Disclosures

• Off Label use: N/A
• Consultant/Advisory Board: Bioconnect, Pervasis, WL Gore, NanoVasc, Proteon, Shire, Medtronic
• Grant/Research Support: Bioconnect, WL Gore, Proteon, Shire
• Clinical Trial Support: Proteon, WL Gore

Radiological presentation of dialysis vascular access dysfunction

AVF
Vein
AVG

• Perianastomotic stenosis
• AVF non maturation

• Stenosis at the graft-vein anastomosis
• Graft thrombosis

What You Need to Know About Neointimal Hyperplasia!!

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Histological presentation of dialysis vascular access dysfunction

\[\text{SMA} \quad \text{Vim} \quad \text{Des}\]
\[
\begin{array}{ccc}
\text{SMCs} & + & - & + \\
\text{Myofib} & + & + & - \\
\text{Fib.} & - & + & - \\
\end{array}
\]

• Migrated in from the media and perhaps the adventitia
• Response to endothelial and smooth muscle cell injury

Outline

• Pathology and pathogenesis of neointimal hyperplasia
• Why is AVF and AVG patency so poor?

VNH is characterized by significant angiogenesis
Perigraft macrophages play a role in VNH

Cytokines (TGF beta) and oxidative stress markers present in clinical and experimental dialysis access stenosis

MCP-1 enhances neointimal hyperplasia

Vascular Injury in the Setting of Hemodialysis Vascular Access Dysfunction

Adapted from Robbins Pathology
Angioplasty: the Good, the Bad and the Ugly

Outward remodeling due to intimamedia rupture

Neointimal hyperplasia

Angioplasty

Restenosis due to neointimal hyperplasia

Adapted from Peter Ballyk

Angioplasty: Decreased cumulative AVF survival in patients requiring angioplasty for AVF maturation

Patient Surviving

100.0%

90.0%

80.0%

70.0%

60.0%

50.0%

40.0%

30.0%

20.0%

10.0%

0.0%

Days

0

500

1000

1500

2000

Bad!!

No interventions

≥ 1 Intervention

≥ 2 Interventions

Double Edged Sword!!

(Lee et al. CJASN 2010)

In fact our results really suck!!!

Post Angioplasty Primary Patency Results

- Coronary Angioplasty 90% @ 9 months
- Carotid Angioplasty 90% @ 1 year
- Iliac Angioplasty 70% @ 5 years
- Femoral Angioplasty 50% @ 2 years
- PTFE graft angioplasty 50% @ 6 months(p)
- AVF angioplasty 40% @ 3 months (t)
- AVF angioplasty 50% @ 1 year

Why are the results of dialysis vascular access surgery and post surgery intervention so poor?

A vein is not an artery

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- Anatomical: Veins have a poorly defined internal elastic lamina
- Physiological: Veins release less nitric oxide and prostacyclin
- Molecular: Significant differential expression of gene products between normal vein and artery

We are not doing very well!!

Primary Patency Results

- CABG (LIMA) 90% @ 10 years
- CABG (SV) 50% @ 10 years
- Aorto-bifemoral bypass 90% @ 5 years
- BK Femoro-popliteal bypass 33% @ 5 years
- AVG Surgery 23% @ 1 year
- AVF Surgery 40% @ 1 year

CABG (LIMA) 90% @ 10 years

AVG Surgery 23% @ 1 year

AVF Surgery 40% @ 1 year
Uremia results in an upregulation of oxidative stress and inflammation

![Diagram showing the relationship between uremia, inflammation, oxidative stress, and neointimal hyperplasia.]

Looking Forward

- Neointimal Hyperplasia in the setting of dialysis vascular access is due to the downstream effects of vascular injury.
- Most prominent mechanisms for these downstream effects are oxidative stress and inflammation on a background of uremia which accentuates both mechanisms.
- Therapeutic Standpoint: Develop interventions that target vascular injury and oxidative stress/inflammation.
- Not easy but just look at the presentations at this meeting: clearly grounds for optimism!!

Uremic mice have increased AV fistula stenosis

![Image showing non-uremic and uremic AV fistula samples, with measurements of neointimal volume and media/neo-intima ratio.]

VNH in Proximal Vein

![Image showing smooth muscle cells and myofibroblasts in a proximal vein.]

Uremia and oxidative stress can result in neointimal hyperplasia independent of hemodynamics

![Image showing histological sections of media and neointima with measurements of stenosis and thickness.]

Looking Forward

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PTFE graft failure is due to Venous Neointimal Hyperplasia (VNH)

Alternative Origins for Neointimal Cells: Role of the Bone Marrow

- Upto 60% of neointimal cells may be bone marrow derived in animal models of atherosclerosis and arterial neointimal hyperplasia
- 20% bone marrow contribution in venous neointimal hyperplasia (Diao et al. AJP 2008)

60% for artery
? 20% for vein

Alternative Origins for Neointimal Cells: Role of the Adventitia

Dialysis access stenosis is a balance between vascular remodeling and neointimal hyperplasia

- Upto 60% of neointimal cells may be bone marrow derived in animal models of atherosclerosis and arterial neointimal hyperplasia
- 20% bone marrow contribution in venous neointimal hyperplasia (Diao et al. AJP 2008)

VNH at the Graft-Vein Anastomosis

VNH is characterized by significant angiogenesis

- Upto 60% of neointimal cells may be bone marrow derived in animal models of atherosclerosis and arterial neointimal hyperplasia
- 20% bone marrow contribution in venous neointimal hyperplasia (Diao et al. AJP 2008)