

MEET, Cannes, June 28, 2008

Carotid Course

*Why I stop antihypertensive drugs &
use selective atropin*



Thomas Ischinger, MD, FESC, FACC
Heart Center Bogenhausen, Munich, Germany

Disclosure Statement of Financial Interest

I DO NOT have a financial interest/arrangement or affiliation with one or more organizations that could be perceived as a real or apparent conflict of interest in the context of the subject of this presentation.

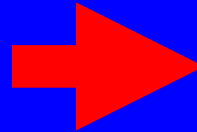
MEET 2008

What are the risks in
CAS?

Carotid Stenting: Risks & remedies

Proc steps & risks

- Access procedure: emboli
- Lesion passage: emboli
- intra procedural (stent, balloon): thromboatheromatous debris / air embolization
obstructive dissection / spasm



vaso/cardio depressant effects

vasospasm

- peri/postprocedural (< 48h)
bleeding vs stent thrombus
impaired microcirculation

Measures to avoid them

technique (one step), antithrombotics
flow reversal protection

medical pretx: ASS & Clopidogrel!
stent design + *distal embolic protection*
technique

technique

hemodynamic management

vasodilators, eg: Nitroglycerin i.a.

antithrombins: ↓
antiplatelet tx: clopidogrel+ASS
IIb / IIIa blockers?

20% of events occur pre / post embolic protection. 10% contralat.

Cardiodepressant effects in CAS

how they happen.....

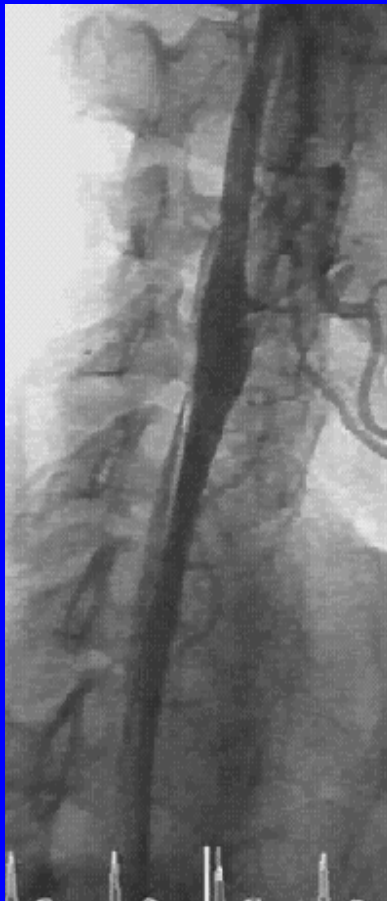
- Cardiodepression = *Hypotension & Bradycardia*
occurs in all pts upon stimulation of carotid sinus reflex -
yet degree varies
- Pathophysiology
 - increased endovascular pressure (local balloon dilatation)
results in cellular shift, possibly edema, hematoma
 - increase in impulse from afferent baroreceptors fibers to
medulla oblongata - for minutes / hours / days
 - triggers inhibiting response by activating cardiac vagal
nerves & decreasing periph sympatic vascular tone

Cardiodepressant effects in CAS

magnitude of the problem

- Stimulation of reflex does not occur in all target lesions - but in most of bifurcational de novo lesions
- Rare in distal ICA or CCA (if no balloon trauma to bifurcation)
- Rare in post CEA or instent restenosis, post radiation stenosis
- Incidence:
 - > 50% short (minutes) cardio depressant effects
 - > 25% sustained postproc hypotension..up to 4 days
 - > 15% sustained postproc bradycardia ..up to 4 days

Morphology and location of the target lesion and risk of cardiodepressant effects



Spontaneous dissection



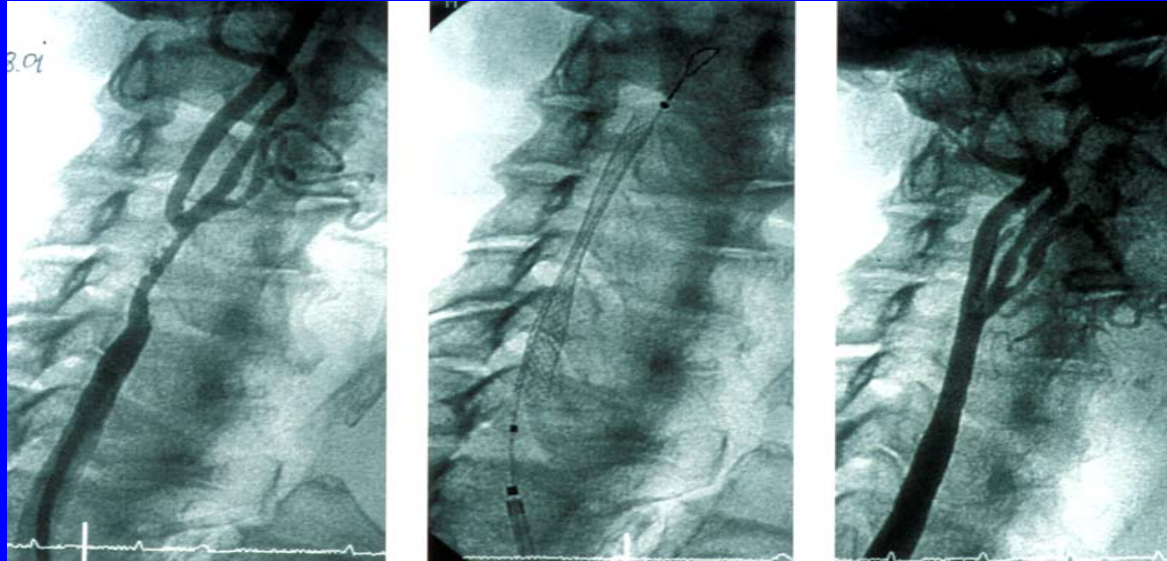
Ulcerative & thrombotic, at bifurcation



Tubular and / or proximity to bifurcation

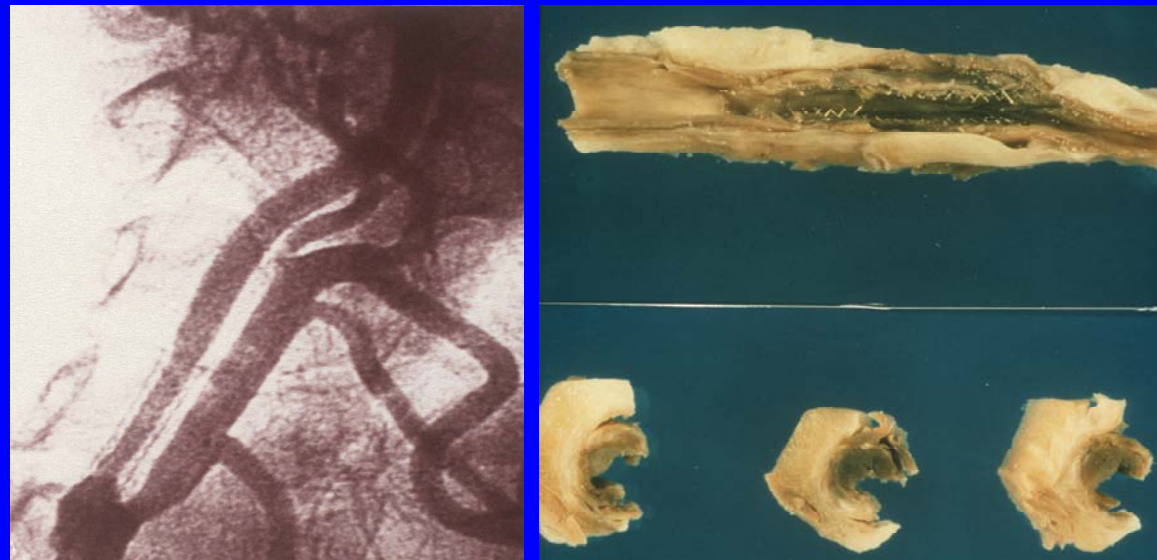


Recurrent lesions less sensitive



Recurrence
post CEA

Recurrence
post Stent



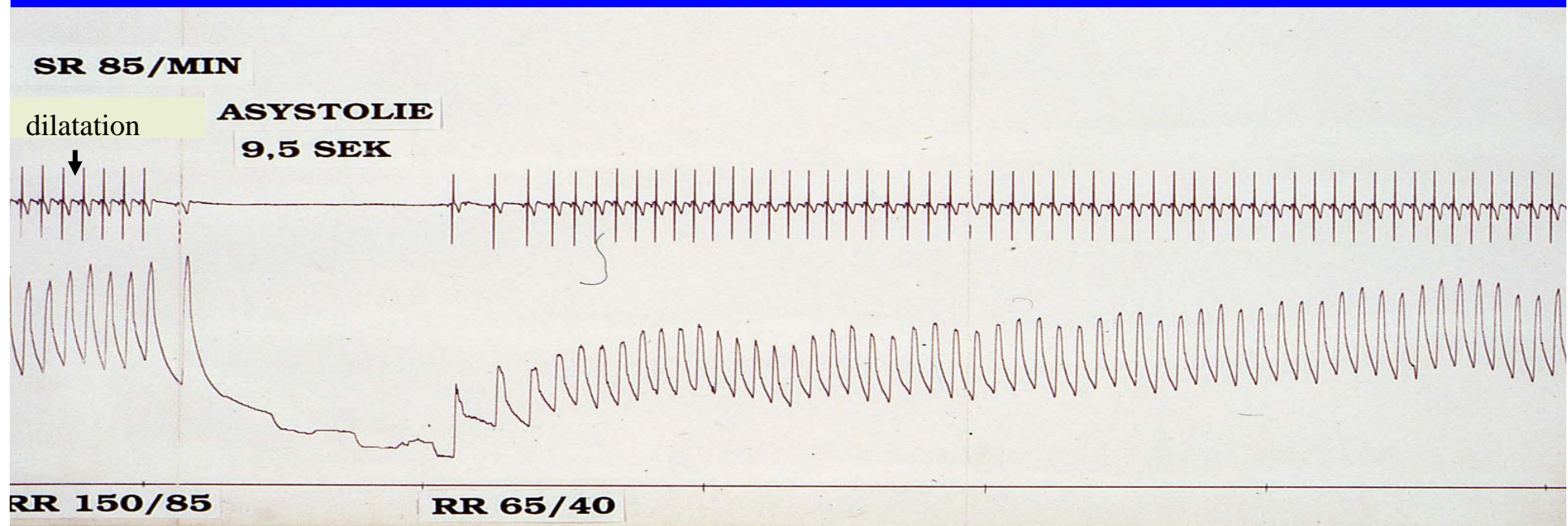
Carotid stenting Heart Center Bogenhausen:

Acute results < 30 days stroke & all deaths: 3.2%

(n=360)

• <u>primary success</u>		99%
stenosis reduction		82%-11% (60-99/0-40)
• <u>Complications procedural < day1</u>		
-reversible spasm (distal of stent)		6%
-brief neuro-symptoms (20 sec-<3 min)		6%
-asystole (2-20 s), Tx for bradycardia		
Tx for prolonged hypotension		17%
TIA (<24 hrs)	9	2.5%
minor stroke, reversible by DC	5	1.3 0%
Stroke	2	0.6%
• <u>Complications delayed >day1</u>		
PRIND day 2 (lack of antiaggr)	1	
death neuro (hemorrhage, hirudin, day 2)	1	0.3 %
<u>death cardiac/other (day 3 & 10 & 20</u>	3	<1. %
puncture site bleed		4 (2 surg.rev., 2 transfusion)

**Hyperactivation of Sinus Caroticus reflex by carotid dilatation:
acute asystole & hypotension, followed by prolonged hypotension.**



Degree of cardioinhibitory & vasodepressive reactions vary

Patient & procedural factors predisposing to cardiodepressant effects

- Old age (> 13% of pts > 80 years), tubular high grade lesions, location at bifurcation, dilatation of bifurc
- Antihypertensives (except β blockers?)
- Hypovolemia
- Late time in the day....
- Large balloon (avoid oversize), large stents
- High pressure or long balloon inflation
- Most frequent with post dilatation

Mendelsohn AJC 1998; Whitlow Stroke 2002; AlMubarak Stroke 2001; Brooks JACC 2001; D`Audiffret J Vasc Surg 2001; Dangas JET 2001; Qureshi Stroke 1999; Nonaka Neurosurgery 2005; ALKK registry JACC 2007

The ugly Trio:

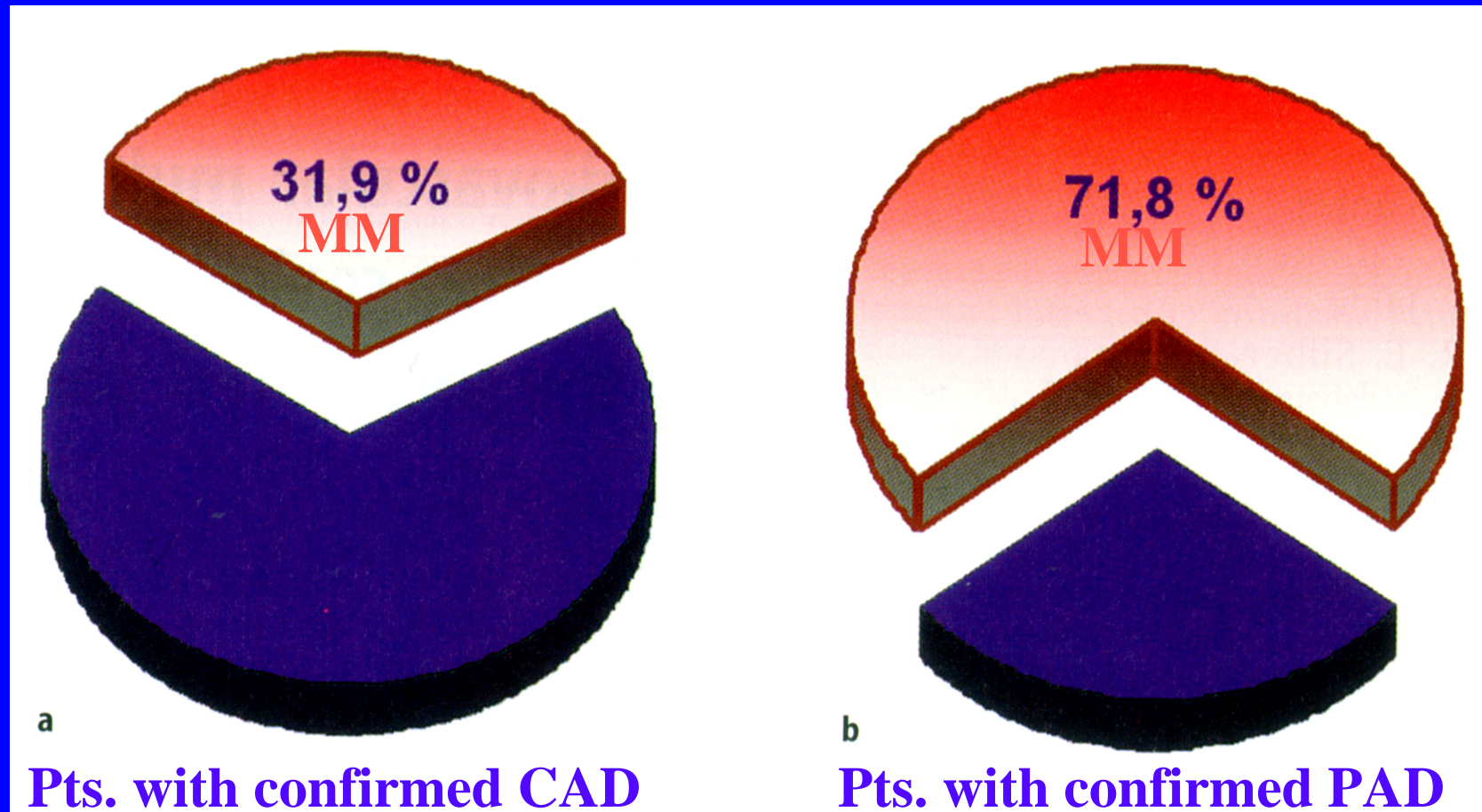
- Antihypertensive drugs on board
- Hypovolemia (late schedule)
- Dilatation of de novo lesion at carotid bifurcation

and no functioning venous access.....

Adverse clinical consequences

- Increased neurological ischemic events (intracranial stenoses, contralateral carotid S)
- Increased myocardial ischemia, (significant CAD, left main disease!)
- Increased risk of heart failure (Low ejection fraction, aortic stenosis)
- Increased LOS in intensive/monitored care
- Increased LOS in hospital

Increased risks for Carotid pts with Cardiovascular multimorbidity (MM)



CAS Patient Characteristics

ALKK registry n=3070

Comorbidity:

- CAD 67% / post MI 30%
- PAD 25%
- Arrhythmia: AF 15%
- Other cardiac disease: 6% HF
- Hypertension 91%
- Hyperlipidemia 85%
- Diabetes 33%

Drugs:

- ACEI 65%
- β Blockade 65%
- Ca Antag 20%
- Statins 82%


CAS pts angiographic characteristics

- Previous CEA: 7.3%
- Previous stent: 4.5%
- Bifurcation involved: more than 50%
- Severe calcific stenosis > 30%
- Stenosis length > 10mm: 50%
- Tubular high grade lesions > 25% (KMB)

Challenge of Cardiovascular Comorbidity

- In general increased procedural cardiovascular risk with interventional & surgical therapies
- Reduced prognosis post invasive procedures
- More difficult balance of bleeding risks & antithrombotics
- **Peri-procedural challenges include maintenance of hemodynamic stability** to minimize
 - cardiac and neurological (and renal) risks

Therefore I propose

- No antihypertensive (except β Blocker?) in the morning of the procedure - except in malignant hypertension and late timing of procedure
- 1.0 mg of Atropine 2 minutes before carotid bifurcational dilatation of de novo lesions in pts **w/o**
 - significant CAD
 - hypertension
 - tachycardia (AF) (HR > 90)
 - non-cardiac contraindications

Selective use...
- 1.0 -2.0 mg of Atropine if Bradycardia/Hypotension occurs upon dilatation despite pretx or w/o pretx w Atropine

Hemodynamic tx pre and periprocedurally

<u>atropin</u>	Prophylactic use prior to dilatation at bifurcation: 1.0 mg Tx of periprocedural hypotension: 1.0-2.0 mg
dopamine	<ul style="list-style-type: none">- Low dose (<2ug/kg/min): dopamine receptors (<i>splanchnicus area</i>)- Intermediate dose (2-5ug/kg/min): cardiac β1-receptors and α-receptors, <u>minor vasoconstriction</u>- high dose (>5ug/kg/min): <u>progressive vasoconstriction</u>-initial bolus: 0.5 - 1.0 ml = 2.5-5.0mg (ampoule: 250mg/50ml)-subsequent tx: > 1.0 ml/min depending on hemodynamics
epinephrine suprarenin	Initial test dose: 0.01 - 0.04 ug / kg / min, followed by titrated dosing

Risks of stopping antihypertensives?

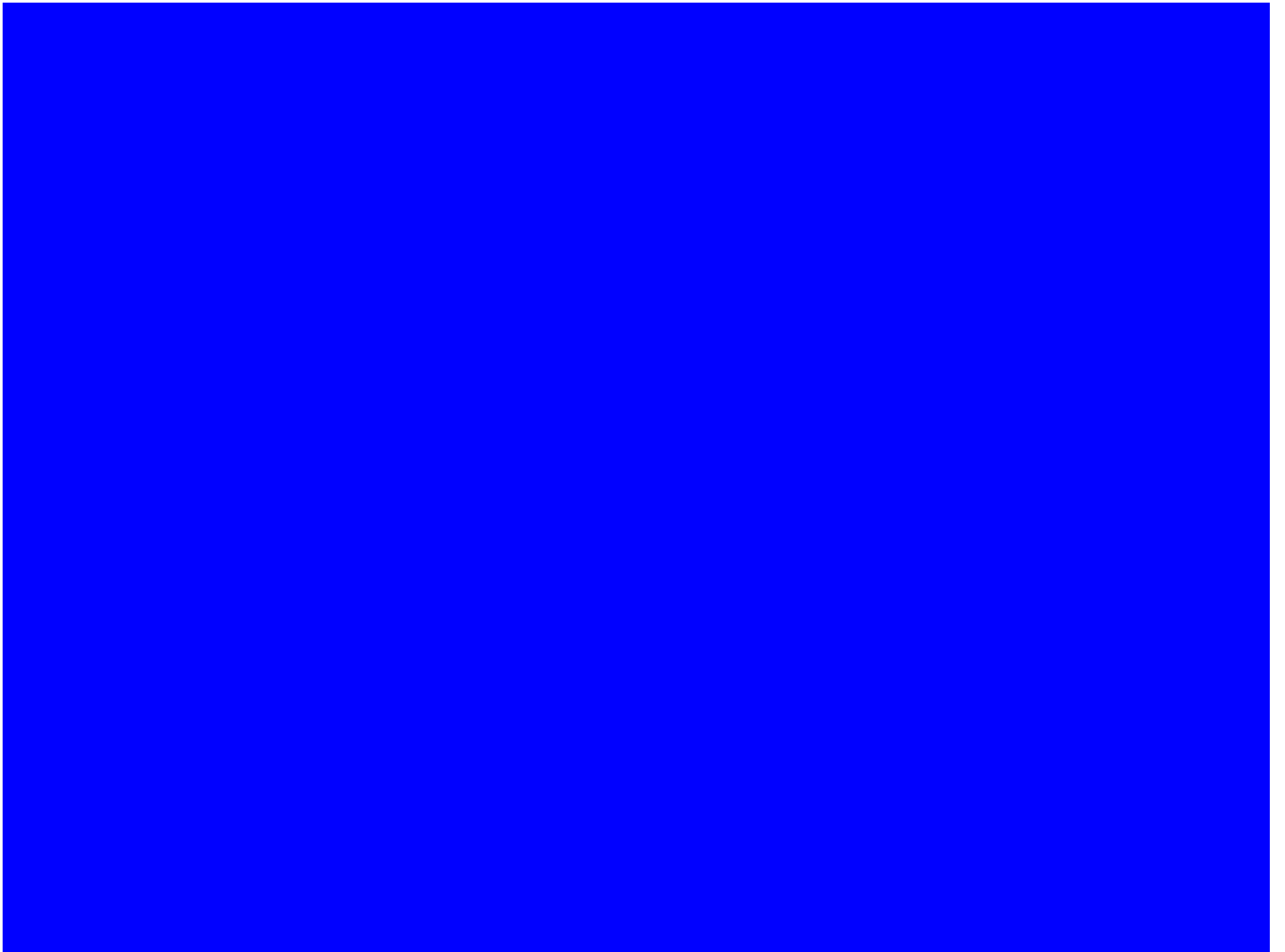
Risks of Atropine administration?...*yes, but manageable*

- Lack of Antihypertensives: Hypertension
Counteraction periinterventionally by vasodilators
i.v. is effective and safe
(Nitrates, Urapidil, Dihydralazin, Nitroprussid-Na,
i.v. Beta-Blocker = Esmolol)
-in hyperperfusion syndrome: β Blocker, Clonidin
- Risk of Atropine: myocardial ischemia, accelerated
tachyarrhythmia
-manageable by Verapamil (AF), β Blockers iv

I recommend...

- Schedule the procedures early in the day
- Avoid hypovolemia
- Avoid Atropine in specific situation (severe CAD, glaucoma, urologic problems...)
- Consider pacing lead in „high hemodynamic risk“ (AV block, aortic stenosis, left main, severe heart failure)
- Have vasopressor agents ready (dopamine, epinephrine)
- Select & tailor periprocedural medical strategy (antihypertensives and atropine) to individual (comorbid) patient and

always permit exceptions from the rule...



Drugs for Hemodynamic Tx

- **Atropin:** selective treatment or routine prophylactic administration to prevent vagal mechanism induced bradycardia & hypotension...?
- **Vasopressor agents** (with persistent hypotension)
 - Dopamine:** peripheral vasoconstriction / positive inotropy (specific β_1 and α receptor activation)
 - Suprarenin / Epinephrine:** heart rate increase & inotropy (unspecific α , β_1 and β_2 activation)

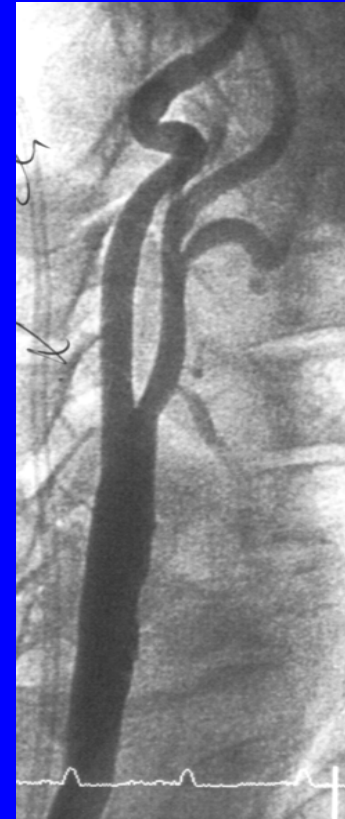
cave: excessive effects with risks of intracerebral bleeding, hyperperfusion sx and myocardial ischemia (coronary pts)
- **Antihypertensives periprocedural:** Ca Antagonists, Nitro;
in Hyperperfusion syndrome: β Blocker, Clonidin

Specific procedure related pharmacology

- Pre-Stenting
 - antithrombotic: ASS and Clopidogrel
 - renoprotective: hydration, contrast sel, metformin discon., Theophylline*, Accetylcysteine? Fenoldopam (dopamin 1 rec agonist)
 - antiallergic: Methylprednisolon, H1 Anthistamins, H2 Blocker,
- Intraprocedural
 - antithrombotic: Heparin UF / Bivalirudin
 - rescue: lytics: tPA for identified thrombus
 - antiplatelet: IIb / IIIa antagonist (short acting)
 - hemodynamic: Atropin / Dopamin / Suprarenin (Epinephrine)**
 - anti-spasm: selective i.art. Nitroglycerin 200ug, Ca antag**
- Post-Stenting
 - antithrombotic: ASS and Clopidogrel, select. Heparin
 - Anticoagulation: special clinical indications (cardiac)
 - hemodynamic: Dopamin / Suprarenin (select), Ca-Antag.in**
 - Hypertension**
 - hyperperfusion syn: diuretics, BP control, β Blocker, Clonidin, sumatriptan**?

Arterial spasm with wires / filters

Risk of low or no flow or spasm or thrombus?



Pharmacological therapy: i.a. Nitro 200mcg,
Verapamil 500mcg i.a., flush, IIB / IIIa?

Carotid disease and CAD

- In pts with CAD, significant carotid stenosis occurs in 30-50%
- In pts with Carotid Stenosis, significant CAD occurs in 20-30%

Drugs in carotid disease pts

- **Tx of hypertension**

ACEI, AT1 blockers, diuretics, β -blockers, Ca-antagonists

- Tx of hyperlipidemia:
statins

- plaque / endothelial function deficit:
statins, ACEI, dual antiplatelet tx

- Antithrombotic management (chronic,procedural):

ASS 100-125mg, Clopidogrel 75mg alone (CAPRIE),ASS + Dipyrid. 75mg x3(post stroke,ESPRIT study), ASS 100 mg + Clopidogrel 75mg in complex symp.pts (CHARISMA)+post stent (CLASSICS)

-Heparins (UF,LMWH),DTI - periprocedural

-Coumadin: comorbidity requiring anticoagulation (e.g.AF, valvular D)