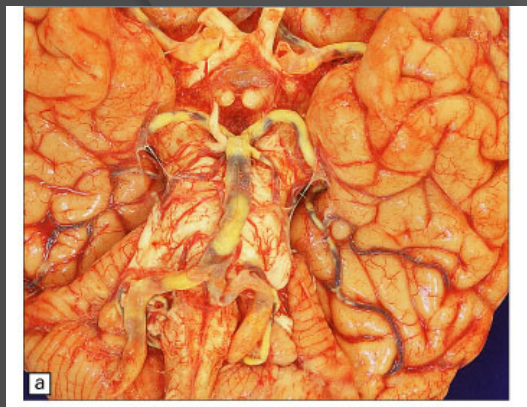
HEMODYNAMIC VS. LOCAL PERFORATOR MECHANISM IN ICAD STROKE- DOES IT MATTER?

Alex Abou-Chebl, MD
Director of Neurointerventional Services
Professor of Neurology
Director of Vascular and Interventional Neurology Fellowships
University of Louisville School of Medicine

Why Differentiating Hemodynamic vs. Perforator Ischemia Matters

- Volume of Territory at Risk
- Eloquence of Tissue at Risk
- Maximizing Benefit from Revascularization
- Reducing Risk of Revascularization

Pathophysiology



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- Thrombotic occlusion
  - Acute plaque rupture → Thrombosis → Vessel Occlusion → Ischemia
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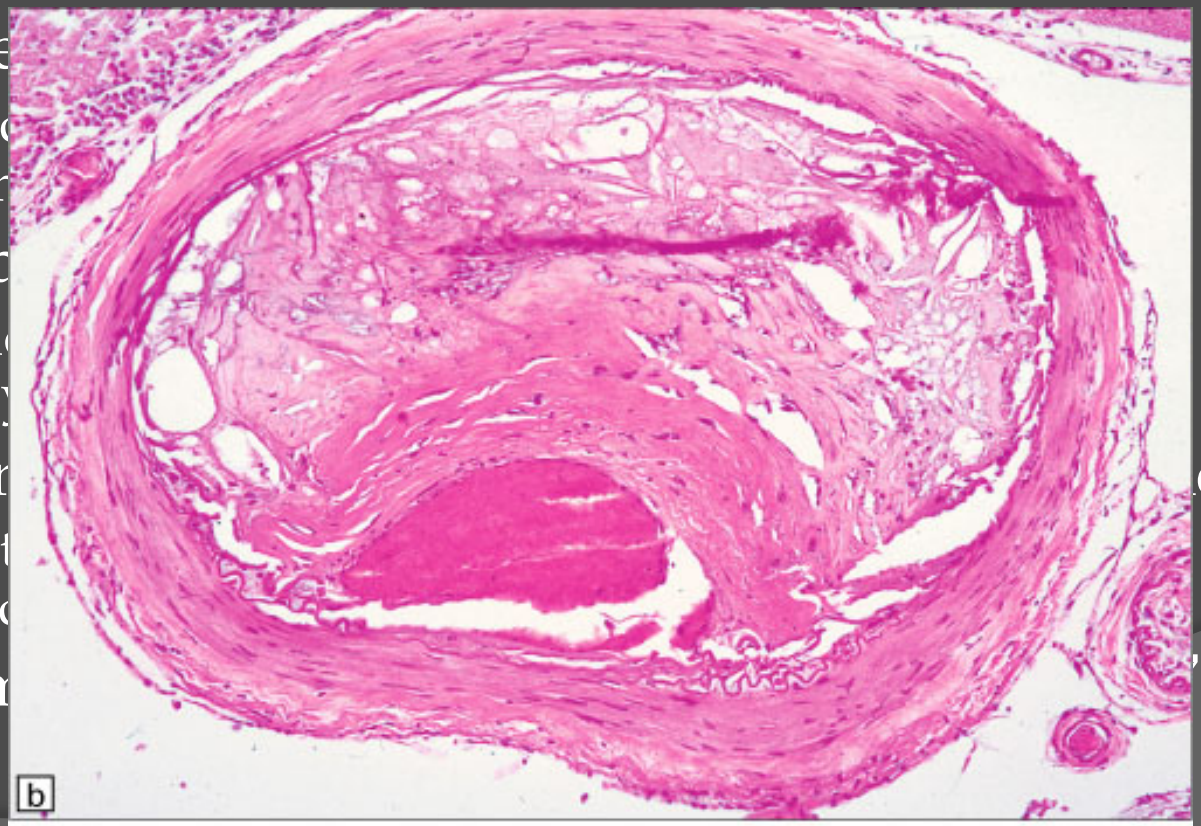

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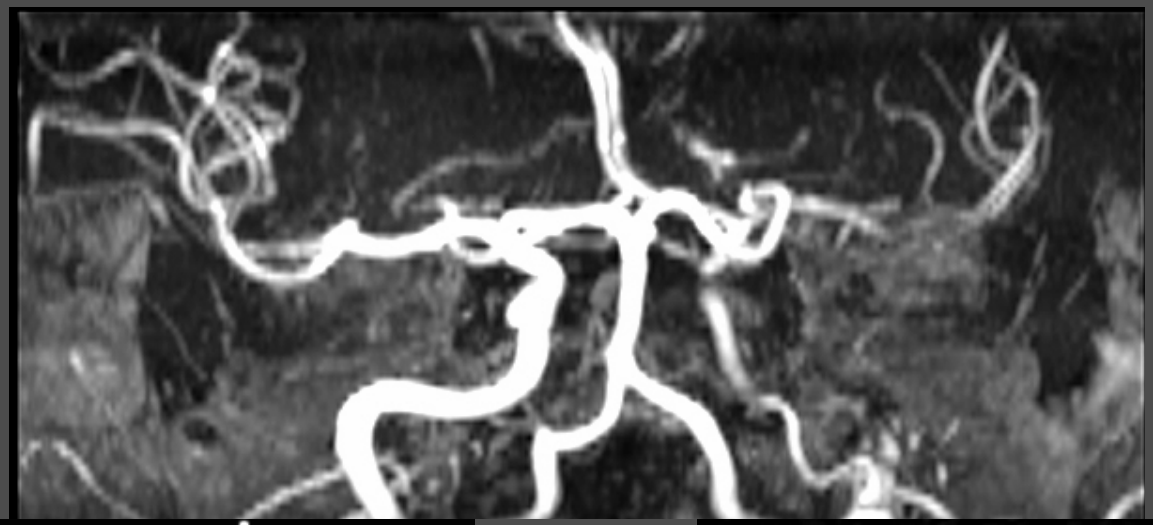
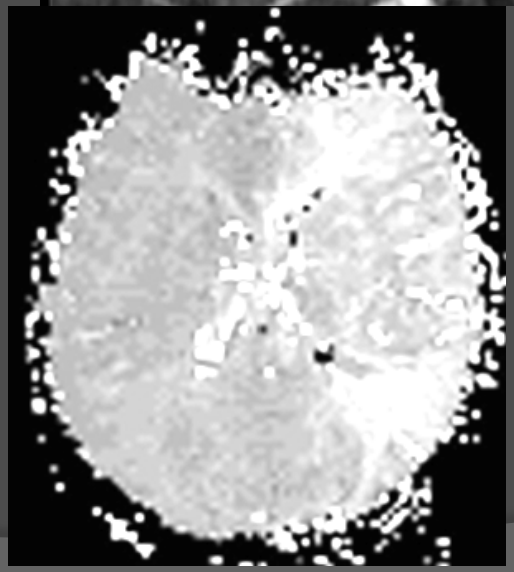
Patterns of Ischemia
MCA Stenosis

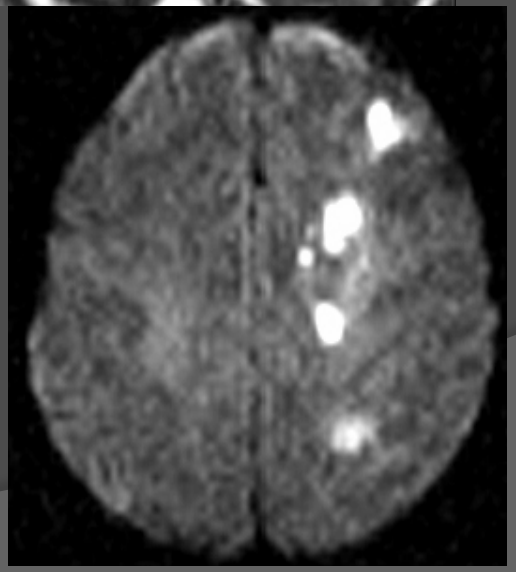
- MRI & TCD study of 30pts
  - 50% Single infarcts % 50% Multiple
    - Single- 67% penetrator strokes
    - Multiple- 73% unilateral, deep, “chainlike” border zone infarcts
  - HITS in 9 with Multiple Strokes vs. 1 with single stroke
    - HITS Predicted # of DWI lesions

Wong KS et al. Ann Neurol 2002;52:74-81

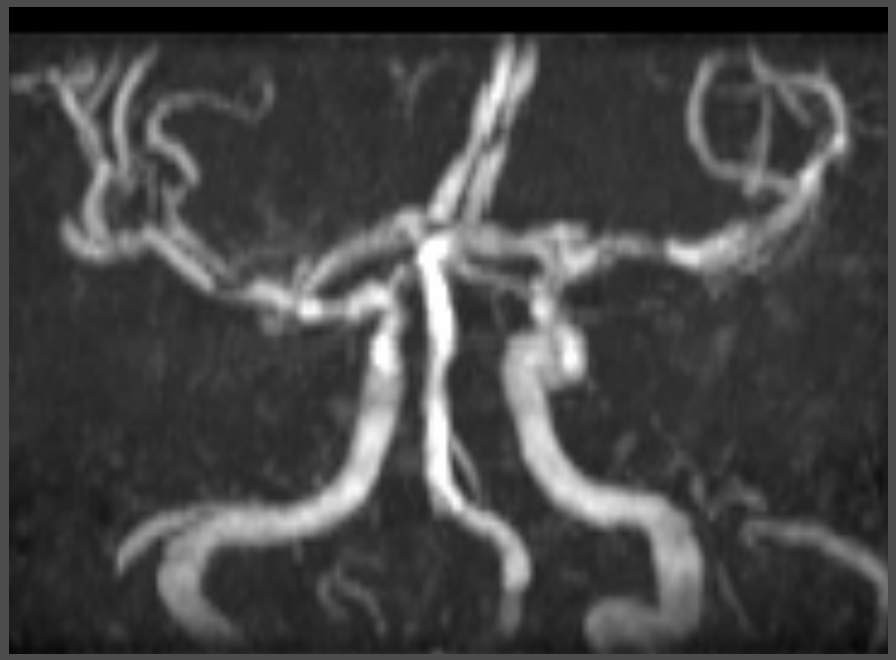
Distal Territory Borderzone Strokes







Penetrator Infarcts



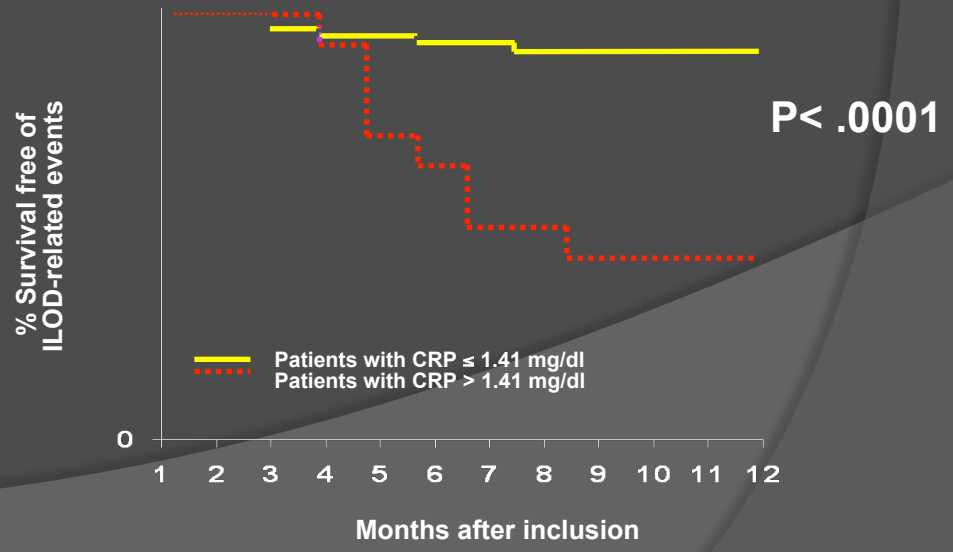
WASID Recurring Stroke Subtype

- 106/569 (18.6%) pts. had an ischemic stroke
- Stroke occurred in territory of symptomatic artery in 77/106 (73%)
  - 70 (91%) were non-lacunar (Cortical or deep >1.5cm)
    - 34 (44%) were disabling
  - 7 (9%) lacunar

Famakin B. Stroke 2009:40;1999-2003

Determinants of Risk & Severity of Clinical Manifestations

- Stenosis Characteristics
- Collateral Blood Flow
  - Cerebrovascular Reserve
- Freq & Size of Embolism
- Severity of Hypoperfusion
- Duration of Ischemia
- Underlying Brain Substrate
  - Neuronal Reserve
- Age
- Medical Co-morbidities
  - Hyper/Hypoglycemia
- CRP & Fibrinogen predictors of recurrent CAD and stroke
  - Bang OY teal. JNNP 2005
  - Arenillas JF et al. Stroke. 2003;34:2463-2468.



Importance of Collaterals

- WASID Angiographic Dataset N=287 (of 569)
- "Across all stenoses extent of collaterals was a predictor for subsequent stroke in the symptomatic arterial territory"
  - None vs. good HR 1.14, CI 0.39-3.30
  - Poor vs. good HR 4.36; 95% CI, 1.46-13.07; $p < 0.0001$
- 70-99% stenoses, more extensive collaterals diminished risk of subsequent territorial stroke
  - None vs. good HR 4.60; 95% CI, 1.03-20.56
  - Poor vs. good HR 5.90; 95% CI, 1.25-27.81, $p = 0.0427$
- 50-69%, presence of collaterals associated with greater likelihood of subsequent stroke
  - None vs. good HR 0.18; 95% CI, 0.04-0.82
  - Poor vs. good HR 1.78; 95% CI, 0.37-8.57; $p < 0.0001$
- Multivariate analyses extent of collaterals independent predictor for subsequent stroke
  - None vs. good HR 1.62; 95% CI, 0.52-5.11
  - Poor vs. good, 4.78; 95% CI, 1.55-14.7; $p = 0.0019$

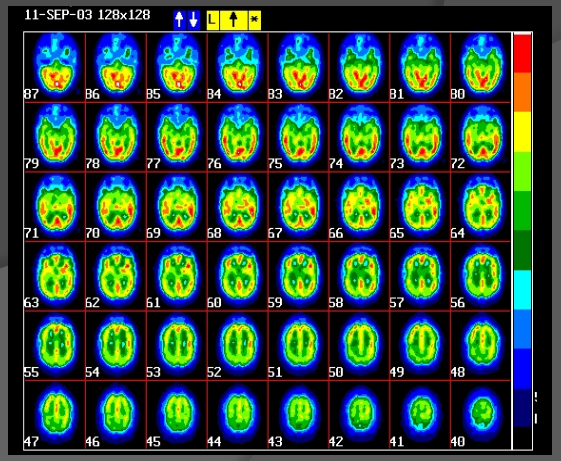
Liebeskind D et al Ann Neurolo 201;69:963-74

Impaired angiographic Collaterals

- Lau et al. created a “composite circulation score” from DSA
- N=69 with ≥50% stenosis
  - Compromised antegrade flow (TICI 0-2a) was observed in 26 (36%)
  - Poor composite circulation score was observed in 8 (12%) patients.
  - Good circulation score (n = 61, 88%) more favorable outcome (OR 7.50, 95% CI 1.11-50.7, p = 0.04) and less recurrent TIA or stroke (OR 0.18, 95% CI 0.04-0.96, p = 0.04)

Assessment of Cerebrovascular Reserve

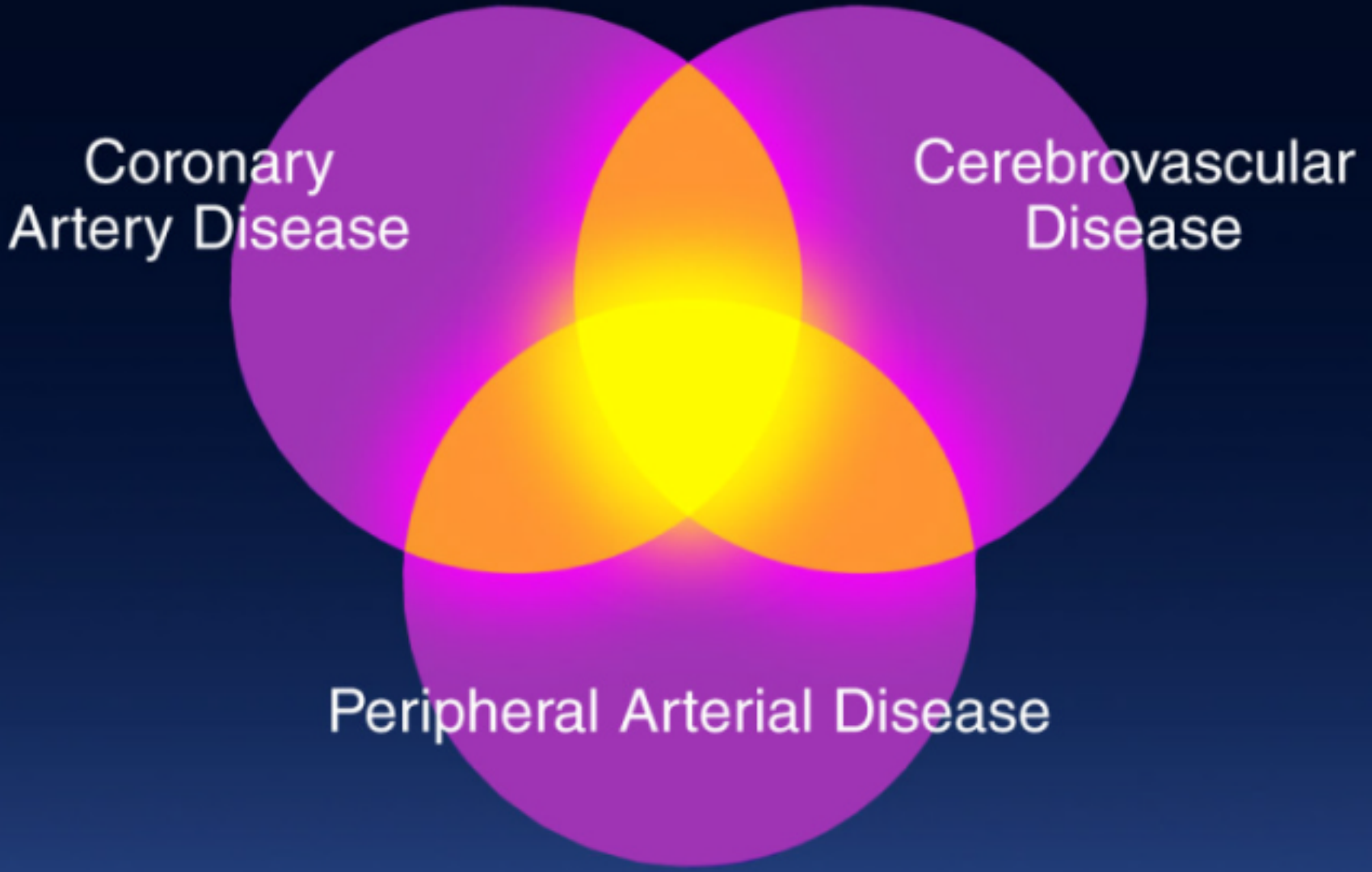
- Acetazolamide SPECT
  - Useful in combination with an anatomical study
  - Measures hemodynamic significance of stenosis
  - Identify pts. who may benefit from revascularization
  - Annual Stoke Rates as high 25%
    - Eskey & Sanelli Neuroimag Clin N Am 2005;15
    - Ozgur H, et al. AJNR 2001



Microemboli

- N=114 MCA stenoses
- MES detected in 25 (22%) patients.
- MES more common with severe stenosis (48% vs. 15%) (p=0.02).
- Mean 13.6 months f/u
  - 12 (12%) patients had recurrence: 10 strokes and 2 TIA
  - Presence of MES was the only predictor of a further ischemic stroke/TIA by Cox regression (adjusted OR 8.45, CI 1.69 to 42.22; P=0.01)
  - Gao S et al. Stroke 2004;35:2832-6

Overlap of Atherosclerotic Disease



Patients with one manifestation
often have coexistent disease in other vascular beds

Common Pathophysiology of Intracranial Atherosclerosis & CAD?

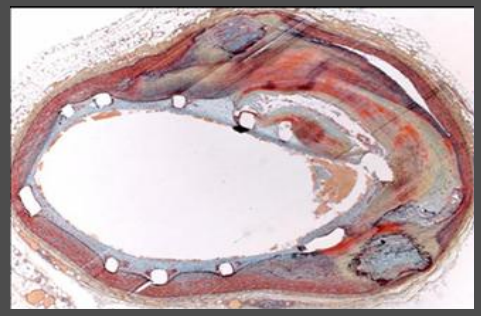
- Do the vessels behave the same?
  - Same risk factors
  - Same markers of disease
  - Responds to same medical treatment
  - Risk of instent restenosis same as with same sized coronary vessels
  - Looks the same pathologically
  - Must be the same disease

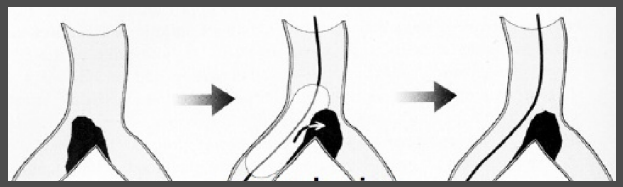
Stenting

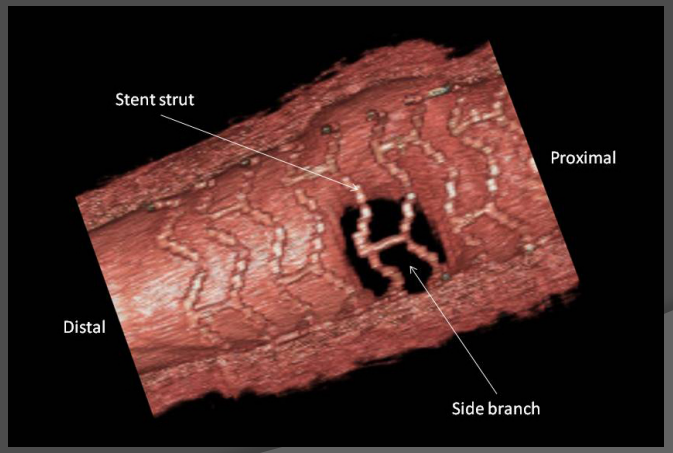
- Palmaz developed coronary stent in early 1980's
- Purpose of Stenting
  - Prevent acute vessel closure due to recoil
  - Tack down dissection flaps
  - Preserve flow to the distal territory

Do Perforators Matter in the Cardiac Bed?

- Plaque shift- lateral dislocation of plaque with PTA
  - Soft Lipid-rich plaque
- “Snow-plowing”
- Carina Shift
- Occlusion of Perforator Ostia by Stent Struts
- Dissection
- Spasm?
- Increased peri-procedural MI

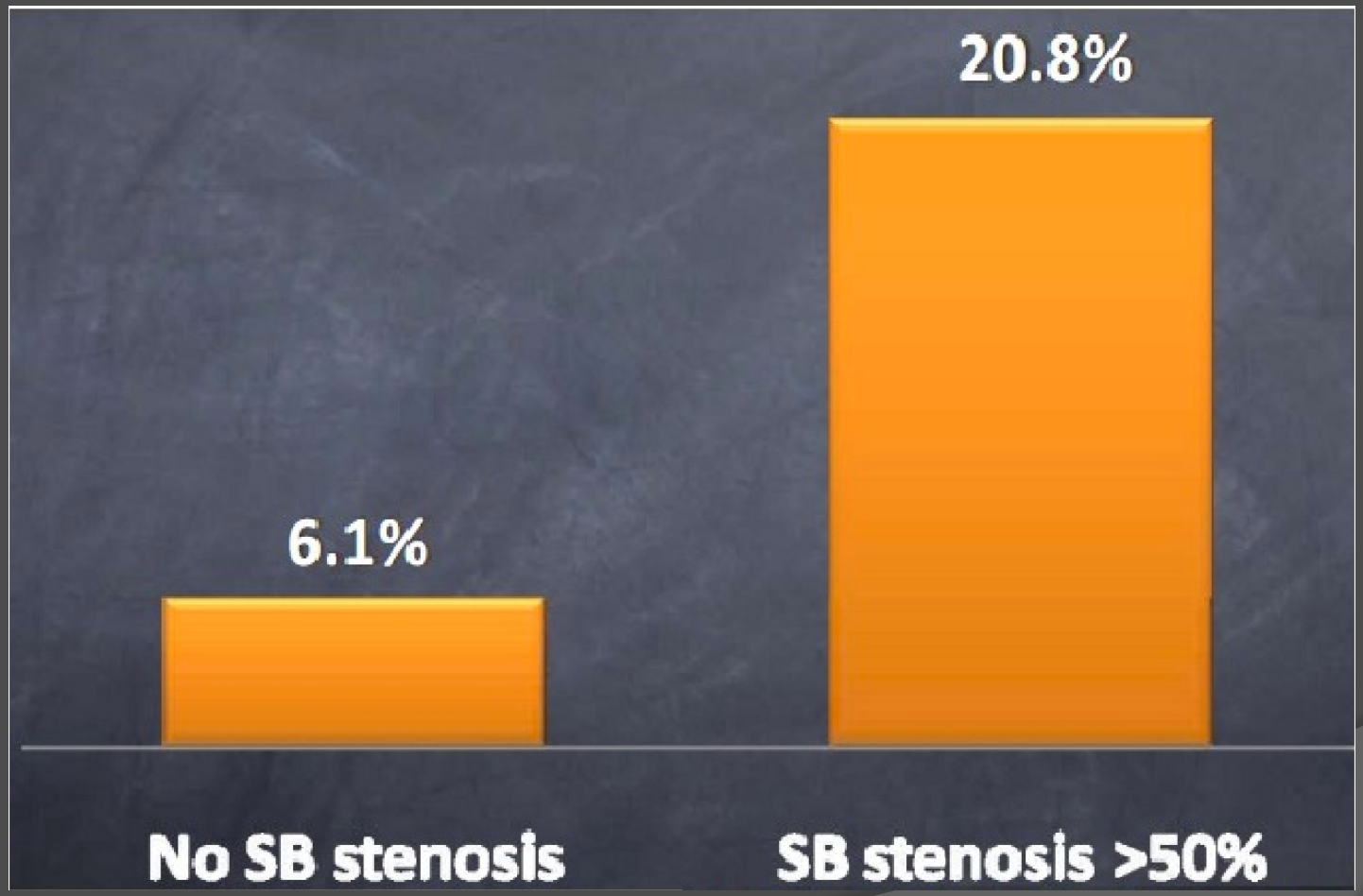






Karanasos A, et al. Card Diag Ther 2012;

Predictors & Incidence of Perforator and Sidebranch Occlusion with PTCA



Furukawa E, et al. Circ 2005

Decreased Flow Reserve in Coronary Circulation

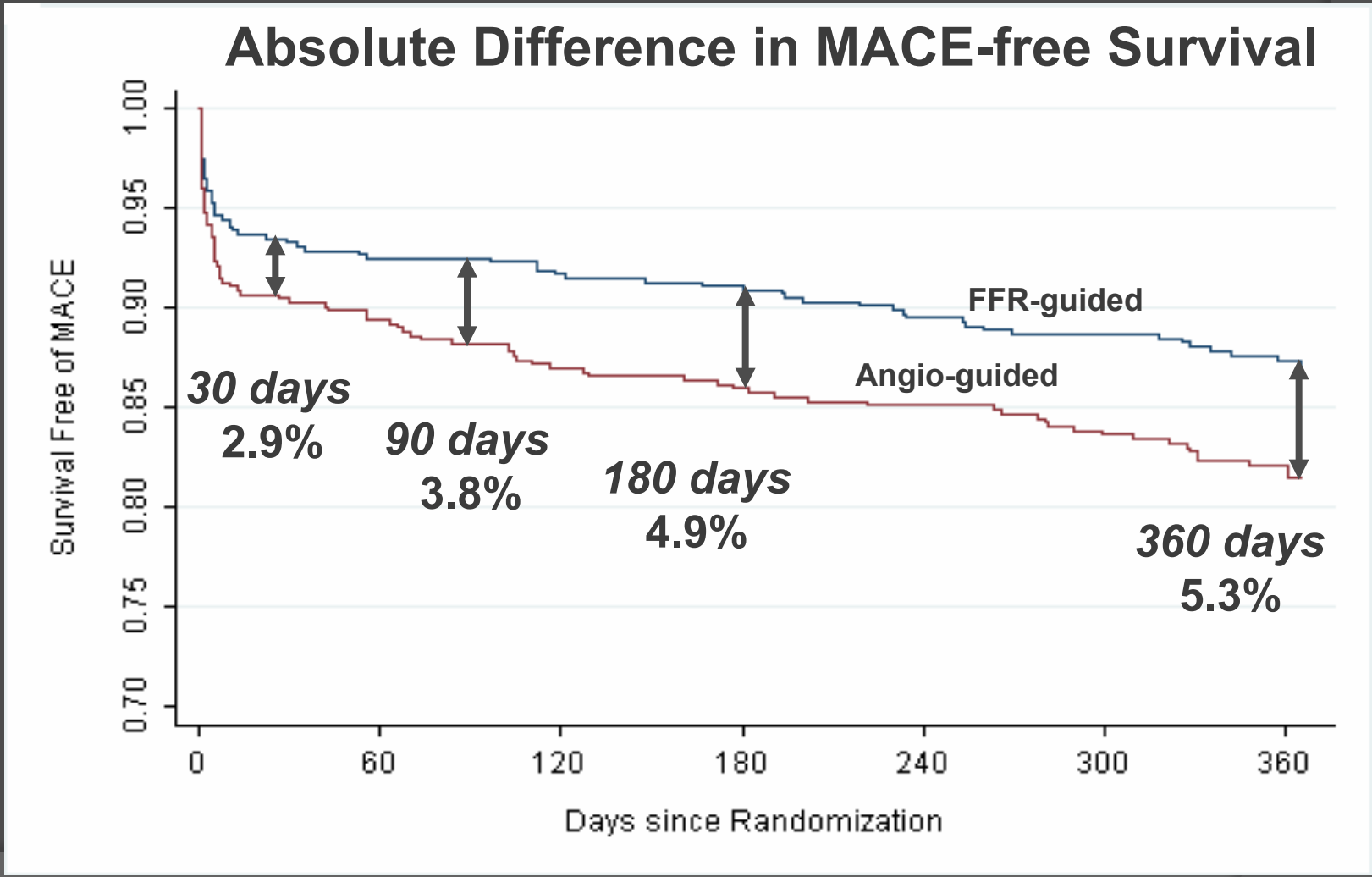
- Stenting of non-ischemic stenoses has no benefit compared to Med Rx only
- Stenting of ischemia-related stenoses improves Sx and outcome
- In multivessel CAD (MVD), identifying which stenoses cause ischemia difficult:
  - Non-invasive tests often unreliable
  - Coronary angiography often results in under- or overestimation of functional stenosis severity

FAME Study: Rationale

- Fractional Flow Reserve (FFR), is most accurate & selective index to indicate whether a particular stenosis is responsible for inducible ischemia
- FFR can be easily determined in the cathlab just prior to stenting

- FFR guidance of PCI in patients with multivessel disease may improve outcome

FAME Study: Event-free Survival Death/MI/CABG/Repeat PCI



Illustrative Case 1

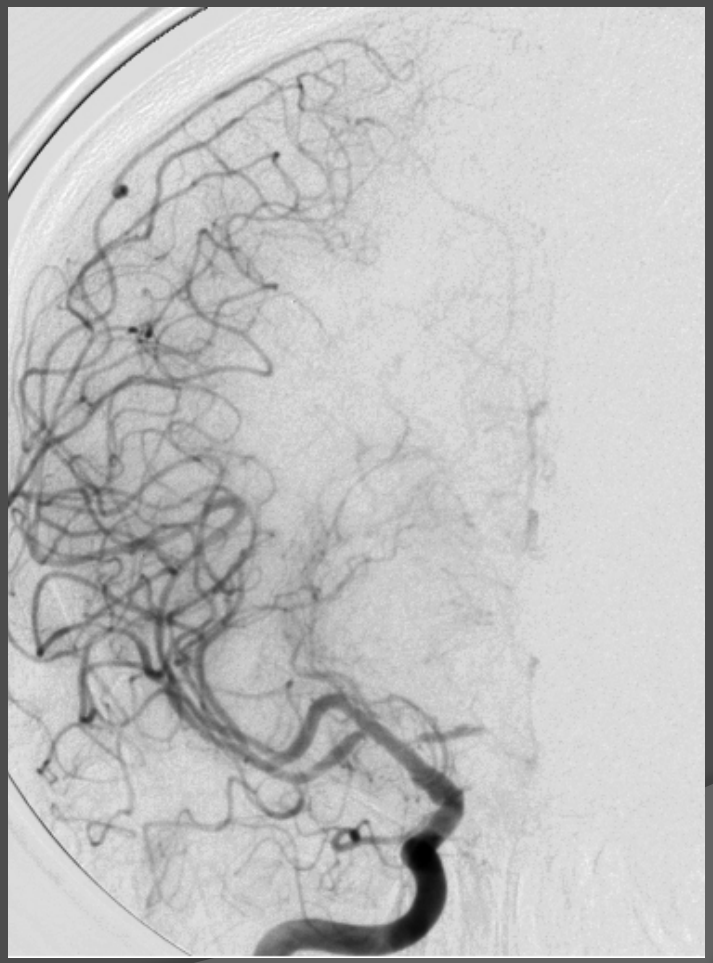
- 42yo Woman with Hx Cigs, HTN
- Presented with SAH and cortical infarct
- Recurrent cortical stroke 6 months later despite ASA & Plavix
- Diamox SPECT- Marked reduction cerebrovascular reserve

Angiographic Findings

- Le CA bi

Outcome

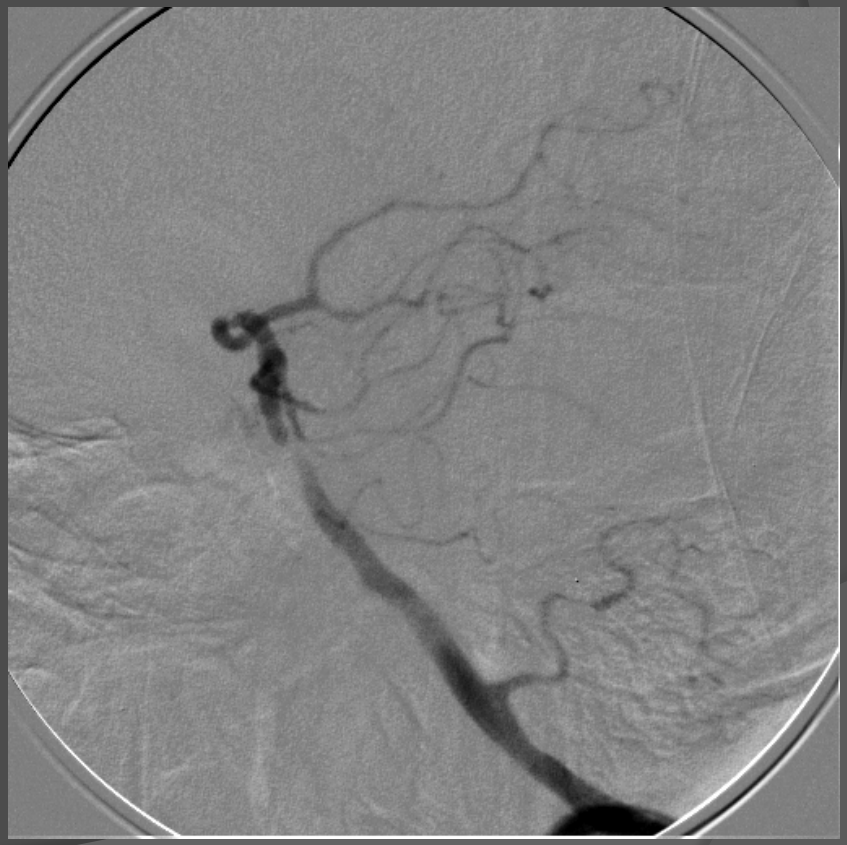
- No Complications
- D/C next AM
  - ASA & Plavix
- 36months F/U asymptomatic



Illustrative Case 2

- 81y.o. WM with DM, HTN,CAD,PVD
  - Platelet Count 70k
- Recurrent VB TIAs and Strokes with BA stenosis by MRA and TCD
  - Stereotyped spells of
    - Dysarthria
    - Left Hemiplegia
    - Gait Unsteadiness

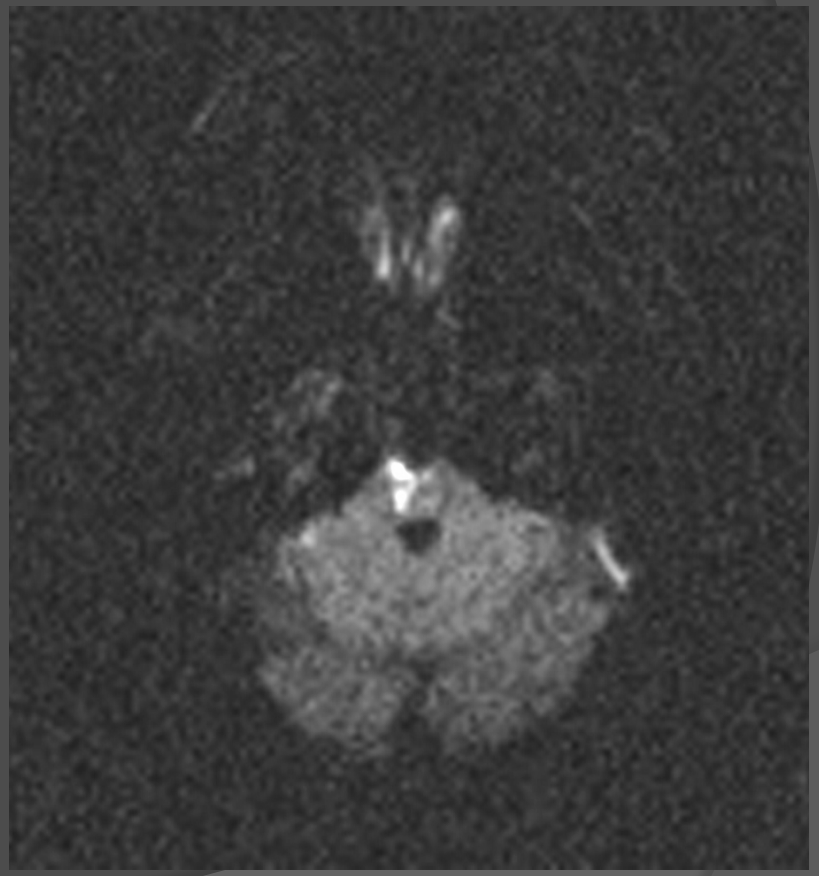
Angiographic Findings



Endovascular Approach

Outcome

- Normal Post-Op
- 4 hours later TIA Sx recurred and resolved
- Recurred again and progressed slowly
- MRI showed Perforator Infarct
- To NH, mRS=4



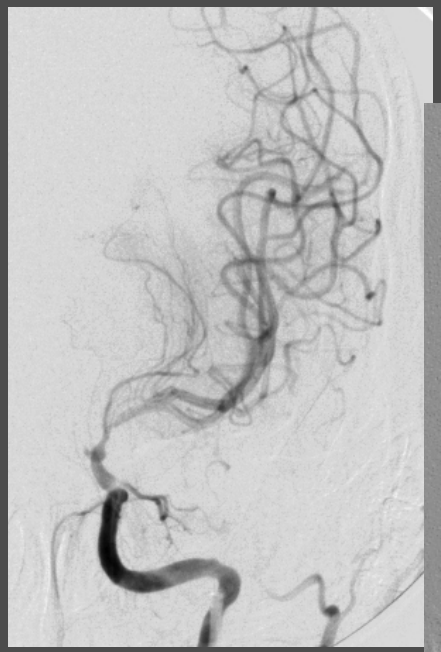
Does Stent Type Affect Risk of Perforator Strokes

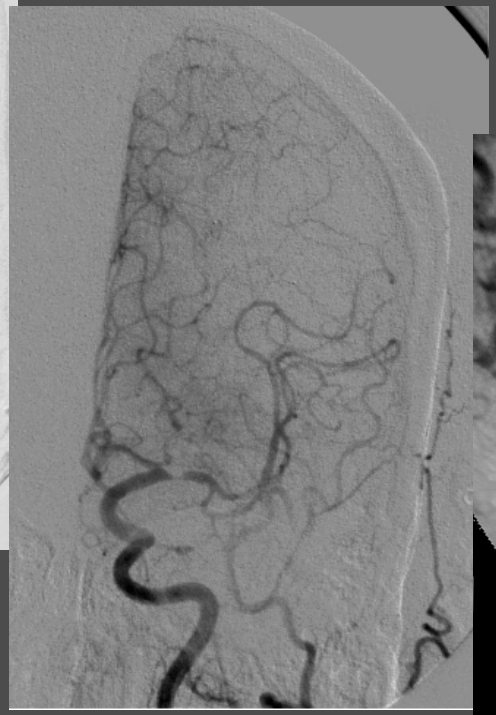
- Al-Ali et al AJNR 2011 (N=140) and Kurre W et al. INTRASTENT Registry. Neuroradiology 2012 (N=409, 254 BES, 155 SES)
  - More perforator strokes with BES in segments with perforators
- Aggressiveness of Angioplasty?

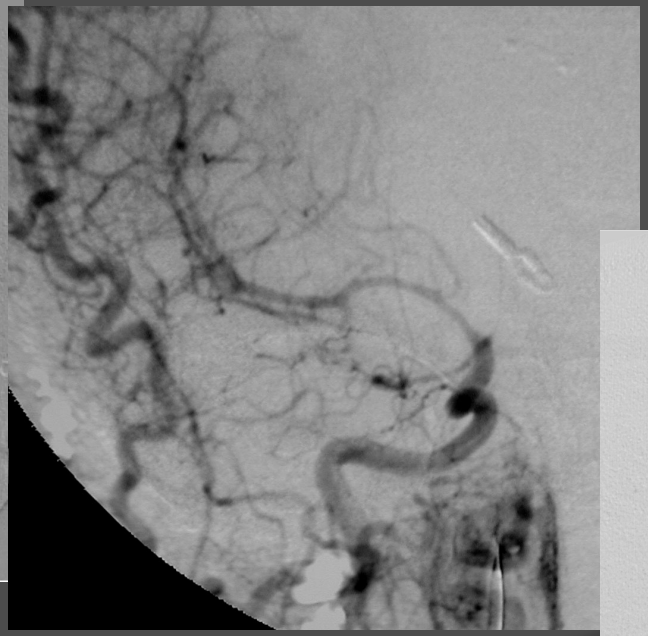
Medical vs. Endovascular Treatment Algorithm

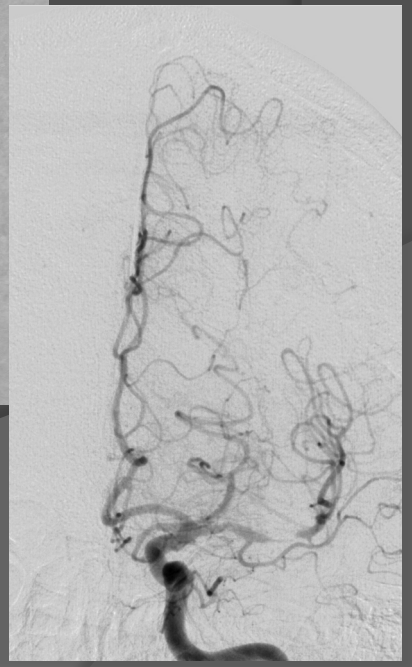
- Recurrent Event in Territory distal to Stenosis
- Impaired Cerebrovascular Reserve
  - Hemodynamic TIAs
- Failure of Medical Therapy
- Lesion Progression
- Lesion Characteristics
  - Tandem Lesions
  - Multi-focal Disease
  - Eccentricity of Plaque
  - Presence of perforators in plaque
- Elevated HSCRP, etc.

No Perforator Strokes in 12yrs









Conclusion

- It is essential to differentiate hemodynamic from perforator stroke
  - Patients with perforator ischemia only are effectively asymptomatic in the territory of the stenosis
  - They have less to gain from revascularization
  - Angioplasty and stenting are most beneficial in patients with hemodynamically significant stenoses