Covered Stents to Treat Hemodialysis Access Stenosis in Central Veins

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How much does this matter?

- In the U.S. alone, $2.9 billion, i.e. ~15% of the total cost of hemodialysis care is spent on managing access dysfunction
- Much of the longstanding PTA literature, i.e. ‘standard therapy,’ is built upon retrospective literature—equally quoted in DOQI
- Shouldn’t it bear more critical review?
- Doesn’t clinical research warrant replicative studies?

Places They Go

- Emergent use: ruptures
- Central vein stenoses and occlusions

Central Stents are prone to iatrogenic Events:
Migration After Unaware Operator Placed TDC Through Stent

Early Signal

SVC Syndrome: handmade PTFE-stent grafts I sewed in 1998
- Impra 4 mm PTFE sewn over Wallstents
- Impra 4 mm PTFE stent grafts

Late Signal

Virtually every device has been shown, fractured, in a central location

Bare venous stents restenose centrally just like they do in the periphery

Iatrogenic causes of most CV stenosis

Emergent use: ruptures
Functioning arm: Early Signal: 2000

On-label ePTFE central vein stent grafts is a desirable goal

Would be nice to have a mission-specific device, beyond revision use of existing designs

18 month follow-up

PTFE graft placed after many recurrent, symptomatic, bare stent stenoses

Revision

SVC Syndrome Treated with ePTFE Central Vein Stent Grafts

Had repeated central vein PTA, nitinol stent, intranitinol stent PTA <3-3 week effect, in final 2 rounds

3 month follow up after 13mm Viabahn in left inominate

Peripheral Long lengths reach into ‘central’ roles:
 Arm Swelling, AVG (renal transplant)

−17+cm

Central Veins Subset Cephalic Arch Stenoses

Cephalic arch stenosis in 26/177 (15%)

• 2/116 Radiocephalic (2%)

• 24/61 Brachiocephalic (39%)

• Cephalic arch PTA 50 cases

• 29/50 (58%) required “Ultra-high pressure” (>27 ATM)

• Higher rupture risk, high restenosis

Edge stenoses: Current designs are not site-specific

• Unique forces at these sites

• Some stent designs may prove better: match adjacent vessel elastic modulus, stress sensitive

Small Comfort in that biological response is similar in other veins: Hepatic Vein Outflow Block and Budd-Chiari Syndrome

42 yo man with recurrent chronic BCS

2/3/15 Returns with ‘edge’ stenosis and recurrent ascites and renal insufficiency

PTA. Time for a new plan
Venous Stent Grafts: What Evidence Do We Have?

- May benefit from different elastic modulus,
- Different flexibilities to reduce torque, shear stress, edge effects
- Heparin coating might be important

Cephalic Arch Stent use: Dukkipati et al

- 45 cephalic arch stent patients, retrospective. Time to repeat PTA after prior PTA in TPA only vs ‘Stent’ patients
- Median PTA patency was 91.5 days with suggested improved bare metal stent patency with a median patency of 152 days.
- Although patency appeared improved with bare metal stents for CAS in this study, there is no description of intervention, follow-up methodology, points of censure or definitions and estimation of patency were provided
- We do not know which stent(s) were placed—do not even know if they were covered or not....
- Is this not a failure of the review process?
- Even the table lists ‘PTCA’, which is: Percutaneous transluminal coronary angioplasty

Viabahn ePTFE stent grafts

- Retrospective; n=25
- 11 x 5 Viabahn or 13 mm Fluency
- 8% thrombosis (n=2) at 30, 90d
- 12% edge PTA req’d
- 1st Stent patency: 56% 12 mos

Cephalic arch stenosis in autogenous haemodialysis fistulas: treatment with the Viabahn stent-graft

- 11 consecutive AVF patients (2005-11), retrospective
- 1st access patency: 82 % at 6 mos; 73 % at 12 mos
- 2nd access patency rates: 91% at 6 mos

Long-term results of stent-graft placement to treat central venous stenosis and occlusion in hemodialysis patients with arteriovenous fistulas.

- 42 Viabahn stent grafts in 30 patients
- Prior PTA and/or bare stents in 77%
- 16 stenoses, 12 occlusions
- Mean 705d follow-up; Fistulography
- 1st patency 6 mos: 81%; 100% asst’d
- 1st patency 12 mos: 67%; 80% asst’d
- 1st patency 24 mos: 45%; 75% asst’d

Early randomized data (2008) and signal

Cephalic Arch Bare Stent V. PTFE

- Luminex vs. Fluency
- 25 consecutive patients, >50% stenosis
- Endpoint: >50% stenosis at 3 mos (11 p)

Limitations:
- Study had no sample size calculation
- Many devices were extended into subclavian vein (excluding the axillary vein)
Covered Stents to Treat Hemodialysis Access Stenoses in the Cephalic Arch and Central Veins (U. Toronto), NCT01200914 (n=140): Hep Bonded Viabahn

- Prospective 1:1 RCT of PTA vs Viabahn at 3,6,12 mos. Investigator sponsored study
- After several years, study closed after failing to enroll more than 14 AVF patients across 3 centers (5 randomized to PTA, 9 to SG)
- PTA mean patency 100d
- SG mean patency 300d
- Lessons?

Rajan et al.

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**RESCUE Study**

Prospective, Multi-Center RCT, Concurrently-Controlled Study of Fluency® Plus for In-stent Restenosis in the AV Access Venous Outflow Circuit

- 23 U.S. investigational sites
- Randomization PTA vs. PTA & Fluency® Stent Graft
- 265 patients randomized / treated
  - 220 patients included in 6 month effectiveness analysis
- Follow Up at 1, 3, 6, 12, 18 and 24 months
- Mandatory angiogram at 90 Days to evaluate binary restenosis (core lab)

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**RESCUE Study**

Core Lab Analysis

**Baseline Data**

Access Circuit Characteristics (n=265)

- AV Fistulae: 94%
- AV Grafts: 6%
- Peripheral: 9%

Central vs. Peripheral Lesions – Post-Intervention Lesion Patency (PLP)

- Central Lesions Greater Benefit: Yes, statistical significance between central vs. peripheral veins (p=0.023)

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**RESCUE Results**: Percentage of Access Circuit Primary Patency at 6 Months (95% CI)

- Fluency® PLUS: 16.7%
- PTA: 2%

Statistically powered to test superiority

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**RESCUE at 6 months**: Access Types and Lesion Locations – Post-Intervention Lesion Patency (PLP)

- No significant difference between AV Graft and Fistula Outcome (p=0.151)
- Access Type Did Not Matter

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ASDIN 2015
...Drug Eluting Balloons?

Questions For All Access?
- Any results so far?
- Control of dosing and amounts?
- Control of release kinetics of drug into a vein wall (is not an atherosclerotic artery), etc.

Immunofluorescence micrographs after staining with a monoclonal anti-tubulin antibody:
- Control animal 7 days after PTA: heterogeneous staining within the neointima.
- Rx animal 7 days after local paclitaxel delivery: intensely stained “fluorescence band” at luminal cell lining.

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But... Did it provide some Signal?

Paclitaxel-Coated versus Plain Balloon Angioplasty for Dysfunctional Arteriovenous Fistulae: One-Year Results of a Prospective Randomized Controlled Trial

- All pts completed 1 yr f/up
- Superior 1 yr patency for DEB (paclitaxel) in AVF pts
- SIR Reporting Standards endpoints (<30% resid stenosis, ITT, clinical success, etc)

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Conclusions

- Hemodialysis access life extension is dramatically potentiated by the use of ePTFE stent grafts– for revision, repair, conversion, etc.
- In-stent restenosis is a current and reasonable approach for central lesions.
- Purpose-designed devices would expand treatment of central vein stenoses– and may markedly affect results. This may not happen.
- Initial Rounds will be market driven expansion of existing products, despite limitations (proof of P).

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