Juxta-anastomotic stenoses: angioplasty or surgery ... (or when/why should we wait)?

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Why does stenosis predominate at this location?

- VSMC Phenotype switching from contractile to synthetic
- VSMC proliferation, intimal migration, matrix secretion, microvessel proliferation \(\rightarrow\) neointimal hyperplasia \(\rightarrow\) stenosis
Juxta-anastomotic stenoses

- What are our goals?
  - Decrease primary failure
  - Decrease thrombosis rates
  - Improve cumulative patency
- Angioplasty vs surgery
- Preemptive vs symptomatic intervention
Cumulative patency of AVFs and AVGs

• 1,140 dialysis pts from 2 Canadian Centers
  1,012 (88.6%) AVFs, 128 (11.2%) AVGs

• Primary patency rate
  AVF 60%; AVG 81%

• Primary failure rate 2x > for AVFs than AVGs
  (AVF 40%; AVG 19%) p<0.001

• If we exclude primary failure:
  cum. patency for AVFs > AVGs (61.9 vs 23.8 mo. for 1st access).

• AVGs:
  2X >PTAs (3.2 vs 1.4/1000 days);
  16x more thrombolysis than AVFs to maintain patency
  (0.98 vs 0.06/1000 days)
Salvage of primary AVF failures

# interventions before use

<table>
<thead>
<tr>
<th>Cum. Patency</th>
<th>0 intervention</th>
<th>1 intervention</th>
<th>≥ 2 interventions</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 year</td>
<td>92 %</td>
<td>78 %</td>
<td>68 %</td>
</tr>
<tr>
<td>2 years</td>
<td>85 %</td>
<td>71 %</td>
<td>57 %</td>
</tr>
<tr>
<td>3 years</td>
<td>75 %</td>
<td>57 %</td>
<td>42 %</td>
</tr>
<tr>
<td># interventions to maintain patency</td>
<td>0.76 ± 0.10</td>
<td>1.37 ± 0.31</td>
<td>3.51 ± 2.20</td>
</tr>
</tbody>
</table>

Angioplasty vs surgery

P = 0.0001 for all three groups
P < 0.0001 for zero vs ≥2 interv.
P = 0.0620 for zero vs 1 interv.

PTA in AVFs

<table>
<thead>
<tr>
<th>Initial intervention</th>
<th>Number</th>
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</thead>
<tbody>
<tr>
<td>PTA</td>
<td>178</td>
</tr>
<tr>
<td>PTA / bare metal stent</td>
<td>22</td>
</tr>
<tr>
<td>PTA / covered stent</td>
<td>3</td>
</tr>
<tr>
<td>PTA / cutting balloon</td>
<td>3</td>
</tr>
<tr>
<td>PTA / vein ligation</td>
<td>1</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Follow-up @ 24 mos.</th>
<th>Number</th>
</tr>
</thead>
<tbody>
<tr>
<td>Add. Perc. interventions</td>
<td>247</td>
</tr>
<tr>
<td>Mean # interventions per pt</td>
<td>2.2</td>
</tr>
<tr>
<td>Pts reaching end of follow-up</td>
<td>107</td>
</tr>
<tr>
<td>Died with functioning AVF</td>
<td>44</td>
</tr>
<tr>
<td>Kidney transplant</td>
<td>9</td>
</tr>
<tr>
<td>Switched to PD</td>
<td>3</td>
</tr>
<tr>
<td>Lost to follow-up (transfer)</td>
<td>4</td>
</tr>
<tr>
<td>SR: AVF declotted, abandoned</td>
<td>40</td>
</tr>
</tbody>
</table>

Neuen, B. J Vasc Interv Rad 2014
Surgical revision vs PTA in AVF JAS

- **SR: not directly comparable to PTA**
  - Traditional treatment of choice
  - No treatment of original lesion
  - Neoanastomosis, interposition graft
  - Selection bias +++

- **PTA**
  - Less invasive, safe
  - Potentially treat all stenoses
  - Poor long-term results → restenosis
  - Repeat PTAs for similar 1st assisted patency

- **SR vs PTA**
  - Sig. better primary patency (<0.05)
  - No sig. difference in primary assisted patency

- **Recommendation**
  - PTA first
  - Reserve SR for PTA failure

Endovascular versus Surgical Preemptive Repair of Forearm Arteriovenous Fistula Juxta-Anastomotic Stenosis

Unadjusted primary patency rates in surgery and PTA groups.

Unadjusted assisted primary patency rates (including initial procedure failure)

«... equally valid, complementary alternatives in the preemptive treatment of juxta-anastomotic stenosis in forearm AVF »

Tessitore N et al. CJASN 2006;1:448-454
Results

Access thrombosis:
- 8/43 (Tx group)
- 18/36 (Control group)

Surgery:
- 12/43 (38%)
  (5 neo-anast., 7 jump grafts)

AVFs at risk:
- Treatment: 43, 35, 25, 20, 16, 12
- Control: 36, 31, 24, 13, 8, 3

P = NS

p = 0.056

Why perform vascular access screening and preemptive angioplasty in asymptomatic stenosis?

Vascular access screening: often the cause for preemptive angioplasty in non-hemodynamically significant stenoses

- Subclinical but anatomically significant stenoses (> 50%) in normally functioning AVFs with \( Q_a > 500 \text{ ml/min} \) and
- No prolonged bleeding, cannulation difficulties or poor clearance
- Adequate dialysis with low risk of failure\(^1\)
- Unnecessary angioplasty for stable/slow growing stenoses may impair access survival
  - aggressive restenosis due to accelerated neointimal hyperplasia\(^2,3\)
- Preemptive repair not warranted nor cost-effective in well-functioning AV access with sub-clinical stenosis.
- «Stenotic lesions should not be repaired merely because they are present\(^3\) ».
- Don’t treat a picture

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1. Sivanesan S. Nephrol Dial Transpl. 1999
Should current criteria for detection and timing of repair of arteriovenous fistula stenosis be reconsidered?

“Our study also confirms that revising asymptomatic stenosis may exacerbate stenosis and trigger thrombosis, supporting concerns that early PTA may even be harmful.”

Tx group
initial: (n=28) 23 PTA + 5 surg.
Restenosis: (n=20) 18 PTA + 2 surg + 1 stent + 2 stent grafts

28 pts: 10/51 procedures (19.6%) other than PTA

~ 20%
Monthly access flow monitoring with increased prophylactic angioplasty did not improve fistula patency

- **Sequential observational trial**
  - Impact of UDT monitoring on patency of first AVF
  - 222 patients
  - 2 groups
    - Group 1: Clinical criteria; 146 patients
    - Group 2: Clinical criteria + UDT screening; 76 patients

- **Referral for angio**
  - Group 1: clinical criteria
  - Group 2: Clinical criteria + UDT screening

- **UDT monitoring**
  - 7 X increase in angioplasty procedures (0.67 vs. 0.09 per access-year)
  - shortened primary unassisted patency
  - no decrease in thrombosis rate
  - no improvement in cumulative fistula patency.

Is preemptive angioplasty an effective solution for AV access stenosis/restenosis?

• Increases the number of procedures, shortens primary assisted patency and decreases the number of thrombotic episodes.

• *Does not* prolong cumulative AV access survival.

• *Would you recommend/perform preemptive surgery on subclinical stenosis, based upon declining flow rates alone?*

• *If not, why would you recommend/perform angioplasty?*
Conclusions

• Angioplasty, surgery equally effective in treating JAS.
• Angioplasty:
  – less invasive, preserves vascular capital, does not preclude subsequent surgery.
  – Preferred choice: delayed maturation from stenosis or interval restenosis.
  – Mostly ineffective in early immature AVF thrombosis.
  – May cause aggressive, early restenosis. Treatment of subclinical lesions?
• Surgery
  – Failure/contraindication/unavailability of first-line endovascular intervention.
  – Treatment of aneurysms, inaccessible lesions, rapid, aggressive recurrent stenosis, anastomotic defects.
NH: right target  Angioplasty: wrong weapon

Histology of progressive AV access dysfunction

A. Non-CKD

B. Advanced CKD

C. AVF Non-Maturation

D. AVF Restenosis

- Uremia
- Uremia Hemodynamics
- Angioplasty Uremia Hemodynamics
Demographics affecting primary failure rates

Baseline demographics by number of interventions to promote AVF maturation

<table>
<thead>
<tr>
<th></th>
<th>Zero Interventions</th>
<th>One Intervention</th>
<th>Two or More Interventions</th>
<th>P</th>
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<tbody>
<tr>
<td>Patients (n = 173)</td>
<td>96 (55.5%)</td>
<td>54 (31.2%)</td>
<td>23 (13.3%)</td>
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<tr>
<td>Sex</td>
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<td>female</td>
<td>17 (17.7%)</td>
<td>16 (29.6%)</td>
<td>11 (47.8%)</td>
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<tr>
<td>male</td>
<td>79 (82.3%)</td>
<td>38 (70.4%)</td>
<td>12 (52.2%)</td>
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<tr>
<td>Race</td>
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<td>0.2664</td>
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<tr>
<td>black</td>
<td>71 (74.0%)</td>
<td>38 (70.4%)</td>
<td>20 (87.0%)</td>
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<td>white</td>
<td>25 (26.0%)</td>
<td>16 (29.6%)</td>
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<tr>
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<tr>
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<td>41 (42.7%)</td>
<td>30 (55.6%)</td>
<td>16 (69.6%)</td>
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<td>55 (57.3%)</td>
<td>24 (44.4%)</td>
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<td>9 (39.1%)</td>
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<tr>
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<td>78 (81.2%)</td>
<td>47 (87.0%)</td>
<td>14 (60.9%)</td>
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<td>Access site</td>
<td></td>
<td></td>
<td></td>
<td>0.7710</td>
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<tr>
<td>upper arm</td>
<td>66 (68.8%)</td>
<td>38 (70.4%)</td>
<td>14 (60.9%)</td>
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<tr>
<td>forearm</td>
<td>30 (31.3%)</td>
<td>16 (29.6%)</td>
<td>9 (39.1%)</td>
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<td>Age ≥65</td>
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<td>24 (25%)</td>
<td>16 (28.3%)</td>
<td>9 (39.1%)</td>
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<tr>
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<td>72 (75%)</td>
<td>38 (71.7%)</td>
<td>14 (60.9%)</td>
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<td>BMI ≥30</td>
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<tr>
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<td>28 (29.2%)</td>
<td>17 (31.5%)</td>
<td>13 (56.5%)</td>
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<tr>
<td>no</td>
<td>68 (70.2%)</td>
<td>37 (68.5%)</td>
<td>10 (43.5%)</td>
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<tr>
<td>First versus subsequent fistula</td>
<td></td>
<td></td>
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<td>0.1727</td>
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<tr>
<td>first</td>
<td>61 (63.5%)</td>
<td>38 (70.4%)</td>
<td>19 (82.6%)</td>
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<tr>
<td>subsequent</td>
<td>35 (36.5%)</td>
<td>16 (29.6%)</td>
<td>4 (17.4%)</td>
<td></td>
</tr>
</tbody>
</table>

Consensus

“To date, randomized controlled trials have not consistently shown that surveillance improves outcomes in grafts”

“There is limited evidence that surveillance reduces thrombosis without prolonging the life of native fistulae”

“Current evidence does not support the concept that all accesses should undergo routine surveillance with intervention.”

Paulson W, Lok C. Kidney Int 81(2): 132-142
Do surveillance and preemptive angioplasty improve thrombosis rates and access survival?

- 5-yr randomized, controlled open trial (79 patients)
  - Control group (n=36)
    - Standard monitoring + intervention based on clinical criteria alone
    - Intervention for decline in dialysis dose (Kt/V<1.0 after 4 hrs) or thrombosis
  - Pre-emptive Treatment group (n=43)
    - Surveillance (Qa, Qb) + pre-emptive repair of subclinical stenoses
  - Each group subdivided into failing/functional subgroup
    - 350 ml/min < Qa > 350 ml/min, absence/presence of recirculation

Angioplasty accelerates neointimal hyperplasia

- VSMC Phenotype switching from contractile to synthetic
- \(\Rightarrow\) VSMC proliferation, intimal migration, matrix secretion, microvessel proliferation \(\Rightarrow\) neointimal hyperplasia \(\Rightarrow\) stenosis
<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Surgery</th>
<th>PTA</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fistula age (mo)</td>
<td>18.0 ± 11.8</td>
<td>15.6 ± 11.5</td>
<td>0.443</td>
</tr>
<tr>
<td>Anastomosis site (wrist/midforearm)</td>
<td>16/5</td>
<td>32/11</td>
<td>1.000</td>
</tr>
<tr>
<td>Proportion of multiple venous stenoses (%)</td>
<td>19.0</td>
<td>30.2</td>
<td>0.386</td>
</tr>
<tr>
<td>Proportion of long venous stenoses (&gt;2.5 cm; %)</td>
<td>33.3</td>
<td>16.3</td>
<td>0.196</td>
</tr>
<tr>
<td>Proportion of critical venous stenoses (≥90%; %)</td>
<td>23.8</td>
<td>9.3</td>
<td>0.140</td>
</tr>
<tr>
<td>Proportion of associated arterial stenoses (%)</td>
<td>14.3</td>
<td>7.0</td>
<td>0.385</td>
</tr>
<tr>
<td>Pretreatment degree of stenosis (%)</td>
<td>83 ± 6</td>
<td>79 ± 6</td>
<td>0.008</td>
</tr>
<tr>
<td>Pretreatment Qa (ml/min)</td>
<td>343 ± 161</td>
<td>438 ± 127</td>
<td>0.035</td>
</tr>
<tr>
<td>Posttreatment degree of stenosis (%)</td>
<td>0</td>
<td>2 ± 5</td>
<td>0.071</td>
</tr>
<tr>
<td>Posttreatment Qa (ml/min)</td>
<td>774 ± 309</td>
<td>778 ± 238</td>
<td>0.866</td>
</tr>
</tbody>
</table>
Endovascular *versus* Surgical Preemptive Repair of Forearm Arteriovenous Fistula Juxta-Anastomotic Stenosis: Analysis of Data Collected Prospectively from 1999 to 2004
Adjusted primary patency rates in surgery and PTA groups.

Adjusted assisted primary patency rates (including initial procedure failure)

«... equally valid, complementary alternatives in the preemptive treatment of juxta-anastomotic stenosis in forearm AVF »

Tessitore N et al. CJASN 2006;1:448-454
Juxta-anastomotic stenoses

- Natural history of AV access
- What are our goals?
  - Preemptive vs symptomatic intervention
  - Surgery vs angioplasty
    - Neoanastomosis
    - PTFE interposition graft
- Decrease thrombosis rates
- Improve primary assisted patency
- Improve cumulative patency
Conclusions

- Angioplasty, surgery equally effective in treating JAS.
- Angioplasty:
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  - Preferred choice: delayed maturation from stenosis or interval restenosis.
  - Mostly ineffective in early immature AVF thrombosis.
  - May cause aggressive, early restenosis. Treatment of subclinical lesions?
- Surgery:
  - Failure/contraindication/unavailability of first-line endovascular intervention.
  - Treatment of aneurysms, inaccessible lesions, rapid, aggressive recurrent stenosis.
  - Avoid routine use of stents.
- Ultimate solution
  - Understanding of vessel wall molecular biology
  - Genetic tools to modulate the factors that downregulate the genetic response to injury → DCBs, other medications, miRNAs.