999, \(P = .010\), respectively).

Conclusions. Our results suggest that AV access thrombosis occurs more frequently during the early postoperative period, particularly in female patients or patients with low flow access, whereas it is a rare event in male patients or patients with high access flow, especially in the late postoperative period.

A WELL-FUNCTIONING ARTERIOVENOUS (AV) access is a crucial element for effective hemodialysis (HD) in patients with end-stage renal disease (ESRD). Nevertheless, it is usually forgotten and left in place in the patient because it is not required after successful kidney transplantation (KT). The remaining AV access in kidney transplant recipients (KTRs) may be spontaneously closed, surgically ligated, functioning until patient death, or reused for HD after renal allograft failure. However, there is no consensus on the management of unused AV access. Some authors advocate performing systematic closure of a functioning access because it may lead to complications of the access itself or high-output cardiac failure [1–3]. On the

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other hand, others recommend preserving an AV access that could be useful if it is necessary to resume HD [4,5].

To decide whether and when AV access should be ligated in patients with successful transplants, it is important to understand the natural history of AV access and the risk factors associated with access thrombosis. Nevertheless, there is scant information on the natural history of AV access in KTRs [6,7]. Furthermore, the risk factors of access thrombosis have never been studied. The object of this study was to investigate the natural history of vascular access and identify factors associated with spontaneous access closure in KTRs who had a well-functioning AV access on the day of transplantation.

METHODS
Selection and Description of Participants
We performed a retrospective review of patients undergoing KT with functioning AV access from June 2010 to July 2012 to identify the risk factors associated with spontaneous closure of the AV access. During this period we performed 284 KTs. Among them, 115 patients with functioning AV access on the day of surgery were included in this study. Various demographic and clinical characteristics of the patients and AV accesses were recorded prospectively on a separate case report form. AV access patency was checked and recorded on the case report form daily during the hospital stay and at every visit to the outpatient clinic after June 2010. Ninety of 115 patients underwent duplex ultrasonography to evaluate AV access flow just before or immediately after KT. Access patency was followed up until patency was lost or the study was closed on October 31, 2012. The patients were divided into 2 groups according to patency of AV access, and factors contributing to spontaneous closure of AV access were assessed. The following characteristics were included in the analysis: recipient age, recipient sex, cause of ESRD, comorbidities (diabetes mellitus, hypertension, cerebrovascular disease, and cardiac disease), presence of antiplatelet therapy, history of rejection, type of AV access (native fistula vs artificial graft), location of AV access (radial artery vs brachial artery), side of AV access, outflow volume of AV access, number of AV accesses formed, duration of AV access use before KT, and history of intervention or surgical revision of current AV access. This study was approved by the institutional review board at Seoul St. Mary’s Hospital.

Statistical Techniques
Descriptive statistics and frequencies were obtained and comparisons were made using the SPSS Version 15.0 statistical package (SPSS Inc., Chicago, Ill, USA). Statistically significant differences between groups were assessed using the Pearson χ² test or the Fisher exact test for categorical variables and the Student t test for continuous variables. The Mann-Whitney U test was used to compare flow volume. A multivariate logistic regression analysis was performed to identify independent predictors of AV access thrombosis. Kaplan-Meier survival curves were used to determine the patency of AV fistula. A value of P < .05 was considered statistically significant.

RESULTS
Patient Characteristics
A total of 115 patients met the inclusion criteria for this study. Demographics and clinical characteristics of the study group are listed in Tables 1 and 2. The mean age of the patients was 46.8 ± 9.3 years, and most were male (61.7%). The mean body mass index was 22.9 ± 3.8. The most common cause of ESRD was chronic glomerulonephropathy in 42 (36.5%) patients. In total, 104 (90.4%) patients were hypertensive, 20 (17.4%) were diabetic, 11 (9.6%) had ischemic heart disease, and 3 (2.6%) experienced a cerebrovascular accident. Fifty-six (48.7%) patients were taking antiplatelet agents at the time of KT. The majority of patients (85.2%) had a native AV access. The arteries used for AV access anastomosis were 80 (69.6%) radial arteries on wrist (80 radiocephalic AV fistulas) and 35 (30.4%) brachial arteries on elbow (20 brachiocephalic AV fistulas, 12 brachioantecubital AV grafts, 2 brachioaxillary AV grafts, and 1 brachiobasilic AV fistula). Mean duration from AV access construction to KT was 1937 ± 1864 days, and mean follow-up after KT was 385 ± 225 days.

AV Access Patency After KT
At the end of follow-up, 18 (15.7%) AV accesses were spontaneously closed. Primary AV access patency using censored data was 87.8% (standard error [SE] .030), 85.6% (SE .034), 83.8% (SE .037), 81.8% (SE .042), 81.8% (SE .042), and 81.8% (SE .042) at 6, 12, 18, 24, and 30 months, respectively (Fig 1). AV access thrombosis occurred more

Table 1. Demographics of 115 Patients Who Received Kidney Transplant With Functioning Arteriovenous Access

<table>
<thead>
<tr>
<th>Variables</th>
<th>Total Patients (%)</th>
<th>Thrombosed Group (%)</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age 46.8 ± 9.3</td>
<td>47.0 ± 9.4</td>
<td>45.8 ± 8.9</td>
<td>.455</td>
</tr>
<tr>
<td>Male sex 71 (61.7)</td>
<td>65 (67.0)</td>
<td>6 (33.3)</td>
<td>.007</td>
</tr>
<tr>
<td>Body mass index 22.9 ± 3.8</td>
<td>23.0 ± 3.8</td>
<td>22.4 ± 3.9</td>
<td>.453</td>
</tr>
</tbody>
</table>

All continuous variables are presented as mean ± standard deviation, and all categorical variables are presented as the total number with the percentage in parentheses.

Abbreviations: ESRD, end-stage renal disease; CGN, chronic glomerulonephropathy; IHD, ischemic heart disease; CVA, cerebrovascular accident.

*Including polycystic kidney disease, lupus nephritis, and chronic pyelonephritis.
frequently in the early postoperative period. Two thirds of AV accesses were occluded within 3 months after KT (including 4 cases of AV access that closed on the day of surgery), whereas only 2 cases of AV access became thrombosed more than 1 year postoperatively (Fig 2). Mean time to closure after transplantation was 119/163 days.

Risk Factors for Loss of Patency

Various patient demographics and clinical characteristics of AV access were compared to identify the factors associated with AV access thrombosis (Tables 1 and 2). There were significant differences between the patent and thrombosed groups with respect to patient sex, type of access, location of access, and flow volume of access. AV access spontaneously closed in 6 (8.5%) male patients compared with 12 (27.3%) female patients ($P = .007$); 12 (12.2%) cases of native AV access compared with 6 (35.3%) of artificial AV access ($P = .016$); and 9 (11.3%) with wrist AV access compared with 9 (25.7%) with elbow AV access ($P = .049$). Spontaneously closed AV access tended to have lower mean access flow when comparing functioning access (1095/645 mL/min vs 2086/1493 mL/min, respectively, $P = .019$). A logistic regression was performed using 4 statistically significant variables from univariate analysis as independent variables and AV access thrombosis as a dependent variable (Table 3). Female sex of KTR and flow volume of AV access were independent predictors of AV access thrombosis after KT (odds ratio [OR] 4.749, 95% confidence interval [CI] 1.919–14.963, $P = .008$ and OR 0.998, 95% CI 0.996–0.999, $P = .010$, respectively).

**DISCUSSION**

What is the best way to manage a retained AV access after a successful KT? There is still debate on this issue, and no consensus has been reached. The general conclusion that can be drawn from the few available studies is that a functioning AV access with complications such as arterial steal syndrome, venous hypertension, infection, and high-output cardiac failure should be ligated [1,3,7]. However, it is still unclear whether systematic closure of a well-functioning AV access without complications is beneficial to a patient who received a successful KT. Although closure of a functioning AV access helps to prevent complications associated with a retained AV access, it can also jeopardize a valuable access that the patient might need for further HD.

| Table 2. Clinical Characteristics of 115 Arteriovenous Accesses in Kidney Transplant Recipients |
|---------------------------------|----------------|----------------|----------------|----------------|
| Variables                      | Total Patients (%) | Patent Group (%) | Thrombosed Group (%) | $P$ Value |
| N = 115                        | N = 97          | N = 18          |                |             |
| Type of access                 |                |                |                | .016        |
| Native fistula                 | 98 (85.2)      | 86 (88.7)      | 12 (66.7)      |             |
| Location of access             |                |                |                | .049        |
| Wrist                          | 80 (69.6)      | 71 (73.2)      | 9 (50.0)       |             |
| Side of access                 |                |                |                | .290        |
| Left                           | 113 (98.3)     | 96 (99.0)      | 17 (94.4)      |             |
| History of access repair*      | 18 (15.7)      | 16 (16.5)      | 2 (11.1)       | .564        |
| Flow volume of access†         | 1931 ± 1439    | 2086 ± 1493    | 1095 ± 645     | .000        |
| Duration (d)‡                   | 1937 ± 1864    | 1882 ± 1781    | 2235 ± 2300    | .936        |

All continuous variables are presented as mean ± standard deviation, and all categorical variables are presented as the total number with the percentage in parentheses.

*History of intervention or surgical revision to salvage current access.

†Respectively, 79 patients and 11 patients were examined with color duplex ultrasound in the patent group and thrombosed group.

‡Arteriovenous access construction to kidney transplantation.

**(Fig 1. Kaplan-Meier survival curve of arteriovenous access after kidney transplantation.**

**(Fig 2. Time of occurrence of arteriovenous access thrombosis after kidney transplantation.**

| Table 3. Multivariate Analysis of Risk Factors Associated With Access Thrombosis |
|---------------------------------|----------------|----------------|----------------|
|                                | B              | OR (95% CI)    | $P$ Value |
| Sex (female)                   | 1.558          | 4.749 (1.507–14.963) | .008 |
| Type of access (graft)         | 0.893          | 2.443 (0.425–14.029) | .317 |
| Location of access (wrist)     | 0.945          | 0.240 (0.532–12.453) | .240 |
| Flow volume of access          | −0.002         | 0.998 (0.996–0.999) | .010 |

Statistics were analyzed by a backward stepwise method in logistic regression analysis.

Abbreviations: B, regression coefficient; OR, odds ratio; CI, confidence interval.
Some authors propose systematic closure of functioning AV access because of the significant role of AV access in left ventricular hypertrophy and the increased cardiovascular disease risk [3,8,9] as well as the effectiveness of AV access closure in improving some cardiac mass indices in stable asymptomatic KTRs [2,10]. On the other hand, reports that do not show a relationship between cardiovascular risk and patency of AV access or a significant alteration in cardiac indices after AV access closure are against routine ligation [4,5,11]. There is also disagreement regarding the reuse of AV access. In 2 recent studies on the feasibility of creating a new AV access after resuming HD, most new AV accesses were created without difficulty [12,13]. On the contrary, some authors recommend preservation of a functioning AV access because the creation of a new access may be extremely difficult and is not feasible in some cases [14].

Systematic AV access closure in KTRs is not recommended until prospective and randomized studies establish evidence-based criteria for a benefit in reducing cardiac morbidity and mortality. Until then, the management of a functioning AV access should be individualized according to the status of the patient and the access. Our study could provide useful information for deciding whether and when AV access should be ligated in successfully transplanted patients.

The results of our study showed that a relatively small number of AV accesses closed spontaneously, and one third of the closures occurred within 3 weeks after the operation. Only female sex and lower access flow volume were statistically significant risk factors associated with access thrombosis.

The incidence of AV access thrombosis in our study differs from that in other reports, although the time pattern is similar [6,7,15]. In our study, 18 of 115 (15.7%) patients experienced AV access thrombosis after KT. This is a relatively low rate compared with reported incidences of 25.6% to 39.7% in other studies (excluding surgically ligated cases) [6,7,15]. There are 2 possible reasons for this difference. The first is the shorter follow-up time in our study compared with others (mean 12.8 ± 7.5 months vs median 69 months) [6], and the second is the high access flow volume in our patients. It is well known that AV access flow is very closely related to access patency. Soleimani et al. [15] reported that 25.6% of AV fistulas spontaneously closed during a mean follow-up period of 13.9 ± 4.8 months. Compared with our study, the mean follow-up period was very similar but the incidence of AV access closure was nearly double. The flow volume of patent AV access in their patients was only one quarter of that in our patients with patent access (560.9 ± 405.8 mL/min vs 2086 ± 1493 mL/min, respectively). Our results also show that the incidence of access thrombosis is high in the early postoperative period and decreases over time after KT (Figs 1 and 2). In our study, two thirds of spontaneous AV access thrombosis occurred within 3 months after KT and one third occurred within 3 weeks. This time pattern is very similar to that reported by Patard et al. [6], who demonstrated that nearly one half (45%) of AV access thrombosis occurred within 3 weeks after KT. The high incidence of access thrombosis in the early postoperative period may be mainly associated with perioperative events such as hypotensive periods secondary to hypovolemia, patient position, operating table handling, and possibly thrombosis of a poorly functional AV fistula that had not been identified before surgery. As expected, the 2-year primary patency of AV access was better in our KTRs than in hemodialyzing patients reported in the literature (81.8% vs 40% to 50%, respectively) [16,17]. There are 2 possible reasons for this difference. AV access in our KTRs was maintained without damage from repeated HD such as traumatic injury by the cannulation itself, thrombosis caused by compression to control bleeding, and hypotension caused by volume removal. Another important reason is that the AV access in KTRs is already matured, whereas a newly created AV access has a 50% risk of maturation failure [18].

There are many reports on the risk factors associated with access failure in hemodialyzing patients, and numerous factors such as demographics, hemodynamics, and hypercoagulability were studied in these reports [19,20]. However, there are no reports on renal transplant recipients in the literature. Our data show that the only independent risk factors of thrombosis in KTRs were female sex and lower flow volume of AV access, which were also risk factors in patients who received HD with AV access. There is some controversy over whether female sex itself is a risk factor in HD patients [21,22]. Some studies showed that female sex is an independent risk factor, but others reported that the smaller vessel size in female patients is associated with access thrombosis. Although there is no definitive cutoff value of access flow associated with access thrombosis, most reports agree that AV access blood flow is a predictor of access thrombosis [23,24].

Although our study has some limitations, such as its retrospective nature and short follow-up periods, this is the first study evaluating the risk factors associated with access thrombosis in KTRs. Our results suggest that AV access thrombosis occurs more frequently during the early postoperative period, particularly in female patients or patients with low flow access, whereas it is a rare event in male patients or patients with high access flow, especially in the late postoperative period. To prevent unnecessary surgery on an access with a high chance of spontaneous closure or prolonging the wait time in the case of an access with a low chance of spontaneous closure, a detailed knowledge of the natural history of AV access and risk factors associated with access thrombosis is important when deciding whether and when access should be closed in patients with successful transplantations.

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