Endovascular versus Surgical Preemptive Repair of Forearm Arteriovenous Fistula Juxta-Anastomotic Stenosis: Analysis of Data Collected Prospectively from 1999 to 2004

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Surgery is the traditional treatment for juxta-anastomotic stenoses in forearm arteriovenous fistulas (AVF), but percutaneous transluminal angioplasty (PTA) is a suitable alternative. No prospective comparative trials between the two have been reported to date, however. A retrospective analysis of prospectively, concurrently collected data was performed to compare the outcome and cost of surgery and PTA in the preemptive repair of juxta-anastomotic stenosis in lower forearm AVF. Sixty-four AVF with >50% venous juxta-anastomotic stenosis were considered: 21 were treated surgically (11 proximal neo-anastomosis and 10 polytetrafluoroethylene interposition graft) and 43 by PTA. After treatment, AVF were monitored by quarterly ultrasound dilution access blood flow measurement. End points were restenosis and procedure failure rate (re-intervention by another technique or access loss), and determinants were analyzed using Cox hazard model. Initial procedural success was 100% for surgery and 95% for PTA (P = 0.539). Restenosis rate was 0.168 and 0.519 events/AVF-year for surgery and PTA, respectively (P = 0.009). The type of procedure was the only variable that was significantly associated with restenosis, the adjusted relative risk being 2.77-fold higher (95% confidence interval 1.07 to 7.17; P = 0.036) after PTA than surgery. The procedure failure rate was 0.110 and 0.097 events/AVF-year for surgery and PTA, respectively (P = 0.736). The cost profile also was similar for the two procedures. This prospective comparative study confirms a higher restenosis rate after PTA than surgery, but with strict surveillance for restenosis, the two procedures show similar assisted primary patency and cost, suggesting that they should be considered equally valid, complementary alternatives in the preemptive treatment of juxta-anastomotic stenosis in forearm AVF.

applied for the treatment of juxta-anastomotic stenoses in forearm AVF, and guidelines suggest that each institution decide which procedure is best for its patients on the basis of the available expertise (1). We performed an analysis of prospectively and concurrently collected data to compare the outcome (restenosis and procedure failure rate) and cost of surgical versus endovascular preemptive repair of venous juxta-anastomotic stenoses (within the first 5 cm of the vein) in functioning, mature, virgin AVF located in the lower half of the forearm.

Materials and Methods
This is a retrospective analysis of data that were collected prospectively between January 1999 and December 2004 at the Hemodialysis Unit, Ospedale Policlinico (Verona, Italy). During the study period, two prospective, controlled, randomized or quasi-randomized trials that evaluated the role of PTA (30) and surveillance combined with preemptive stenosis repair (by surgery and PTA) on AVF survival (31) were completed in our institutions. Many of the data in our study were collected for these trials and now are analyzed to answer the question of whether the two stenosis treatment modalities, surgical and endovascular, had different outcome and cost. All patients gave their informed consent to the study protocol.

Access Eligibility
The study focused on AVF that were functioning (able to provide adequate dialysis delivery, i.e., spKt/V ≥1.2), mature, virgin (with no previous surgical or endovascular procedure), and located in the lower half of the forearm with an angiographically proven significant (>50%) juxta-anastomotic venous stenosis (first 5 cm of the draining vein). The stenosis was identified by a surveillance program that measured access blood flow rate (Qa) by ultrasound dilution with a Transonic HD01 monitor (Transonic System Inc., Ithaca, NY) every 3 to 4 mo and monitoring dialysis blood pump flow rate (Qb) at every dialysis session. Indications for fistulography were a Qa <750 ml/min or a decrease in Qa >25% or inability to achieve the prescribed Qb in at least two consecutive hemodialysis sessions (31).

During the study period, 64 such AVF in 64 patients met the criteria and were enrolled in the study: 55 were referred for fistulography because of Qa parameters and nine because of inability to achieve the prescribed Qb, triggering an immediate Qa measurement. Fistulography was performed before dialysis, as described elsewhere (30).

Access Allocation
The choice of intervention procedure was made case by case at the discretion of and depending on the availability of the radiologist and the attending vascular surgeon, with a view to correcting the stenosis without any major reduction of the venous capital available for puncture. Any vein loss <6 cm was arbitrarily considered irrelevant because it did not interfere with cannulation or change the nature of the access in our experience. Two AVF underwent surgery because they were deemed technically unsuitable for endovascular treatment as a result of the presence of multiple critical venous stenoses. The lesions in the remaining AVF all were amenable to treatment with either procedure. On the whole, surgery was preferred for lesions in which PTA was expected to be least effective, e.g., critical (≥90% reduction in luminal diameter) or long (>2.5 cm) venous stenoses, or stenoses that were associated with the presence of a small or calcified or stenotic feeding artery (5,13,14), whereas PTA was preferred to treat multiple stenoses or whenever surgery was expected to sacrifice a long segment of the vein (≥6 cm). Nonetheless, critical, long, and arterial stenoses also were treated by PTA, and multiple stenoses were treated by surgery in many instances.

Surgery was the primary procedure in 21 AVF. Forty-three AVF underwent preemptive PTA, which failed in three. Two of the latter were corrected surgically (and they were excluded from subsequent analyses), and one underwent successful re-PTA within 1 mo. Follow-up in the PTA group consequently was available in 41 AVF (Figure 1). Forty AVF (10 in the surgical group and 30 in the PTA group) were in the treatment arm of the previously described prospective trials (30,31).

Intervention Procedures
Preemptive surgery was performed as an inpatient procedure under axillary plexus anesthesia and consisted of either the creation of a more proximal re-anastomosis of the cephalic vein to the radial artery a few centimeters above the stenotic venous segment (neo-anastomosis) or the insertion of a short (3 to 5 cm long) interposition polytetrafluoroethylene (PTFE) arteriovenous graft to replace the stenosed venous segment (interposition graft). These short grafts were not intended for cannulation. Posttreatment fistulography and Qa measurement were performed within 2 wk of the procedure. The procedure was considered anatomically successful when the residual stenosis was <30%. Thrombectomy and access replacement with a PTFE graft also were done as inpatient procedures.

PTA of stenotic segments was performed as a day procedure as described elsewhere (31). Balloons 6 to 9 mm in size were used, and their diameter was oversized by 1 mm in comparison with the size of the adjacent nonstenotic vessel. Balloons were inflated to a pressure of 10 to 12 atmospheres for 60 to 90 s. Dilation-resistant lesions were sequentially subjected to multiple dilations up to 20 atmospheres for 3 min. Lesions with early restenosis and elastic recoil after repeated angioplasty underwent intravascular stent placement. Intravascular stent deployment took place with self-expanding Wallstent-Uni stents (Boston Scientific Medi-Tech, Natick, MA). Stent size approximated the angioplasty balloon size used in the particular case and ranged 6 to 10 mm in diameter. The length of the stent used was determined by the length of the lesion to be covered, allowing for approximately 10 mm of

![Figure 1. Participants and outcomes flow diagram.](image-url)
Postintervention Surveillance

After initial treatment, all AVF continued to have surveillance, monitoring Qa every 3 to 4 mo and dialysis Qb at every session, and the inability to obtain the prescribed Qb for at least two consecutive hemodialysis sessions triggered additional Qa measurement (31). All AVF had at least one follow-up angiogram, as a result of a drop in Qa >25% or a Qa <750 ml/min, or when patency was measured. The Qa parameters for fistulography were chosen for their high sensitivity (95%) in detecting stenosis (32). The frequency of Qa measurement was based on an observed median time to stenosis in forearm AVF of 10 mo (10th to 90th percentiles 5 to 20 mo), in our experience (32).

Outcomes

Postintervention patency rates were evaluated and defined according to the criteria of Sidawy et al. (33). Postintervention primary patency was defined as the interval between the surgical or endovascular procedure and the next intervention (as a result of restenosis or access thrombosis). Because preemptive re-intervention always was performed within 2 wk of identification of restenosis and behind any thrombotic episode there always was a restenosis, postintervention primary patency was considered equivalent to restenosis-free interval. Postintervention assisted primary patency was defined as the interval between the surgical or endovascular intervention and re-intervention by any procedure other than the initial one (e.g., PTA for surgery and vice versa), access thrombosis, or abandonment (as a result of conversion to an elbow or upper arm fistula or replacement by a PTFE graft or a permanent central venous catheter), so postintervention assisted primary patency meant the time up to procedure failure. Patients were censored in the event of death, transplantation, or transfer to another unit or when they ended the study with an event-free access. Outcomes also were expressed as rates (restenosis rate, procedure failure rate and access loss rate) and presented as events/AVF-year (34).

Cost Analysis

A direct access care–related cost was estimated for each procedure, including all expenses for correcting stenosis, for detecting restenosis, and for treating procedure failure (e.g., for surgery after failed PTA and vice versa) or for thrombectomy, and the placement of a new access or a central venous catheter after surgery and PTA (35). Specifically, the cost per procedure was determined according to Azienda Ospedaliera di Verona financial data system, which calculated costs in 2004 euro. Operating room and PTA costs included professional fees but not material other than angioplasty balloons. The cost of access monitoring by the ultrasound dilution technique was based on the number of measurements per year and the working life of the machine (7 yr).

Statistical Analyses

Data are reported as percentages, means ± SD, or medians (10th to 90th percentiles) or medians (range), as appropriate. Normally distributed continuous variables were analyzed using the nonpaired t test, and skewed variables were analyzed using the Mann-Whitney U test. Categorical variables were analyzed using the Fisher exact test.

Cox multivariate proportional hazard regression model was used to identify variables that were associated with outcome (35). Adjusted survival curves were obtained by plotting survival function values from Cox model. The Generalized Linear Model-Poisson log linear statistical procedure was used to test for associations between restenosis and procedure survival rates in the study groups. All tests were two sided, and differences were considered significant at P ≤ 0.05.

The Generalized Linear Model-Poisson log linear procedure was computed using EGRET Version 1.02.10 (SERC Corp., Seattle, WA). All other statistical analyses were performed using the SPSS software, version 11 (SPSS, Chicago, IL).

Results

The characteristics of the patients and of the stenosed AVF are given in Tables 1 and 2, respectively. The two groups were...
similar in terms of patient characteristics (age, gender, and prevalence of diabetes and cardiovascular disease, defined as the presence of coronary artery and/or cerebral and/or peripheral vascular disease). They also were comparable in terms of certain AVF characteristics before treatment, e.g., anastomosis site, age of access (defined as the time of access construction to stenosis), proportion of multiple and long stenoses, and associated arterial stenoses adjacent to the anastomosis, whereas the degree of stenosis was significantly lower and Qa significantly higher in the PTA group.

Anatomic success rates were 100% for surgery (21 of 21) and 95.3% for PTA (41 of 43; \( P = 0.539 \)). No major complications, such as thrombosis or grade 2 or 3 hematoma (36), were observed with either procedure. None of the patients required central venous catheter placement in the immediate posttreatment period, because all AVF were used successfully for dialysis within 48 h of either procedure. In the surgical group, stenosis was corrected by proximal neo-anastomosis in 11 and by graft interposition in 10 AVF (Figure 1). Surgery always was associated with a <6 cm reduction of the puncture area. Successful treatment led to a significant early increase in Qa in both groups (\( P < 0.001 \)). The degree of stenosis and Qa after treatment was comparable in the two groups (Table 2).

The median follow-up was 24.0 mo (10th to 90th percentiles 12.2 to 55.6) for surgery and 22.0 mo (10th to 90th percentiles 6.0 to 60.0) for PTA (\( P = 0.290 \)). Eight (38.1%) AVF restenosed in the surgical group and 25 (61.0%) restenosed in the PTA group (Figure 1). The median time to restenosis was 19.0 mo (10th to 90th percentiles 7.0 to 31.0) after surgery and 10.0 mo (10th to 90th percentiles 3.0 to 24.3) after PTA (\( P = 0.019 \)). The restenosis rates were 0.168 and 0.519 events/AVF-year for surgery and PTA, respectively (\( P = 0.009 \)).

Cox analysis revealed the procedure as the only variable that was significantly associated with restenosis; all other variables (gender; age; diabetes; site of anastomosis; any pretreatment long, multiple, or critical stenoses; and treatment procedure) were unassociated with restenosis. The adjusted relative risk for restenosis was 2.77 times higher (95% confidence interval 1.07 to 7.17) after PTA than after surgery (\( P = 0.036 \)). Adjusted postintervention primary patency rates are shown in Figure 2. The restenosis-free survival rates were significantly higher after surgery than after PTA (\( P = 0.036 \)).

In the surgical arm, the restenosis rates were 0.221 events/AVF-year after neo-anastomosis and 0.120 events/AVF-year after graft interposition (\( P = 0.378 \)). Restenosis was located in the venous juxta-anastomotic area in four of five AVF after neo-anastomosis and in the venous outflow at or near the vein/graft anastomosis after graft interposition.

In the surgical arm, restenosis could be treated only by surgical re-intervention (graft interposition) with no loss of the puncture area in two wrist AVF. Five restenosed AVF were treated by PTA, because additional surgery would have led to a significant reduction of venous capital. One AVF thrombosed during follow-up and was converted into an elbow fistula (Figure 1).

In the PTA arm, 25 AVF restenosed and were treated endovascularly, for a total number of 40 repeat PTA. Four AVF with early restenosis and elastic recoil after repeated angioplasty underwent intravascular stent placement. Four AVF with repeated early restenosis after dilation underwent surgical revision (one neo-anastomosis, two graft interposition, and one conversion into an elbow fistula), and one was replaced by a PTFE graft. Two AVF thrombosed and were deemed unsalvageable: One was converted into an upper arm AVF, and one was replaced by a Tesio catheter (Figure 1). Procedure failure rates, including initial failures, were 0.110 and 0.097 events/AVF-year for the surgical and endovascular groups, respectively (\( P = 0.736 \)).

At Cox analysis, none of the evaluated variables (gender; age; diabetes; site of anastomosis; any pretreatment long, multiple, or critical stenoses; and treatment procedure) were associated with procedure failure. Figure 3 shows the adjusted postintervention primary assisted patency rates: No statistically significant difference was observed between surgery and PTA in terms of procedure survival (\( P = 0.736 \)).

In the PTA group, the procedure failure rate of the four AVF that underwent stenting was not different from a control group.

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**Figure 2.** Adjusted primary patency rates in surgery (Δ) and percutaneous transluminal angioplasty (PTA; ●) groups.

**Figure 3.** Adjusted assisted primary patency rates (including initial procedure failure) in surgery (Δ) and PTA (●) groups.
of eight AVF with repeat PTA and no stenting (0.114 versus 0.051 events/AVF-year; P = 0.731). Access loss rates were 0.018 and 0.032 events/AVF-year for the surgical and endovascular groups, respectively (P = 0.445).

Because the higher prevalence of more complicated and severe lesions (critical and/or long stenoses) in the surgical group (12 of 21 versus 11 of 43 in the PTA group; P = 0.025) may provide biased results, subgroup analysis of the outcome of the surgical and endovascular treatment of these severe lesions was performed. Surgery and PTA showed no statistically significant difference in anatomic success (100 versus 82%; P = 0.217), procedure failure (0.123 versus 0.227 events/AVF-year; P = 0.259), and access loss rates (0.031 versus 0.091 events/AVF-year; P = 0.329).

The results of the cost analysis are shown in Table 3. The median procedure time was 45 min (range 15 to 120 min) for PTA, 82 min (range 35 to 170 min) for preemptive surgical access revision, and 134 min (range 45 to 195 min) for thrombectomy.

**Table 3. Cost analysis**

<table>
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<tr>
<th></th>
<th>Unit Cost in Euros</th>
<th>Surgery</th>
<th>Angioplasty</th>
<th>P</th>
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<tr>
<td></td>
<td>Event per AVF-Year</td>
<td>Cost per AVF-Year (Median [Range])</td>
<td>Event per AVF-Year</td>
<td>Cost per AVF-Year (Median [Range])</td>
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<td>3.664 (21 to 52)</td>
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<td>Fistulogram</td>
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<td>0.567 (25 to 134)</td>
<td>1.069 (20 to 720)</td>
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<td>Angioplasty</td>
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<td>—</td>
<td>0.843 (107 to 2140)</td>
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<tr>
<td>Stenting</td>
<td>650</td>
<td>—</td>
<td>0.043 (0 to 355)</td>
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<tr>
<td>Surgery</td>
<td>1281</td>
<td>0.417 (232 to 1734)</td>
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<tr>
<td>Days in hospital</td>
<td>281</td>
<td>1.307 (157 to 1124)</td>
<td>—</td>
<td></td>
</tr>
<tr>
<td>Procedure failure</td>
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<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>angioplasty</td>
<td>571</td>
<td>0.083 (0 to 798)</td>
<td>—</td>
<td></td>
</tr>
<tr>
<td>surgery</td>
<td>1281</td>
<td>—</td>
<td>0.054 (0 to 4932)</td>
<td></td>
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<tr>
<td>thrombectomy</td>
<td>1895</td>
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<td>0.022 (41)</td>
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<td>PTFE a graft</td>
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<td>0.011 (7)</td>
<td></td>
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<tr>
<td>Tesio catheter</td>
<td>796</td>
<td>—</td>
<td>0.011 (9)</td>
<td></td>
</tr>
<tr>
<td>days in hospital</td>
<td>281</td>
<td>0.202 (0 to 1124)</td>
<td>0.367 (0 to 4496)</td>
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<td>Total cost</td>
<td>—</td>
<td>1287 (525 to 5438)</td>
<td>876 (185 to 13824)</td>
<td>0.080</td>
</tr>
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</table>

*PTFE, polytetrafluoroethylene.*

Discussion

Our analysis of prospectively and concurrently collected data on the outcome of preemptive correction of juxta-anastomotic stenosis in forearm AVF shows a significantly higher restenosis rate after PTA than after surgery, but it also shows a comparable procedure survival, access loss rate, and cost profile for the two methods. Both procedures proved to be safe (no major complications were observed after either treatment) and have much the same, very high immediate anatomic success rates, comparable with those previously reported after preemptive PTA (4–11,13–17) and surgery (12,23,26,28) in AVF.

Both treatments were associated with a significant immediate increase in Qa, which was similar after surgery and PTA (despite a lower pretreatment Qa in the surgical group), indicating that the two methods are equally effective not only in correcting stenosis but also in improving access hemodynamic status. The two procedures also were comparable in that our open surgical approach (either creating a more proximal anastomosis or bypassing the stenotic segment by interposing a short arteriovenous PTFE graft) was associated with no or minimal (<6 cm) loss of the venous capital available for puncture and no change in the nature of the access, so it shared some of the advantages of interventional radiology.

Having shown a three-fold adjusted relative risk for restenosis after PTA by comparison with surgery, our study confirms the results of previous noncomparative studies that reported higher primary patency rates in surgical series than after dilation in failing forearm AVF (3–19,25,26,28). Moreover, the unadjusted 1-yr primary patency rates in our series (91 ± 6% for surgery and 54 ± 8% for PTA) compare favorably with the literature, which reports rates of 64 to 88% after preemptive surgery (12,19,25,26) and 16 to 79% after endovascular procedures (3–18). In addition, restenosis rates after the two surgical techniques were similar in our study, failing to support the concern of any higher complication rates’ being associated with the PTFE interposition graft (24).

Our study also shows that, using a close surveillance program for early detection of restenosis (based on regular access blood flow measurement and using a Qa threshold criterion that is highly sensitive to stenosis), PTA can provide results similar to surgery, despite its higher restenosis rate. Identifying restenoses without delay enables preemptive re-intervention using PTA with no sacrifice of venous capital (which cannot be said for surgery, in our experience). In the surgical group, only two restenosed wrist AVF could be treated without changing the location of the access. In the remaining AVF, restenosis was treated either by converting the access in an elbow AVF or by PTA, which succeeded in correcting the restenosis with no
reduction of the puncturing area or need to extend the access farther up the arm. Our study confirms that a strict surveillance program (coupled with preemptive stenosis correction) enables low access loss rates, regardless of whether stenosis is corrected surgically or endovascularly.

Cost analysis showed no statistically significant difference in cost profile between the two procedures. The median total cost of surgery, however, was higher than PTA, mostly because of the hospitalization expenses associated with surgery. We are aware that our cost analysis is by no means exhaustive because only access-related direct costs were considered, but this should not affect the comparison between surgery and PTA because the same criteria were used to calculate the cost of both procedures.

We recognize that the major drawback of our study is the lack of randomization. The choice of procedure was at the discretion of the investigators, introducing a subjectivity and a consequent allocation bias in the study, suggested by some differences in the two groups’ characteristics before treatment (degree of stenosis and Qa levels, indicating that AVF with greater anatomic and hemodynamic impairment were allocated unintentionally to surgery). Although subgroup analysis suggested that surgery and interventional radiology are equally effective also in correcting the more severe lesions, we cannot rule out a benefit of surgery because outcomes of surgery seem to be superior to PTA and our sample size may not be powerful enough to detect differences between subgroups. In addition, our study may be underpowered for the purposes of detecting differences in procedure survival and access loss rate between the two methods. Obviously, further, larger studies with a randomized design are needed to understand fully the role of surgery and PTA in the preemptive treatment of juxta-anastomotic stenoses in forearm AVF. Finally, we are aware that the results of our study apply only to mature AVF, and they are not generalizable to the treatment of juxta-anastomotic stenosis in fistulas that fail to mature.

Conclusion
Our prospective comparative study shows that restenosis rate after preemptive correction of venous juxta-anastomotic stenosis in lower forearm AVF is higher after PTA than after surgery. However, it suggests that, with a close surveillance program for early detection of restenosis, the two procedures’ failure rate and cost profile are similar, because PTA allows for re-intervention with no loss of the venous capital, whereas surgery usually does not. It therefore is suggested that the two procedures should be considered as equally valid, complementary alternatives for the preemptive treatment of stenosis in lower forearm AVF, the choice between them depending on local expertise and technical availability rather than on any clinical and economic outcome.

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References