Local Drug Delivery for AV Access Dysfunction: Challenges and Opportunities

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Disclosures

• Consultant/Advisory Board: WL Gore, Medtronic, BD Bard, Cormedix, Humacyte, Akebia, Relypsa, Cylerus, Vascular Therapies

• Grant/Research Support: NIH, VA, NSF

• Clinical Trial Support: Bayer, Akebia, Vascular Therapies, Cormedix

Outline

• Biology of vascular access dysfunction
• Basic principles for local drug delivery
• Exciting examples of local drug delivery for vascular access dysfunction
• Message for the future

A message for the present!!

• Current modalities and therapies for dialysis vascular access are not very effective
• Huge unmet clinical need that needs to be addressed
• Local drug delivery is clearly a very attractive modality

Radiological presentation of dialysis vascular access dysfunction

• Perianastomotic stenosis
• AVF non maturation

Histological presentation of AV access failure

• Aggressive venous neointimal hyperplasia
• Smooth muscle cells and myofibroblasts that migrate in from the media and perhaps the adventitia as a result of vascular (hemodynamic) injury
• Inward remodeling or at least a lack of outward remodeling
• Both the NH and inward remodeling made worse by the inflammation, oxidative stress and endothelial dysfunction that is present in our CKD/ESRD patients

Don’t worry, I’ll find a good site soon!!
Translating biology into therapy!

- Anti-proliferative agents that block neointimal hyperplasia
- Nitric oxide like drugs that enhance outward remodeling
- Anti-oxidant and anti-inflammatory therapies that block the negative effects of uremia

Drug eluting cuffs for vascular access dysfunction (Cylerus)

Sirolimus eluting cuffs reduce neointimal hyperplasia in an interposition graft model (Cylerus)

Sirolimus eluting cuffs in a pig model of AVG stenosis

Need to use these novel therapies to...

- Get away from the "one size fits all" vascular access paradigm
- Stratify patients based on clinical, demographic and biological parameters
- Access that is best suited for them
- Right access in the right patient at the right time
Looking to the FUTURE!

- **LOW Risk** = Standard AVF
- **MODERATE Risk** = AVF/AVG + Drug Delivery
- **HIGH Risk** = Catheter + Drug Delivery

**Precision Medicine Approach** → **Population Health** = **ADDED VALUE to Vascular Access Care and to our patients**