Percutaneous Treatment of Thrombosed Arteriovenous Fistulas: Clinical and Economic Implications

Luís Coentrao, Pedro Bizarro, Carlos Ribeiro, Ricardo Neto, and Manuel Pestana

*Nephrology Research and Development Unit, Hospital S. João, and †Institute of Pharmacology and Therapeutics, Faculty of Medicine, University of Porto, Porto, Portugal; and ‡Financial Management Unit, Hospital S. João, Porto, Portugal

Background and objectives: Maintenance of previously thrombosed arteriovenous fistulas (AVFs) as functional vascular accesses can be highly expensive, with relevant financial implications for healthcare systems. The aim of our study was to evaluate the costs and health outcomes of vascular access care in hemodialysis patients with AVF thrombosis.

Design, setting, participants, & measurements: A retrospective, controlled cohort study was performed among local hemodialysis patients with completely thrombosed AVFs between August 1, 2007, and July 1, 2008. Detailed clinical and demographic information was collected and a comprehensive measure of total vascular access costs was obtained. Costs are reported in 2009 U.S. dollars.

Results: A total of 63 consecutive hemodialysis patients with thrombosed AVFs were identified—a cohort of 37 patients treated with percutaneous thrombectomy and a historic cohort of 25 patients with abandoned thrombosed AVFs. The mean cost of all vascular access care at 6 months was $2479. Salvage of thrombosed AVFs led to a near two-fold reduction in access-related expenses, per patient-month at risk ($375 versus $706; P = 0.048). The costs for access-related hospitalizations ($393 versus $91; P = 0.050), management of access dysfunction ($106 versus $28; P = 0.005), and surgical interventions ($35 versus $6; P = 0.001) were also significantly lower in the percutaneous treatment group. At 6 months, most of these patients had a functional AVF as permanent vascular access (91% versus 33%, P = 0.0001).

Conclusions: Salvage of thrombosed AVF is a highly efficient procedure; therefore, intensive efforts should be undertaken to universalize these interventions.

F

Functional vascular access is a prerequisite for adequate hemodialysis treatment in patients with ESRD. Autogenous arteriovenous fistulas (AVFs) are considered superior to synthetic grafts as a hemodialysis vascular access; however, AVFs are not without problems (1). In the last decade, management of thrombosed AVFs has been largely accomplished by surgical or endovascular interventions. Despite the existence of well established endovascular procedures to declot a thrombosed AVF (2–10), attempts to salvage these accesses are not universally used.

Percutaneous treatment of thrombosed AVFs is a relatively highly successful procedure. However, repeated interventions are usually required to achieve long-term access survival (11). Therefore, maintenance of a previously thrombosed AVF could be a highly expensive policy. Published data regarding the economic value of vascular access surveillance and prophylactic angioplasty to prevent AVF thrombosis are controversial (12,13), and information about the cost-effectiveness of AVF salvage procedures has been limited.

In the study presented here, we performed a retrospective analysis among adult maintenance dialysis patients with thrombosed AVFs to estimate the costs and health outcomes of vascular access care during the first 6 months post-thrombosis.

Patients and Methods

Patient Population

The Hospital S. João, Porto, is a university hospital center that serves a large population on regular hemodialysis (approximately 1600 patients). Until the last few years, hemodialysis patients with thrombosed AVFs were referred for surgical revision of the clotted AVF or to our nephrology department for central venous catheterization pending creation of a new AVF. By 2008, endovascular treatment of thrombosed AVFs became a standard procedure in our unit.

Patients were recruited from the Nephrology Unit, Hospital S. João, Porto. All adult maintenance dialysis patients with completely thrombosed AVFs between August 1, 2007 and July 31, 2008, were included in this study. From August 1 and December 31, 2007, patients were referred for central venous catheterization pending creation of a new AVF. From January 1 to July 31, 2008, patients were referred for consideration of a percutaneous thrombectomy.

Sixty-three adult maintenance dialysis patients fulfilled the study criteria. Thirty-seven patients were treated with percutaneous thrombectomy (group A) and 25 patients underwent central venous catheterization to bridge the interval until a new AVF was suitable for...
cannulation (group B). In only one patient the interventionalist deemed that endovascular intervention was not advisable because of the presence of long segmental aneurysms with an extremely large clot burden. This patient underwent central venous catheterization. Three patients were lost to follow-up. In the final analysis, group A included 35 patients and group B included 24 patients (n = 59).

The study was approved by the Ethics Committee for Health of the Hospital S. João, Porto.

Procedures

In our unit, we used the method of manual catheter-directed thromboaspiration (2). If a hemodynamically significant lesion was encountered, a conventional angioplasty balloon, rated burst pressure of 15 atm (Cordis Corporation, Johnson & Johnson Medical N.V/S.A., Waterlool, Belgium), was inflated at the level of the stenotic site. Patients were referred within 72 hours of thrombosis. The only contraindications for percutaneous declotting were infection and the presence of long segmental aneurysms with extremely large clot burdens. Percutaneous thrombectomy was performed as an outpatient procedure. Tunnelled cuffed catheter (TCC) placement (Retro, Spire Biomedical, Inc., Bedford, MA) was performed with ultrasound guidance, as recommended by Dialysis Outcomes Quality Initiatives (14). Postprocedure chest radiography was performed in all patients.

Clinical success was defined as the resumption of dialysis with a blood flow >300 mL/min at the first dialysis session after the intervention (15). Primary (unassisted) patency of the vascular access was calculated from the date of the index procedure to the first subsequent access intervention. Access primary patency ended when any of the following occurred: (1) there was an intervention for the treatment of stenosis or thrombosis anywhere within the AVF; (2) there was an intervention for the treatment of intracatheter thrombosis, catheter malposition, or kinking; or (3) there was an intervention for the treatment of access-related bacteriaemia requiring catheter removal or AVF closure.

Cost Analysis

Our study took the perspective of the healthcare purchaser including direct vascular access care-related costs. All resource use was valued at prices in 2009. All costs were converted to U.S. dollars using an exchange rate of 1 Euro (€) equal to 1.41 U.S.$.

A direct access care-related cost was estimated for each procedure, including all expenses for creation of a new AVF (unitary cost, €420), placement of TCC (unitary cost, €605), and hospitalization for vascular access-related complications (unitary cost for in-hospital care of vascular access infection, €2075). Costs for correcting the AVF stenosis or thrombosis by endovascular means were assessed to be €1401. The cost per procedure was established from the Ministry of Health and Welfare Ordinance Legislation - Diário da República (1st series, no. 147, July 31, 2009, ordinance no. 839 and 2nd series, no. 81, April 5, 2000, dispatch no. 7376/2000).

Information on all vascular access surgeries was captured from our nephrology unit database, which collects surgical data for all patients who undergo vascular access surgery. Information on hospital admissions for management of vascular access-related problems (e.g., local or metastatic infection, limb ischemia, hemorrhage, or thrombosis), endovascular procedures (i.e., all radiology procedures performed as part of access-related care), and catheter placements/local thrombolytic therapy, was collected from our hospital database. Patient’s transport costs required for the vascular access care were also included in the analysis. They principally used a taxi or ambulance for hospital visits (€0.66 for 1 km). In addition, we did not collect information on costs specifically related to outpatient use of intravenous antibiotics for access-related infection.

Follow-Up

Patient follow-up started on the day the vascular access intervention was first performed and continued for 6 months. Clinical and demographic data, as well as data on access type, were collected from hospital and satellite unit records. Demographic information was assessed by means of a questionnaire. The presence of comorbid illness was assessed by a physician as of the enrolment date by complete review of patient’s records. Information was collected for the 19 variables that constitute the Charlson comorbidity index (16), which has been validated for use in patients with ESRD. Follow-up was censored for patient death or transplant.

Study Endpoints

The primary endpoint of this analysis was to determine the economic effect of endovascular intervention in hemodialysis patients with thrombosed AVF. Secondary outcomes of the study included all access-related clinical adverse events (e.g., bacteriaemia, access dysfunction, surgical interventions, hospital admissions, and death).

Statistical Analyses

Data are given as percentages and mean ± SD. Normally distributed continuous variables were analyzed using Student’s unpaired t test and categorical variables using Fisher’s exact test. Rates were calculated for each of the patients by dividing the number of events/procedures by the duration of follow-up in months. Vascular access patency was analyzed using the Kaplan–Meier method and differences between groups were evaluated by log-rank tests. All tests were two sided, and differences were considered significant at P < 0.05. All statistical analyses were performed using the SPSS software, version 11 (SPSS, Inc., Chicago, IL).

Results

Approximately two thirds of the patients were male. Diabetes, hypertension, and vascular disease were commonly present in both study groups. There were no relevant differences between the two treatment groups at baseline with respect to demographic characteristics and medical history (Table 1).

Percutaneous thrombectomy was successfully performed in 34 patients, with prompt restoration of a thrill and bruit. No stent was deployed. Angioplasty was not feasible in one patient with an upper-arm AVF because of the inability to pass the guidewire through a tight stenotic lesion. This patient underwent TCC placement. Clinical success was observed in 34 patients (success rate = 97%). Twenty-four patients (69%) presented with a radial-cephalic AVF (an underlying stenosis lesion was present in the draining vein in 11 patients and concurrent stenoses at the arterial anastomosis and in the draining vein in 13 patients). Eleven patients (31%) presented with a brachial-cephalic AVF (an underlying stenosis lesion was present in the draining vein in five patients and in the arterial anastomosis in six patients). One patient with upper-arm AVF developed steal syndrome and myocardial infarction, approximately 2 weeks postprocedure, requiring hospitalization and further access surgery. Six patients experienced AVF thrombosis during follow-up (five patients with an upper-arm AVF and one patient with a forearm AVF): three patients were treated...
with further percutaneous thrombectomy, two patients were given a TCC placement, and one patient underwent a new AVF creation in the same arm. Two patients died during follow-up because of acute pancreatitis and respiratory infection, respectively. At 6 months, the primary patency rate of the vascular access was 75% (Figure 1). At the end of follow-up, 30 patients (91%) presented a functional AVF as a permanent vascular access (Figure 2).

TCC placement was successfully performed in 24 patients. Nevertheless, clinical success was observed in 22 patients (92%) presented with an internal jugular catheter. During follow-up, hospitalization because of catheter-related bacteremia (n = 4) or central venous thrombosis (n = 2) was required in six patients. Local catheter thrombolysis (total = 16) was necessary in six patients. Thereafter, four patients underwent catheter removal because of late dysfunction. Nine patients underwent a second TCC placement. At 6 months, the primary patency rate of the vascular access was 51% (Figure 1). Although 22 patients underwent a new AVF creation, only eight patients (33%) were performing dialysis with a functional AVF at the end of follow-up (Figure 2). The mean time for the construction of a new AVF was 33 days (3 to 180 days). Table 2 shows the mean values of secondary outcomes for both study groups.

The cost of vascular access care was substantial, with a mean cost per patient at 6 months of $2479 (median $1455; interquartile range [IQR] $647 to $18,848). The total cost for patient-month at risk was lowest for the endovascular group (mean $374; median $241; IQR $228 to $3146 versus mean $706; median $379; IQR $108 to $3018; P = 0.048; Table 3). Furthermore, the mean access-related surgical costs, costs for access-related hospital admissions, and management of access dysfunction were significantly higher for group B patients. The largest expenses for patients treated with central venous catheterization were related with hospitalizations. On the other hand, percutaneous thrombectomy itself was responsible for approximately two thirds of the costs spent with group A patients (Table 3).

Table 1. Baseline characteristics of patients overall and according to treatment group

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>Overall (n = 59)</th>
<th>Group A (n = 35)</th>
<th>Group B (n = 24)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, years</td>
<td>66 ± 13.4</td>
<td>64 ± 14</td>
<td>69 ± 11.8</td>
<td>0.07</td>
</tr>
<tr>
<td>Gender, n (%) male</td>
<td>39 (66%)</td>
<td>25 (71%)</td>
<td>14 (58.3%)</td>
<td>0.29</td>
</tr>
<tr>
<td>Previous fistulas, n (%)</td>
<td>24 (40.7%)</td>
<td>13 (37%)</td>
<td>11 (45.8%)</td>
<td>0.21</td>
</tr>
<tr>
<td>Previous dialysis catheter, n (%)</td>
<td>34 (57.6%)</td>
<td>21 (60%)</td>
<td>13 (54.2%)</td>
<td>0.29</td>
</tr>
<tr>
<td>Time on dialysis, years</td>
<td>3.3 ± 2.6</td>
<td>3.9 ± 2.8</td>
<td>2.4 ± 1.8</td>
<td>0.02</td>
</tr>
<tr>
<td>Charlson comorbidity index</td>
<td>4.7 ± 2.3</td>
<td>4.6 ± 2.3</td>
<td>4.8 ± 2.3</td>
<td>0.4</td>
</tr>
<tr>
<td>Comorbid conditions, n (%)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>coronary heart disease</td>
<td>11 (18.60%)</td>
<td>7 (20%)</td>
<td>4 (16.70%)</td>
<td>0.76</td>
</tr>
<tr>
<td>congestive heart failure</td>
<td>19 (32.20%)</td>
<td>11 (31.40%)</td>
<td>8 (33.30%)</td>
<td>0.86</td>
</tr>
<tr>
<td>peripheral vascular disease</td>
<td>14 (23.70%)</td>
<td>9 (25.7%)</td>
<td>5 (20.8%)</td>
<td>0.65</td>
</tr>
<tr>
<td>previous stroke</td>
<td>11 (18.60%)</td>
<td>5 (14.3%)</td>
<td>6 (25%)</td>
<td>0.31</td>
</tr>
<tr>
<td>diabetes</td>
<td>16 (27.10%)</td>
<td>12 (34.30%)</td>
<td>4 (16.70%)</td>
<td>0.14</td>
</tr>
</tbody>
</table>

Figure 1. Percentage of freedom from subsequent interventions at 6 months. The graph shows the primary patency as of enrollment according to the Kaplan–Meier analysis.

Figure 2. Permanent vascular access type at 6 months of follow-up for each study group. At the end of follow-up, a significantly higher number of group A patients had a functioning AVF as a permanent vascular access.
Table 2. Secondary outcomes at 6 months of follow-up according to study group (median \pm SD)

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Group A (n = 35)</th>
<th>Group B (n = 24)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Access-related surgery</td>
<td>0.08 \pm 0.27</td>
<td>0.33 \pm 0.47</td>
<td>0.01</td>
</tr>
<tr>
<td>Access-related hospital admissions</td>
<td>0.05 \pm 0.32</td>
<td>0.25 \pm 0.43</td>
<td>0.047</td>
</tr>
<tr>
<td>Management of access dysfunction</td>
<td>0.16 \pm 0.43</td>
<td>0.96 \pm 1.45</td>
<td>0.004</td>
</tr>
<tr>
<td>Management of access-related infection</td>
<td>0</td>
<td>0.17 \pm 0.47</td>
<td>0.036</td>
</tr>
<tr>
<td>Patient death, access-related</td>
<td>0</td>
<td>0.08 \pm 0.48</td>
<td>0.072</td>
</tr>
</tbody>
</table>

*Includes all radiology procedures performed as part of access-related care, catheter placements, and local thrombolytic therapy.

Table 3. Cost analysis in U.S. dollars/patient-month overall and according to treatment group (mean \pm SD)

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Overall (n = 59)</th>
<th>Group A (n = 35)</th>
<th>Group B (n = 24)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Index procedure</td>
<td>$182 \pm 45</td>
<td>$232 \pm 3</td>
<td>$109 \pm 20</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Surgical interventions</td>
<td>$18 \pm 25</td>
<td>$6 \pm 14</td>
<td>$35 \pm 32</td>
<td>0.001</td>
</tr>
<tr>
<td>Hospital admissions</td>
<td>$211 \pm 428</td>
<td>$91 \pm 327</td>
<td>$393 \pm 50</td>
<td>0.050</td>
</tr>
<tr>
<td>Management of access dysfunction</td>
<td>$60 \pm 75</td>
<td>$28 \pm 54</td>
<td>$106 \pm 88</td>
<td>0.005</td>
</tr>
<tr>
<td>Patient’s transport</td>
<td>$22 \pm 22</td>
<td>$8 \pm 3</td>
<td>$45 \pm 29</td>
<td>0.002</td>
</tr>
<tr>
<td>Total cost</td>
<td>$510 \pm 466</td>
<td>$375 \pm 355</td>
<td>$706 \pm 563</td>
<td>0.048</td>
</tr>
</tbody>
</table>

*Includes all radiology procedures performed as part of access-related care, catheter placements, and local thrombolytic therapy.

Discussion

Vascular access care is responsible for a significant proportion of healthcare costs in prevalent hemodialysis patients (17). Manns et al. (18) have shown that the high access-related costs of incident hemodialysis patients with primary AVF failure were partially due to the increased number of diagnostic imaging and radiologic interventions. For healthcare systems with strict economic barriers, this issue may be extremely relevant.

Bittl et al. (12) recently published an economic analysis concluding that preemptive angiographic management of AVF dysfunction may represent a less efficient use of healthcare resources than increasing the number of patients with AVF. In the study presented here, we have demonstrated that salvage of clotted AVF by percutaneous thrombectomy rather than waiting for a new mature AVF, was associated with a reduction in access-related costs (Table 2).

Study groups were relatively well matched for baseline parameters and length of follow-up. Despite the relative short time on hemodialysis, near a half of the patients had a previous history of dialysis catheters and vascular access surgeries (Table 1). As such, salvage of the clotted AVF would be of an utmost importance.

Among the previous series (2–10), clinical success and primary patency at 6 months of thrombosed AVFs treated with interventional thrombectomy have ranged between 73% to 96% and 38% to 81%, respectively. For TCC placement, primary patency rates are approximately 60% at 6 months (19). The outcomes of the current series, for endovascular procedure (clinical success 97%, primary patency 75%) and catheter placement (clinical success 92%, primary patency 51%), were at the higher end of these ranges (Figure 1).

In 2006, Allon et al. (20) reported that change in vascular access had relevant clinical implications in hemodialysis patients. In the study presented here, 91% of group A patients had a functioning AVF as a permanent vascular access at 6 months. In contrast, we have found only 33% of group B patients with a functional AVF at the end of follow-up. As a consequence, group B patients presented a higher percentage of hospitalizations and comorbidity (Table 2). Local practice patterns may have been responsible for the observed low rate of functioning AVF in group B patients. However, these results are not surprising because even incident hemodialysis patients (without a previous history of failed AVF) with a functional AVF at 6 months. In the study presented here, 91% of group A patients had a functioning AVF as a permanent vascular access at 6 months. In contrast, we have found only 33% of group B patients with a functional AVF at the end of follow-up. As a consequence, group B patients presented a higher percentage of hospitalizations and comorbidity.
procedure itself was completely offset by the saving associated with lower surgical visits, access dysfunction, and hospitalizations (Table 3). In fact, management of access dysfunction and access-related hospitalizations was nearly 4 times higher in group B patients (Table 3), reflecting the lower access survival and the subsequent comorbidity associated with TCC placement. Interestingly, the usual forgotten patient’s transport cost required for the establishment and management of the vascular access had a relevant economic effect in group B patients (Table 3). Therefore, the guarantee of a functional AVF with a high primary patency rate is an utmost important issue in hemodialysis patients, with obvious economic benefits.

Although patients were followed-up for only 6 months, we were able to find clinical and economic disparities between the two different approaches. Probably, if a long-term follow-up was performed, differences between cohorts would have been similar because both groups would require more vascular-access interventions to establish or maintain a functional vascular access.

Our study had several limitations. First, as a retrospective study, it shares all of the limitations of that approach. Selection of candidates for AVF salvage therapy and the type of procedure performed may differ among centers and countries, and this may have an effect on the external generalizability of our results. Also, the patient population consisted mainly of Caucasian Europeans, which makes it impossible to draw conclusions for other ethnicities. The cost of certain healthcare procedures has been reported to differ between countries (22). However, the relative amount of resources required for intervention and the determinants of vascular access costs are likely to be similar between centers. We are aware that our study cannot provide a definitive answer regarding the efficiency of percutaneous thrombectomy in AVF thrombosis and that further prospective cost-effectiveness analysis comparing endovascular and surgical procedures needs to be undertaken.

In conclusion, the cost of vascular access care is high among patients with AVF thrombosis and highest for patients selected for central venous catheterization pending the creation of a new AVF. Our study suggests that salvage of thrombosed AVFs by percutaneous thrombectomy is a safe and cost-effective policy; therefore, intensive efforts should be undertaken to universalize these procedures.

Acknowledgments

We thank the clinical directors from hemodialysis clinics who kindly agreed to collaborate in this study: A. Baldaia Moreira M.D., A. Caldeira Gomes M.D., A. Castro Henriques M.D., Antunes de Azevedo M.D., Eva Xavier M.D., João C. Fernandes M.D., João M. Fração M.D., Ph.D., Jorge P. Baldaia M.D., José M. Madureira M.D., José Pinheiro M.D., Odete Pereira M.D., Sofia Pedroso M.D., Susana Sampaio M.D., and Vasco Miranda M.D.

Disclosures

None.

References