

Institut

Lorrain du Coeur et des Vaisseaux

ILCV

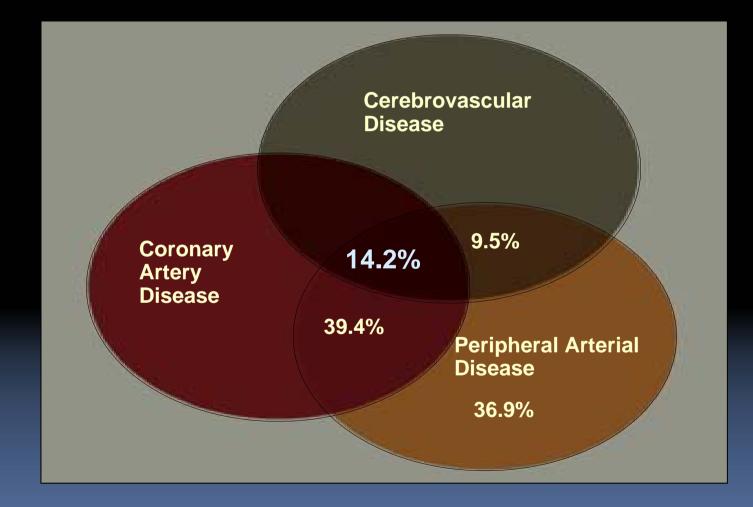
## Management of combined coronary & carotic disease

אות קיטולים גבותיים קילטבילק בוניטל שואילים קיליק קיטוליים אילי אלבצא mach com

# Combined Carotid and coronary artery diseases

- Frequent combination
- Fear of imminent death psychologically traumatic for the patients and their families
- Higher Risk of morbidity and mortality
- Complex and dilemmatic management

#### **Atherosclerosis is a Systemic Disease**



Bhatt DL, et al; for the REACH Registry Investigators. JAMA. 2006;295:180-189.

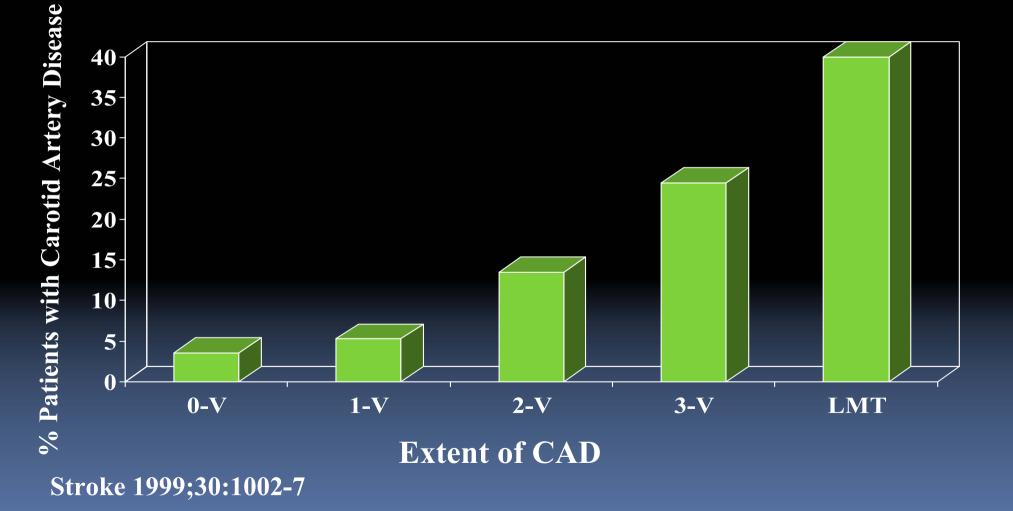
## Management

- At the present time guidelines for adequate treatment of both symptomatic and asymptomatic carotid artery stenoses are vague for patients with symptomatic CAD:
  - Ignoring carotid or coronary lesions
  - Performing staged operations with delay of one of the procedure (or reverse staged: CABG CEA)
  - Combining coronary grafting and CEA during the same anesthesia
  - Performing only carotid stenting and coronary angioplasty

### Points to remember

- Prospective studies have shown that 8 to 14 % of CABG patients have significant carotid stenosis
- Whereas it has been estimated that up to 28 % of patients undergoing exploration for CEA have severe correctable CAD
- Furthermore CAD is the leading cause of both early and late mortality after CEA
- Although the overall incidence of complications after CABG has decreased ,the incidence of neurological complications (neuropsychological, stroke) remains unchanged being reported from 0.8 to 3.2% in retrospective studies and from 1.5 to 6% in prospective studies

### Coronary Artery Disease as a Marker for Carotid Artery Stenosis



## Combined Coronary/Carotid Disease is a Marker of Poor Outcomes



J Vasc Surg 2006;43:959-68

### Perioperative stroke after C.A.B.G

## According to the severity of carotid artery stenosis (symptomatic & asymptomatic)

Carotid stenosis	Stroke
<50%	2%
50-80%	10%
≥80%	11-18,8% (RR 9,87)
+ Contralateral stenosis >80% or occlusion	>20%

Wareing TH. Ann Thorac Surg 1993;55:1400-7

D'Agostino RS. Ann Thorac Surg 1996;62:1714-23

Outcomes following staged and synchronous CEA and CABG

Naylor A.R Eur J Vasc Endovsc Surg 2003; 25 : 380-389

- A recent systematic review of outcomes following staged (CEA then CABG), reverse staged (CABG then CEA) and synchronous CEA & CABG
- Mortality highest with synchronous (4.6%), whereas reversed staged has the highest risk of ipsilateral stroke (5.8%).
- Perioperative MI was lowest following reverse staged procedure(0.9%) and highest in staged procedure (3.2%)
- The risk of death /stroke/MI was 11.5% after synchronous and 10.2% after staged CEA-CABG (not significant)

## Advantages of Carotid Stenting in the presence of coronary artery disease

- Advantages :
  - In contrast to CEA the anti-platelet regimen can be continued and abrupt changes in blood pressure be avoided (less myocardial ischemia & hypotension)
  - When acute myocardial ischemia occurs during procedure intra-arterial access is provided and immediate angioplasty can be performed
  - The procedure does not need to be restricted to the neck (ostial ,Inominate, vertebral ,subclavian)
  - General anesthesia is not required ,CAS can be offered to old sick patients with respiratory disease

## Disadvantages of Carotid Stenting in the presence of coronary artery disease

- Disadvantages :
  - Delay surgical procedures
  - Cardiac death by delaying myocardial revascularization
  - Long term results unknown

## Incidence cumulée des événements

à 30 jours

Jay Yadav, NEJM, 2004;351;15 p1493-1501

EVENEMENT	INTENTION DE TRAITER			PATIENTS TRAITES		
	STENT	CHIR	P value	STENT	CHIR	P value
	N=167	N=167		N=159	N=151	
Décès	2 (1.2)	4 (2.5)	0.39	1( 0.6)	3( 2.0)	0.29
AVC	6(3.6)	5(3.1)	0.77	5(3.1)	5(3.3)	0.94
Majeur Homolatéral	1(0.6)	2(1.2)	0.55	0	2(1.3)	0.15
Majeur Non Homolatéral	1(0.6)	1(0.6)	1.00	1(0.6)	1(0.7)	0.97
Mineur Homolatéral	4(2.4)	1(0.6)	0.18	4(2.5)	1(0.7)	0.20
Mineur Non Homolatéral	1(0.6)	1(0.6)	1.00	1(0.6)	1(0.7)	0.97
Infarctus	4 (2.4)	10( 6.1)	0.10	3 (1.9)	10 (6.6)	0.04
Avec onde Q	0	2 (1.2)	0.15	0	2 (1.3)	0.15
Sans onde Q	4( 2.4)	8 (4.9)	0.23	3 (1.9)	8( 5.3)	0.11
Décès , AVC, infarctus	8 (4.8)	16( 9.8)	0.09	7 (4.4)	15 (9.9)	0.06
Complic vasculaires maj.	2 (1.2)	1 (0.6)	0.57	2 (1.3)	1( 0.7)	0.60

#### A Systematic Review of Outcomes in Patients With Staged Carotid Artery Stenting and Coronary Artery Bypass Graft Surgery

Luis A. Guzman, MD; Marco A. Costa, MD, PhD; Dominick J. Angiolillo, MD, PhD; Martin Zenni, MD; Peter Wludyka, PhD; Scott Silliman, MD; Theodore A. Bass, MD

#### Guzman, L. A. et al. Stroke 2008;39:361-365

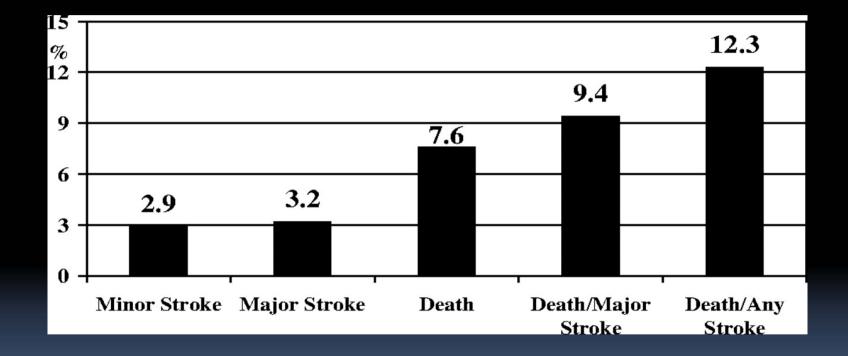
*Methods*—A search of MEDLINE and a manual search of the literature from selected articles were performed. A total of 6 studies with 277 patients reporting carotid stenting followed by staged CABG were available for this clinical outcome analysis. All were retrospective and single-center studies.

Results—The mean age was 69 years; 78% were males. Asymptomatic carotid stenosis was present in 76% of patients. The mean time to CABG was 32 days. The incidence of stroke and death associated with the stent procedure was 4.7%. Only 6 patients (2.2%) developed stroke associated with CABG. The overall combined 30-day event rate after CABG, including all events during carotid artery stenting, were as follows: minor stroke, 2.9%; major stroke, 3.2%; mortality, 7.6%; and combined death and any stroke, 12.3%.

*Conclusions*—In this pooled analysis, the combined incidence of death and stroke in patients undergoing carotid artery stenting and staged CABG remains elevated. These results confirm that the presence of carotid stenosis is per se a marker of risk that might persists independent of its treatment. A systematic or randomized evaluation appears warranted. (*Stroke*. 2008;39:361-365.)

277 pts with a mean time to CABG of 32 days. Overall combined death and any stroke 30-day event rate after CABG : 12.3%

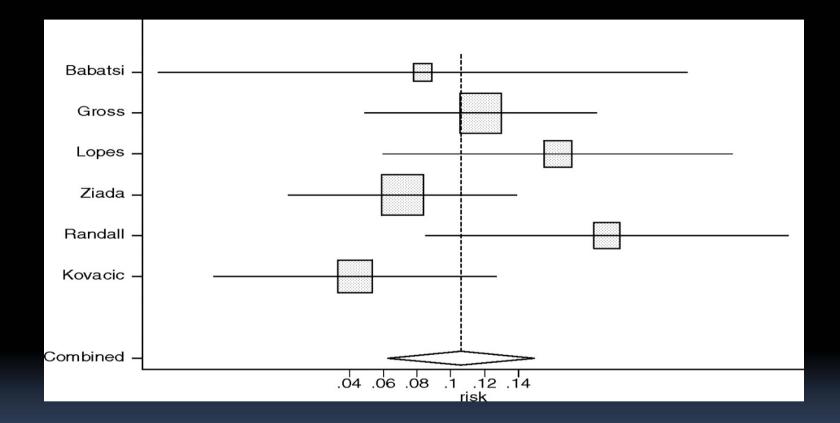
#### Major clinic events from CAS to 30 days after CABG



Stroke

Guzman, L. A. et al. Stroke 2008;39:361-365

#### Heterogeneity evaluation among the different studies





Guzman, L. A. et al. Stroke 2008;39:361-365

## Heterogeneity of distal protection use among the different studies (0 to 100%)

Study	Year	N	Male	Age, years	Diabetes Mellitus	Hypertension	Smoking	Cholesterol	Symp	C Occ	Timing	D.P.
Babatsi	1996	12	12 (100)	71	NA	NA	NA	NA	0	5 (41)	18	12 (100%)
Gross	1999	85	70 (82)	43-89	27 (32)	51 (60)	36 (42)	38 (45)	19 (22)	11 (13)	23	No
Lopes	2002	49	34 (69)	68	20 (41)	32 (65)	NA	NA	16 (32)	9 (18)	15	No
Ziada	2005	56	39 (69)	70	24 (43)	40 (71)	36 (64)	NA	26 (46)*	5 (9)	39	8 (14%)
Randall	2005	52	45 (86)	68	16 (31)	40 (77)	46 (88)*	47 (90)	4 (8)*	20 (38)*	30	31 (69%)
Kovacic	2005	23	17 (74)	68	10 (43)	23 (100)*	19 (82)	22 (95)	8 (32)	5 (21)	69	10 (38%)
Combined		277	217 (78)	69	97 (36)	186 (70)	137 (63)	107 (71)	73 (26)	55 (20)	32.3	61 (32%)

\*P<0.05.

Symp indicates symptomatic carotid stenosis; C Occ, contralateral occlusion; Timing, time in days between the completion of CAS intervention and CABG; D.P., utilization of distal protection device during the carotid stent procedure; NA, not available.

# Occurrence of events after CAS, between CAS & CABG, and after

#### Table 2. Clinical Events in Each Individual Study

			Afte	er Carotid St	ent	Pos	st-CAS to CA	BG	Post-	CABG	Overall	Events
Study	Year	N	Minor Stroke	Major Stroke	Death	Minor Stroke	Major Stroke	Death	Major Stroke	Death	Death/Major Stroke	Death/Any Stroke
Babatsi	1996	12	1	0	0	0	0	0	0	0	0 (0)	1 (8.3)
Gross	1999	85	3	2	2	0	0	0	0	5	7 (8.2)	10 (11.7)
Lopes	2002	49	3	0	2	0	0	1	1	1	5 (10.2)	8 (16.3)
Ziada	2005	56	0	1	0	0	0	2	0	1	4 (7.1)	4 (7.1)
Randall	2005	52	0	0	0	0	0	3	5	4	10 (19.2)	10 (19.2)
Kovacic	2005	23	1	0	0	0	0	0	0	0	0 (0)	1 (4.3)
Combined		277	8	3	4	0	0	6	6	11	26 (9.4)	34 (12.3)

Guzman, L. A. et al. Stroke 2008;39:361-365

#### Table 3. Combined Incidence (%) of Major Clinical Events After Revascularization

	Minor Stroke	Major Stroke	Death	Death/Major Stroke	Death/Any Stroke
Post CAS (at discharge)	2.9	1.1	1.4	1.8	4.7
After CAS, before CABG	0	0	2.2	2.2	2.2
30 days post-CABG	NA	2.2	4.1	5.6	5.6
Overall	2.9	3.2	7.6	9.4	12.3

Guzman, L. A. et al. Stroke 2008;39:361-365

#### Staged Carotid Angioplasty and Stenting Followed by Cardiac Surgery in Patients With Severe Asymptomatic Carotid Artery Stenosis: Early and Long-Term Results

Jan Van der Heyden, Maarten J. Suttorp, Egbert T. Bal, Jef M. Ernst, Rob G. Ackerstaff, Jeroen Schaap, Johannes C. Kelder, Mark Schepens and Herbert W. Plokker

*Methods and Results*—We report the results of a prospective, single-center study designed to evaluate the feasibility and safety of carotid artery angioplasty and stenting (CAS) before cardiac surgery in neurologically asymptomatic patients. The periprocedural and long-term outcomes of 356 consecutive patients who underwent CAS before cardiac surgery were analyzed. The procedural success rate of CAS was 97.7%. The death and stroke rate from time of CAS to 30 days after cardiac surgery was 4.8% (n=17). The myocardial infarction rate from time of CAS to 30 days after cardiac surgery was 2.0% (n=7), and the combined death, stroke, and myocardial infarction rate was 6.7% (n=24). Distal embolic protection devices were used in 40% of the cases.

*Conclusions*—This large cohort of asymptomatic patients who underwent staged CAS and cardiac surgery experienced a low periprocedural complication rate. The high rate of freedom from death and stroke during the 5 years of follow-up supports the long-term durability of this approach. Our findings suggest that this new strategy may become a valuable alternative in the treatment of patients with combined carotid and cardiac disease. (*Circulation*. 2007;116:2036-2042.)

Single center study (Nieuwegen, The Netherlands) 356 consecutive patients treated with CAS (distal protection in 40 %)

N	19783		
Event	CAS Patients (n=356)	Cardiac Surgery Patients (n=354)	Total (n=356)
All deaths	1 (0.3)	12 (3.4)	13 (3.7)
Cardiac deaths	1 (0.3)	7 (2.0)	8 (2.2)
Neurological deaths	0	1 (0.3)	1 (0.3)
Nonneurological/noncardiovascular deaths	0	4 (1.1)	4 (1.1)
All strokes	5 (1.4)	6 (1.7)	11 (3.1)
Major ipsilateral nonfatal strokes	1 (0.3)	3 (0.8)	4 (1.1)
Major contralateral nonfatal strokes	0	2 (0.6)	2 (0.6)
Minor strokes	4 (1.1)	1 (0.3)	5 (1.4)
Transient ischemic attacks	8 (2.2)	5 (1.4)	13 (3.7)
Nonfatal MIs	2 (0.6)	5 (1.4)	7 (2.0)
All deaths and major strokes	2 (0.6)	15 (4.2)	17 (4.8)
All deaths, major strokes, and MIs	4 (1.1)	20 (5.6)	24 (6.7)

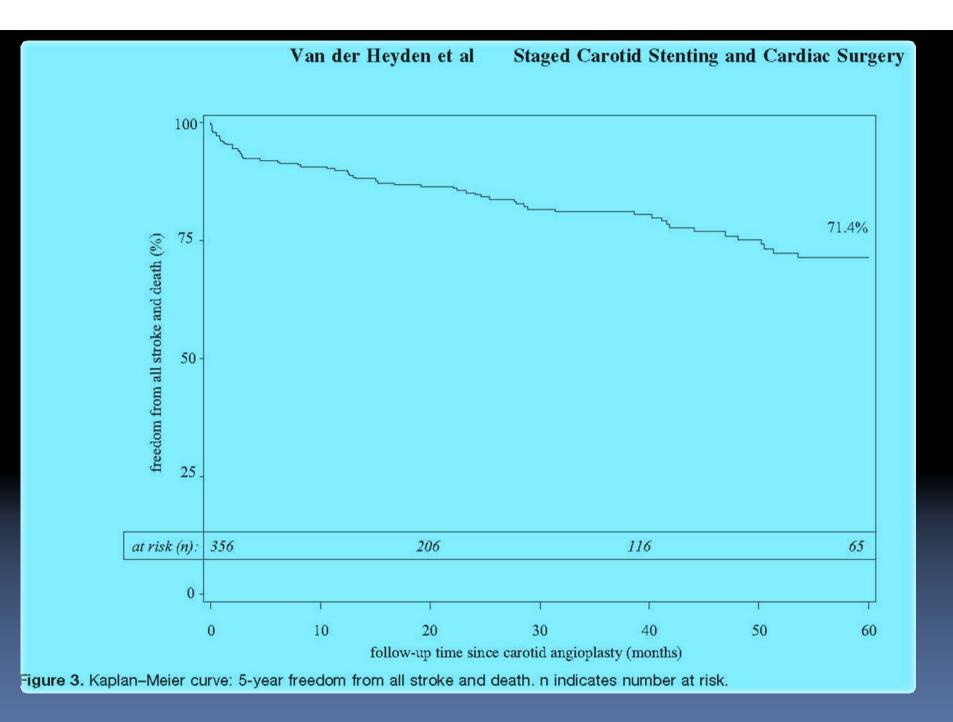
#### Table 2. Periprocedural Event Rate After Staged CAS and Cardiac Surgery

#### Death and strokes : 6.2 %

	Cumulative Event Rate at 5 Years, % (95% Cl)	Р
All cause mortality	24.5 (18.0–31.0)	
Cardiocerebrovascular mortality	16.6 (11.2–22.0)	20100
MI	2.0 (0.5–3.5)	
Major stroke	3.1 (0.1–6.0)	
Minor stroke	2.9 (0.8–5.0)	
Transient ischemic attack	5.6 (2.3–8.9)	
All-cause mortality+minor stroke+major stroke	28.6 (21.8–35.3)	<b></b>
Cardiocerebrovascular mortality+major stroke+MI	20.5 (14.6–26.3)	0.7713
Age <80 y	20.0 (13.5-26.4)	
Age $\geq \! 80$ y	23.0 (8.5–37.4)	
All-cause mortality by sex		0.0505
Men	27.8 (19.9–35.6)	
Women	16.2 (5.5–26.9)	
All-cause mortality by age		0.5404
Age <80 y	23.9 (16.7–31.1)	•••
Age ≥80 y	27.3 (12.1–42.4)	
All-cause mortality by use of distal protection device		0.7654
No distal protection device used*	15.5 (10.3–20.8)	
Distal protection device used*	17.5 (7.3–27.6)	
Transient ischemic attack by age		0.0377
Age <80 y	3.7 (1.2–6.2)	
Age ≥80 y	13.5 (0.5–26.6)	

Cl indicates confidence interval.

\*Denotes event rates at 3-year follow-up.



## Population & methods

 We treated 25 patients with Carotid artery stenosis (5 symptomatic and 20 asymptomatic) with elective stent implantation under Embolic Protection Devices

All patients had severe coronary artery disease, and/or generalized arteriosclerosis

In two patients the opposite carotid artery was occluded; five patients had bilateral stenoses of which two received stent bilaterally

> Clinic Louis Pasteur Data 2002-2005 Mamoun Maksour

#### Table 1 Baseline clinical characteristics of patients

6

	n= 25
Age (in years)	58-8
Male/Female	17/8
Cardiovascular risk factors	
Hypertension	11
Diabetes	~7
Smoker	7
Hypercholesterolemia	10
Peripheral artery disease	5 1
Abdominal aneurysm	1
Cardiac history	
Prior MI, CABG	7
Coronary vessel disease	
1 vd	9
2 vd	6
3 vd	10
Advised for CABG	3
Advised for PTCA	22
Carotid artery stenoses (n=30)	
Right internal carotid artery	12
Left internal carotid artery	18
Symptomatic	5
Transient ischemic attack (TIA)	4
Major stroke	1
Asymptomatic	20
Contralateral carotid occlusion	2
Bilateral stenoses	5

### RESULTS

- All patients had a successful stent implantation
- Complications included four transient ischemic attacks immediately after the deployment of stent, which completely resolved
- At 30 days there was no minor or major stroke or MI, but one death occurred in a patient with bad LV function who was awaiting cardiac surgery
- No neurological events during Cardiac intervention and 30 days after

30-day Death and strokes after Cardiac intervention 4.0 %

Proposed indications for CAS in presence of symptomatic coronary artery disease

1) Patients with Carotid lesions not recommended for CEA

- Neck radiation, hostile neck, recurrent stenosis, contralateral occlusion
- 2) Patients accessible to PTCA
  - PTCA and CAS could be performed during the same hospitalization ,
  - If the renal function allows it ,CAS and PTCA performed synchronically ( abdominal aortic occlusion &radial access)
  - Performed routinely in patients with AAA before surgery
- 3) Patients with bilateral carotid artery lesions
  - Both carotid lesions are treated (we know from surgical series that stroke occurs more frequently in the neglected side)
- 4) Patients with tandem lesions
  - Ostial, Inominate ,subclavian artery

Proposed indications for CAS in presence of symptomatic coronary artery disease

- 5. Patients with co morbidity, old patients
  - Respiratory disease
- 6) Patients with a past thoracic or cardiac surgery
  - Redo cardiac surgery

Proposed indications for CEA in presence of symptomatic coronary artery disease

#### 1) Patients with lesions not recommended for CAS

- Heavily calcified lesions, Thrombus containing lesions
- Inability to use embolic protection device
- Difficult anatomy to access
- 2) Patients allergic to Aspirin or Clopidogrel
- 3) Patients requiring valve replacement?
  - Coumadin + Aspirin
  - Coumadin+ Clopidogrel
  - Coumadin + Aspirin + Clopidogrel

## Points to discuss

#### **PTCA** is the treatment selected

### PTCA feasible

- Perform PTCA first to avoid destabilization of coronary situation induced by hypotension ,bradycardia
- CAS in the elderly require interruption of anti-hypertension drugs and sometimes βblockers
- We do not recommend to perform CAS in the same session
  - Contrast medium
  - Hypotension, Bradycardia (RCA, Dominant LCX)
  - Same access but 2 different technics (EPD, EKG monitoring, Enzymes...)
  - Surveillance : neurological & cardiological different
  - IIb IIIa inhibitors are prohibited in our lab during CAS
- Perform a selective carotid angiography to confirm the feasibility of CAS
- Avoid if possible DES. The CAS may become CEA ! and PTCA a CABG ...

- PTCA performed with good clinical and angiographic results
  CAS is performed at a distance of PTCA

  - The patient is fully informed about this interim period
    The clinical signs that he or she should recognized
    The Dual anti-platelet treatment

    - It is very important to manage his anxiety and to counteract it.
    - A full information of the steps is indispensable
  - How long is this interim period
    - Patient choice between 3 weeks and 2 months
    - It is important to repeat a full neurologic assessment
  - CAS
    - We verify frequently at first the coronary result by a quick coronary anglogram (Healing of a dissection, collaterals evolution...). The information is given to the patient during CAS procedure to reassure him that we are on the right track

**CABG ± Valve replacement are the selected treatment** 

### Staged technic are preferred

- We recommend to start with CAS
- If there is tandem or bilateral lesions there are treated in 2 sessions (To avoid hyperfusion syndrome, profound hypotension, difficult interpretation of neurologic symptoms)
- Usually we keep the introducer in place and perform the second CAS 24 hours later
- The interim period is 2 weeks if CAS results were excellent and 3 weeks if the patient is old (over 80y) and the results not optimal
- Clopidogrel is stopped 5 to 7 days before cardiac surgery
- The patient is placed under Enoxaparin
- The day before surgery Aspirin is stopped (or maintained ?)
- Dual anti-platelet therapy is given ASAP usually 48 hours later
- If the patient require Coumadin the patient is given in addition Aspirin only

(4)

**CABG ± Valve replacement are the selected treatment** 

- Synchronous technics are necessary
- CAS is performed under UF heparin
- An immediate 2 D carotid Echo is performed in the cath lab
- The groin is closed using a PERCLOSE device
- Dual anti-platelet therapy is given ASAP usually 48 hours later

It is a very difficult management that require a close and competent team where each physician is thinking about the next step and the previous step

## Carotid artery symptoms are dominant (1) CAS is the treatment selected

- Patient neurologically stable
  - Perform PTCA first to avoid destabilization of coronary situation induced by hypotension ,bradycardia, interruption of anti-angina drugs such as βblockers
  - This allows if necessary the us of IIb IIIa inhibitors (Integrilin)
  - We do not recommend to perform CAS in the same session
    - Contrast medium
    - Hypotension, Bradycardia (RCA, Dominant LCX)
    - Same access but 2 different technics (EPD, EKG monitoring, Enzymes...)
    - Surveillance : neurological & cardiological different
  - Perform a selective carotid angiography to confirm the feasibility of CAS
  - Avoid if possible DES . The CAS may become CEA !and PTCA a CABG
  - CAS is performed 2 to 3 weeks later . Control coronary anglo is performed if necessary
  - THESE PATIENTS ARE PARTICULARLY ANXIOUS AND THE INTERIM PERIOD NEED TO BE SHORT

### Carotid artery symptoms are dominant (2)

CAS is the treatment **Selected** 

- Patient neurologically unstable
  - If CAS is feasible and PTCA needed, Perform CAS at first. Synchronous procedure are exceptionally needed (Access Problem)
  - PTCA is performed during the same hospitalzation. This allows if necessary the use of IIb IIIa inhibitors (Integrilin).
  - If CAS is feasible and CABG required
    - Staged procedure starting with CAS
    - The interim period is 4 weeks if CAS results were excellent and 6 weeks if the patient is old (over 80y) and the results not optimal.
    - The Brain healing on MRI and CT is followed
    - Clopidogrel and Aspirin are stopped 5 to 7 days before cardiac surgery
    - The patient is placed under Enoxaparin
    - Dual anti-platelet therapy is given ASAP usually 48 hours later if needed
    - If the patient require Coumadin the patient is left under coumadin alone .Aspirin is given if needed

## Coronary+ Neurologic instability

- Exceptional in our practice
- In the few cases that we had we treated the coronary culprit lesion first.
- During the same session the feasibility of Carotid stenting was assessed
- The carotid stenting was performed in the same session if appropriate (Recurrent symptoms despite good medical therapy)

## Several possibilities

	Asymp	tomatic	Sympt	omatic		
	Carotic	Artery	<b>Carotid Artery</b>			
	Unilateral	Bilateral	Unilateral	Bilateral		
		(occl& sten)		(occl&sten)		
1 VD	1St PTCA	1St PTCA	1St PTCA	1St PTCA		
	2nd CAS	2nd CAS	2nd CAS	2nd CAS		
			Synchro?	Synchro?		
2 VD	1St PTCA	1St PTCA	1St PTCA	1St PTCA		
	2nd CAS	2nd CAS	2nd CAS	2nd CAS		
			Synchro?	Synchro?		
3 VD or	1St PTCA	1St PTCA	1St PTCA	1St PTCA		
L MainT	2nd CAS	2nd CAS	2nd CAS	2nd CAS		
			Synchro?	Synchro?		

## **Clinical perspective**

- In the absence of randomized trials, the best management of patients with concomitant severe carotid and coronary artery remains in dispute particularly in asymptomatic patients
- The initial studies of combined or staged carotid endarterectomy in these patients were conceived in an attempt to reduce perioperative mortality
- The effect of carotid stenting on the incidence of death and stroke after carotid stenting remains unclear but may provide a valuable treatment for these patients and avoid a less radical intervention.
- It is reducing the psychological trauma and improves quality of life

## Conclusion

- Our experience indicates that high-risk patients with severe coronary artery disease, three vessel disease and poor ventricular function can be successfully treated for carotid artery stenosis
- Nevertheless, the complexity of these patients require excellent multidisciplinary teams with good understanding of these intricate diseases and excellent experience of carotid stenting and carotid protection
- A cooperative study is indispensable to help us most clinically and increase our patchy knowledge

## Need for randomized studies ? Wise? Realistic?

- The clinical question of possible benefit of combined procedures compared with staged procedures for concomitant coronary and carotid disease could best be addressed in trials where patients are randomized to the 2 strategies and the 2 carotid techniques (CEA/CAS)
- Such a prospective study would require a multi-institutional, multinational effort to achieve the appropriate sample size (approx 1500 pts per group) and therefore would be difficult to achieve
- A retrospective analysis with a rigorous and well described inclusion criterion comparing several approaches performed by the same team would also yield a lot of missing information
- However as most surgical teams use either combined or staged approach and not both ,the collection of data is very difficult

#### **Need for randomized studies ?**

 Requirement also to study the potential role of off pump coronary revascularization

#### Broad spectrum of clinical presentation

- Unstable or stable coronary insufficiency
- Symptomatic or asymptomatic carotid artery stenosis

#### Broad spectrum of therapeutic solution

- Staged : CAS then PTCA,CAS then CABG,CAS then Off pump CABG , CEA then CABG, CEA then Off pump CABG
- Combined : CAS&PTCA ,CEA&CABG, CEA &Off pump CABG

## It is probably safer than still persisting Big scars doest mean always great surgeons