

Optimale timing van Carotis Interventie & “de hoog risico patient”

GJ de Borst

Afdeling Vaatchirurgie

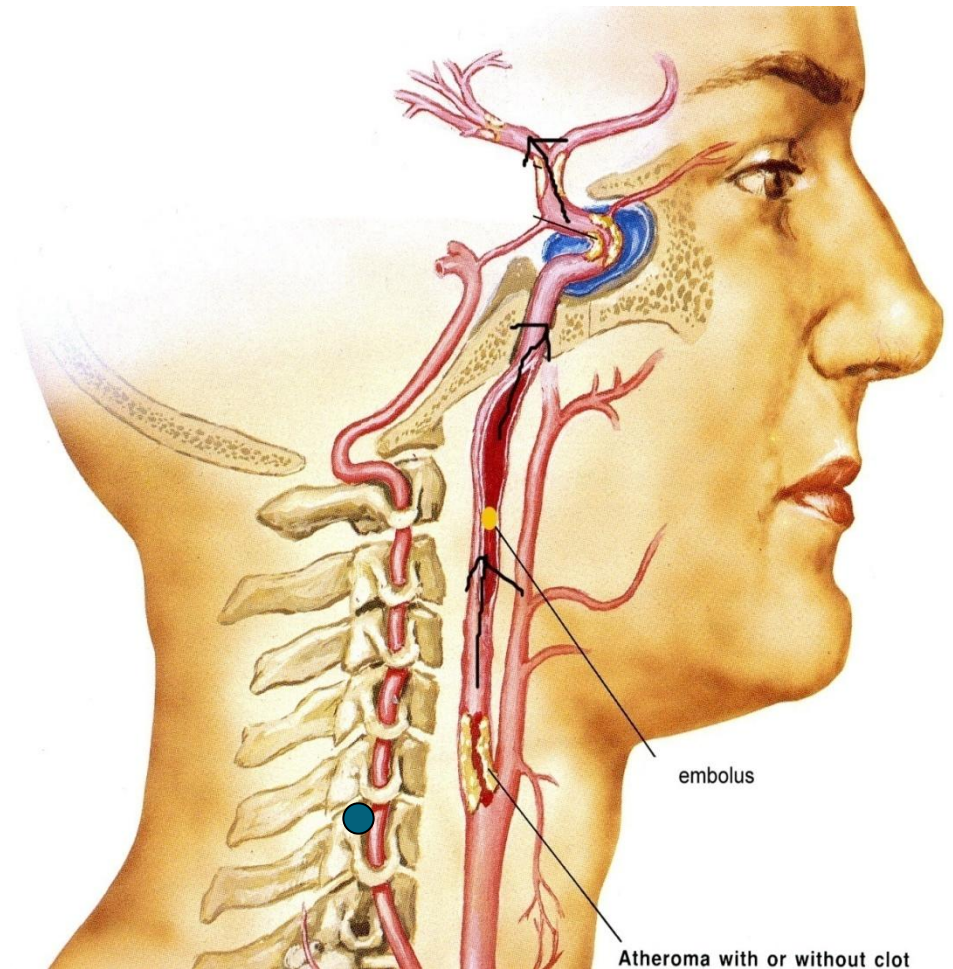


Universitair Medisch Centrum
Utrecht

Doel van carotis interventie

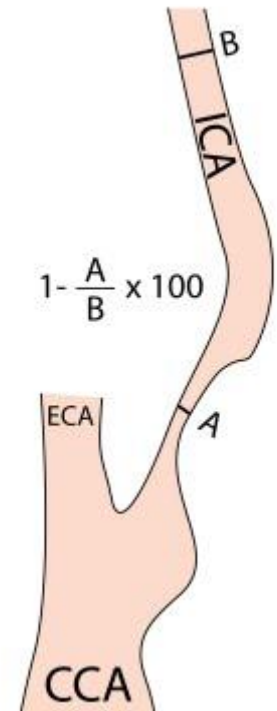
Preventie van CVA !

Niet excellente operatieve
track records !



Indications “Old school”

- Neurological symptomatology
- Degree of stenosis
 - Transient symptoms + stenosis : **>70%**
 - Non-invalidating symptoms + stenosis : **>70%**
 - Symptoms with APT/ anticoagulants : **50% - 99%**



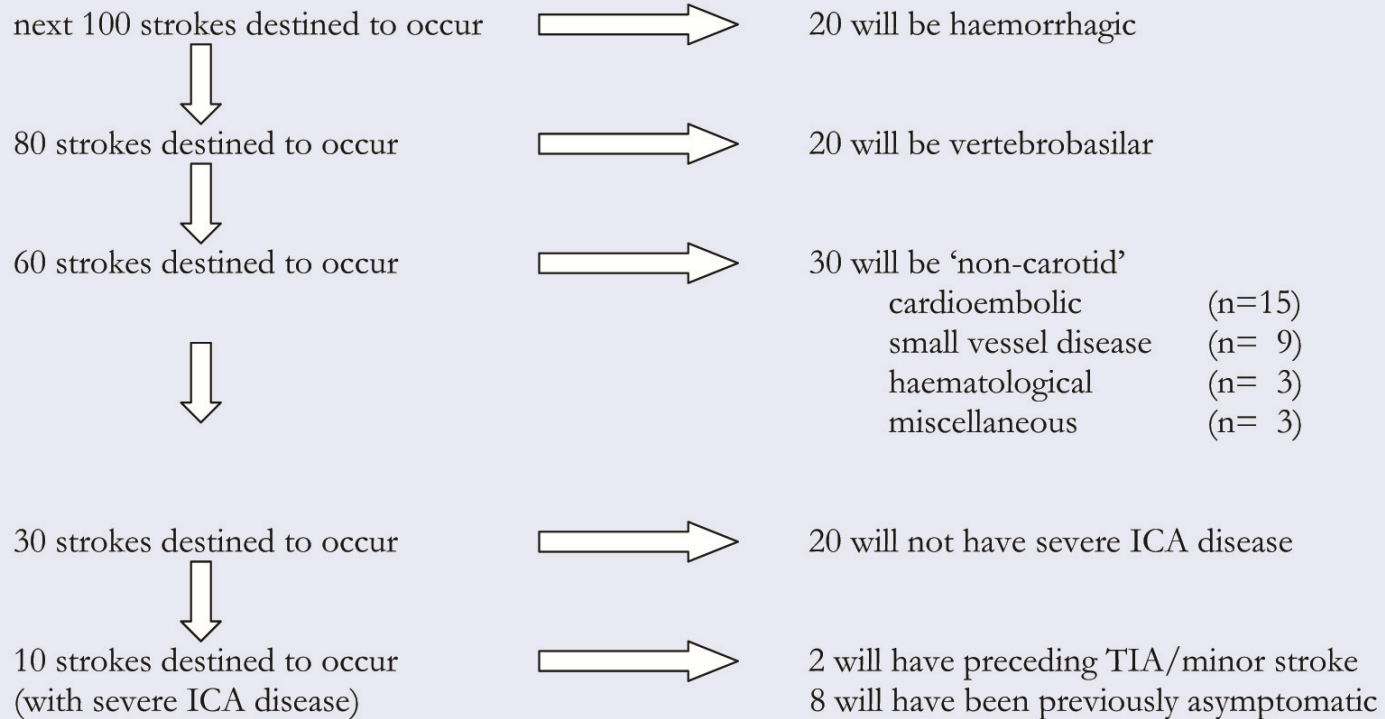






CVA preventie; rol van CEA ?

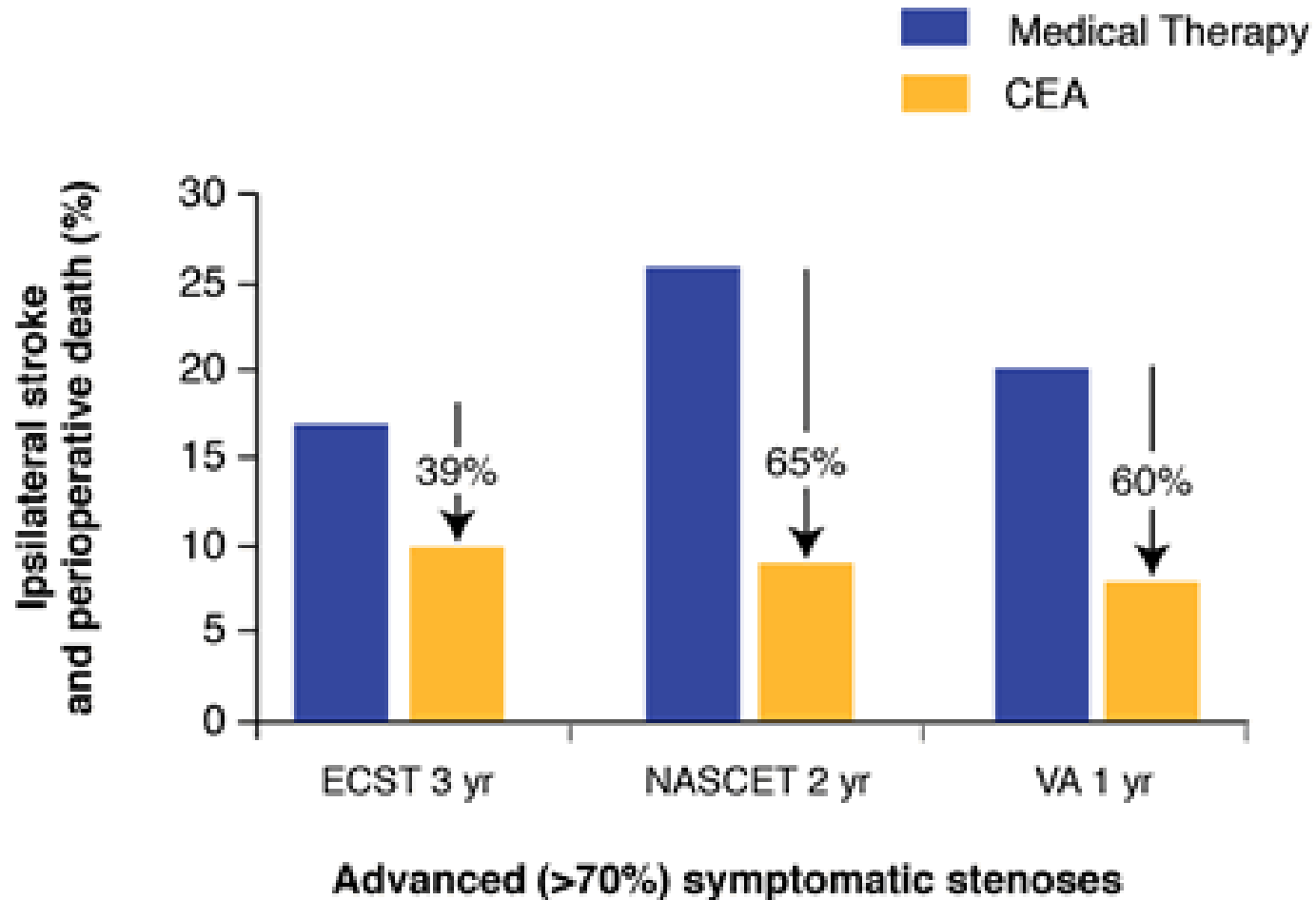
TABLE 1: HOW DOES CAROTID INTERVENTION IMPACT UPON GLOBAL STROKE PREVENTION?



“Old school”

- Risico op CVA in de eerste weken na symptomatische presentatie is waarschijnlijk niet erg hoog
- Snel en volledig herstel van symptomen gezien als teken dat snelle interventie onnodig was
- Vroege chirurgie mogelijk geassocieerd met verhoogd risico op perioperatieve complicaties
- CEA moet worden uitgesteld 6-8 weken na doorgemaakte CVA

CEA vs BMT: Benefit van CEA



Long term benefit of CEA

Any stroke at five years (including operative stroke/death)								
			five year risk					
Trial	Stenosis	Op risk	Surgery	Medical	ARR	RRR	NNT	CVA prevented per 1000 CEAs
CETC	< 30%		18.36%	15.71%	-2.6%	n/b	n/b	none at 5 years
CETC	30-49%	6.7%	22.80%	25.45%	+2.6%	10%	38	26 at 5 years
CETC	50-69%	8.4%	20.00%	27.77%	+7.8%	28%	13	78 at 5 years
CETC	70-99%	6.2%	17.13%	32.71%	+15.6%	48%	6	156 at 5 years
CETC	string	5.4%	22.40%	22.30%	-0.1%	n/b	n/b	none at 5 years

CETC data (combined ECST, NASCET and VA Study)

“Very recent” school

Carotid intervention for recently symptomatic, severe carotid stenosis should be regarded as an emergency procedure in patients who are neurologically stable, and should ideally be performed within 48 hours of a transient ischaemic attack or minor stroke.

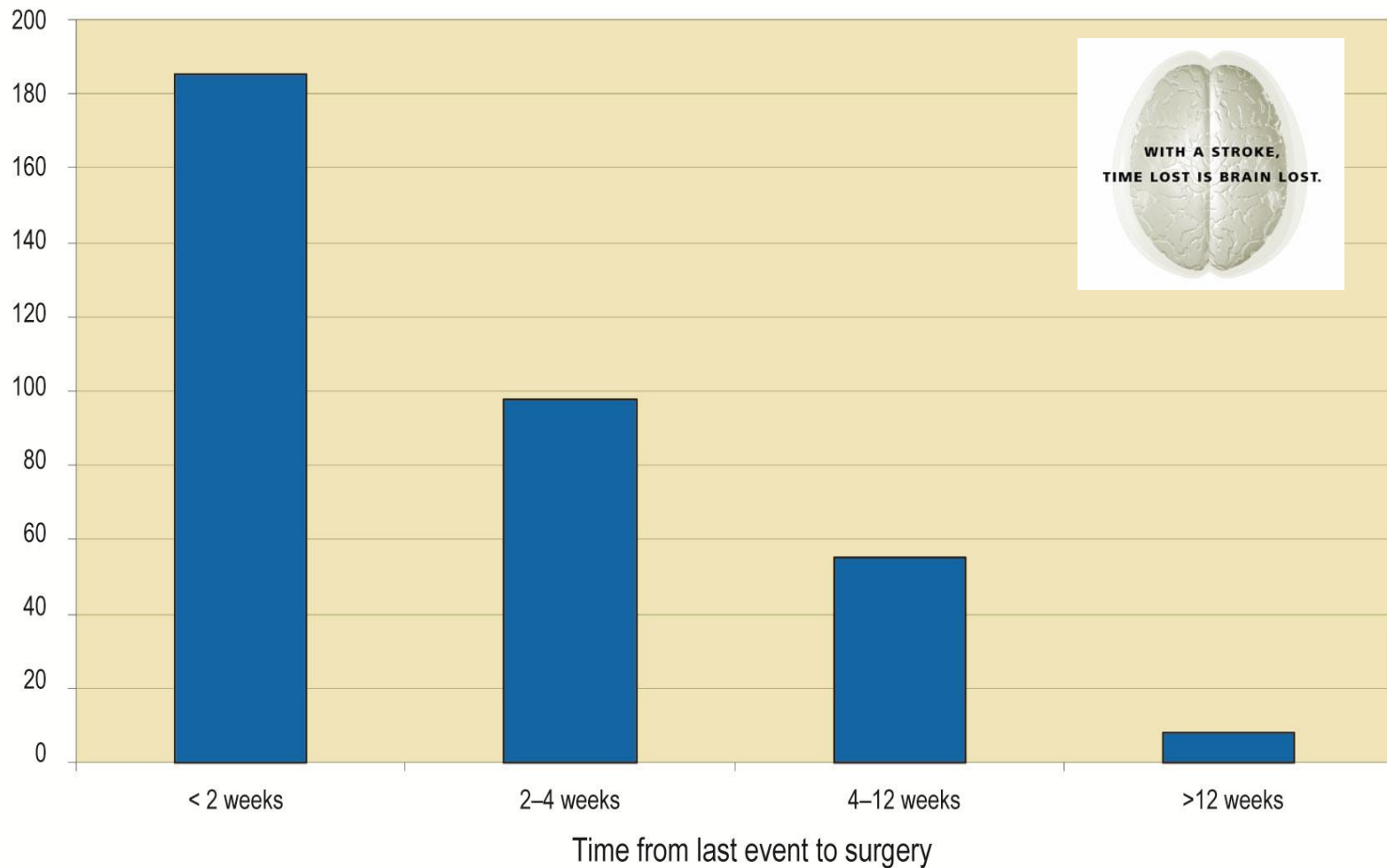
The National Stroke Registry
UK Department of Health, Dec. 2007

Waarom snel handelen ?

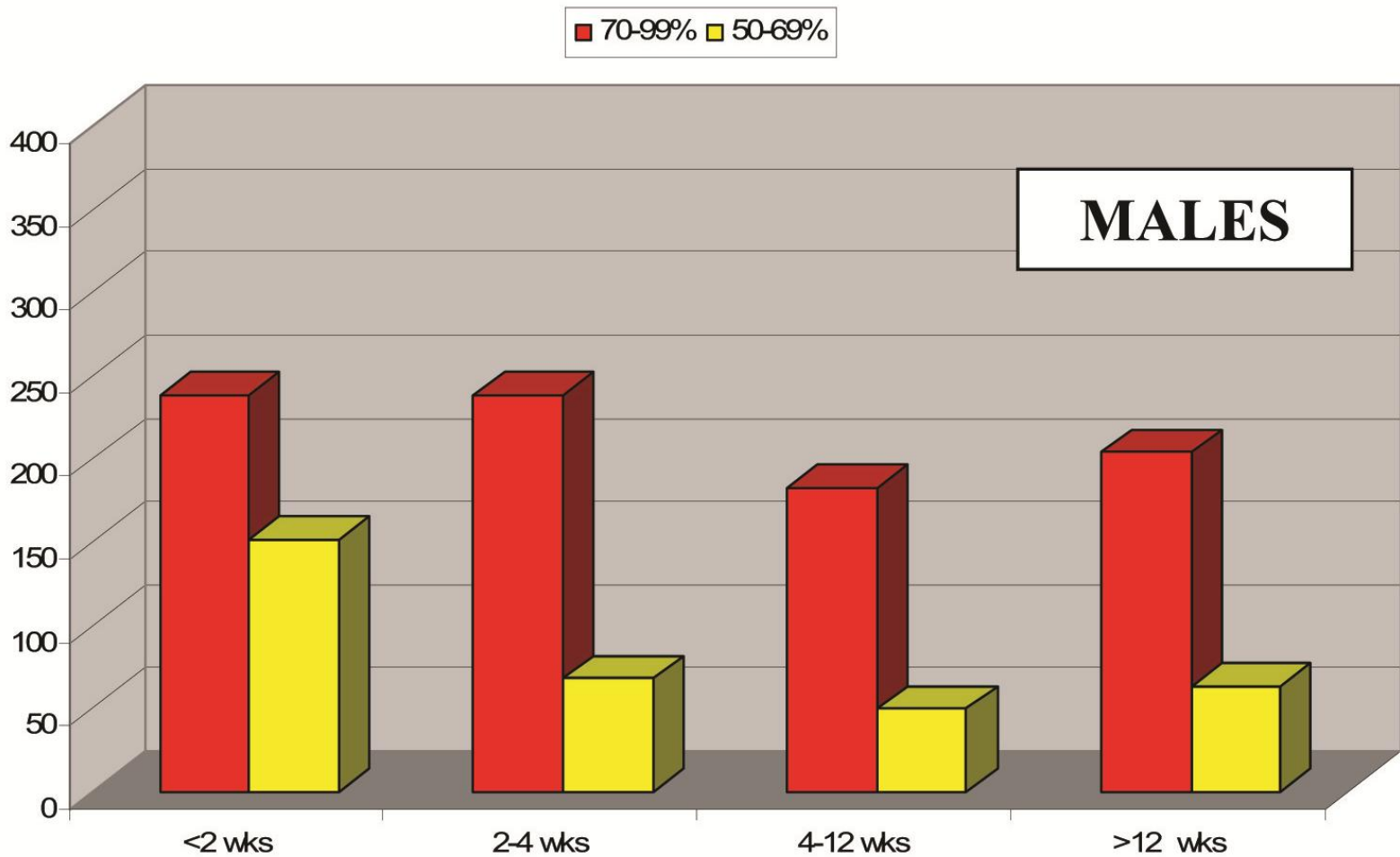


Timing van carotis chirurgie ?

Ipsi CVA / 5 y/ 1000 CEA / Sx patienten/ 50-99% stenosis (CETC re-analyse)

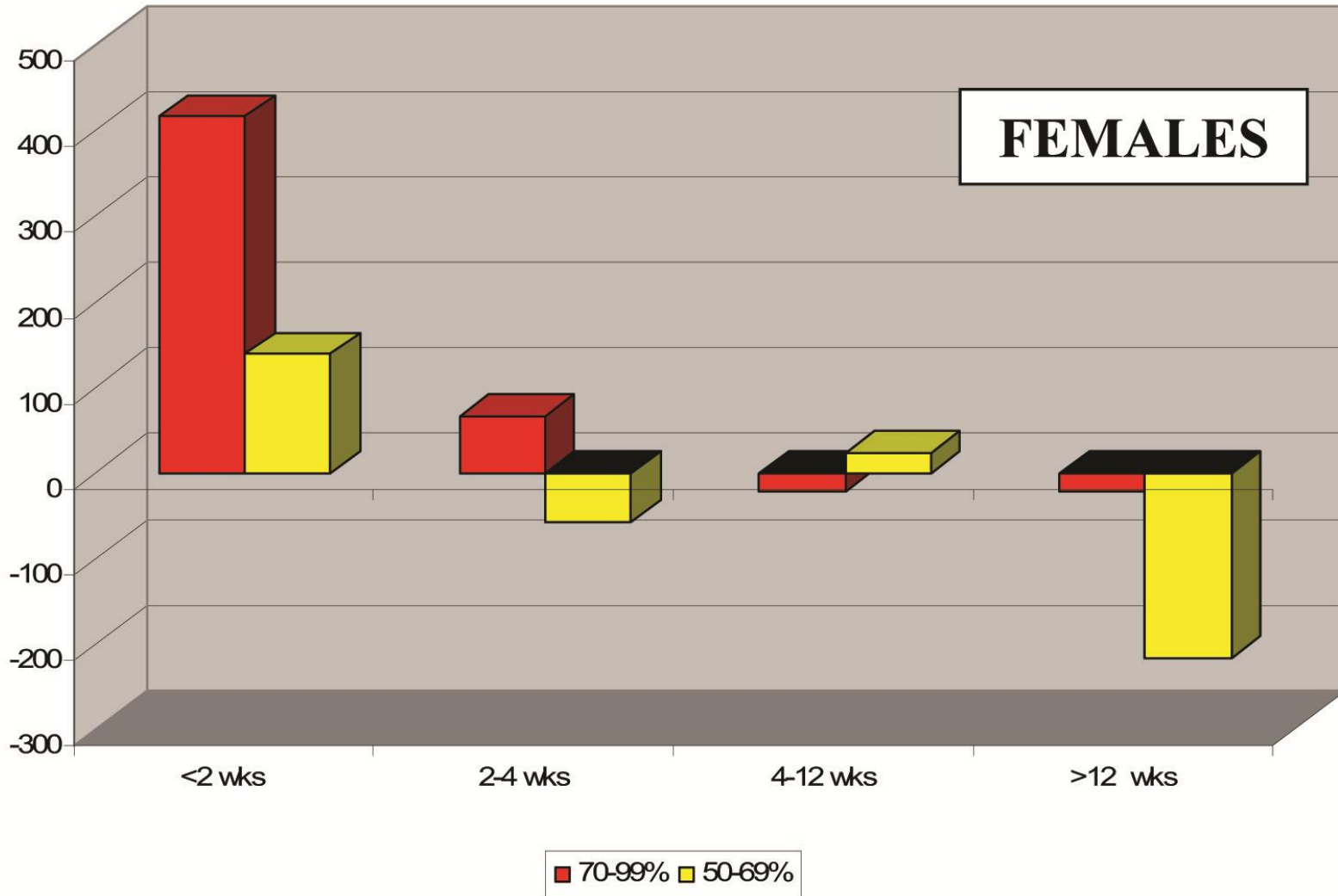


Strokes prevented per 1000 CEA at 5 years



AR Naylor The Surgeon 2007;5: 23-30

Strokes prevented per 1000 CEA at 5 years



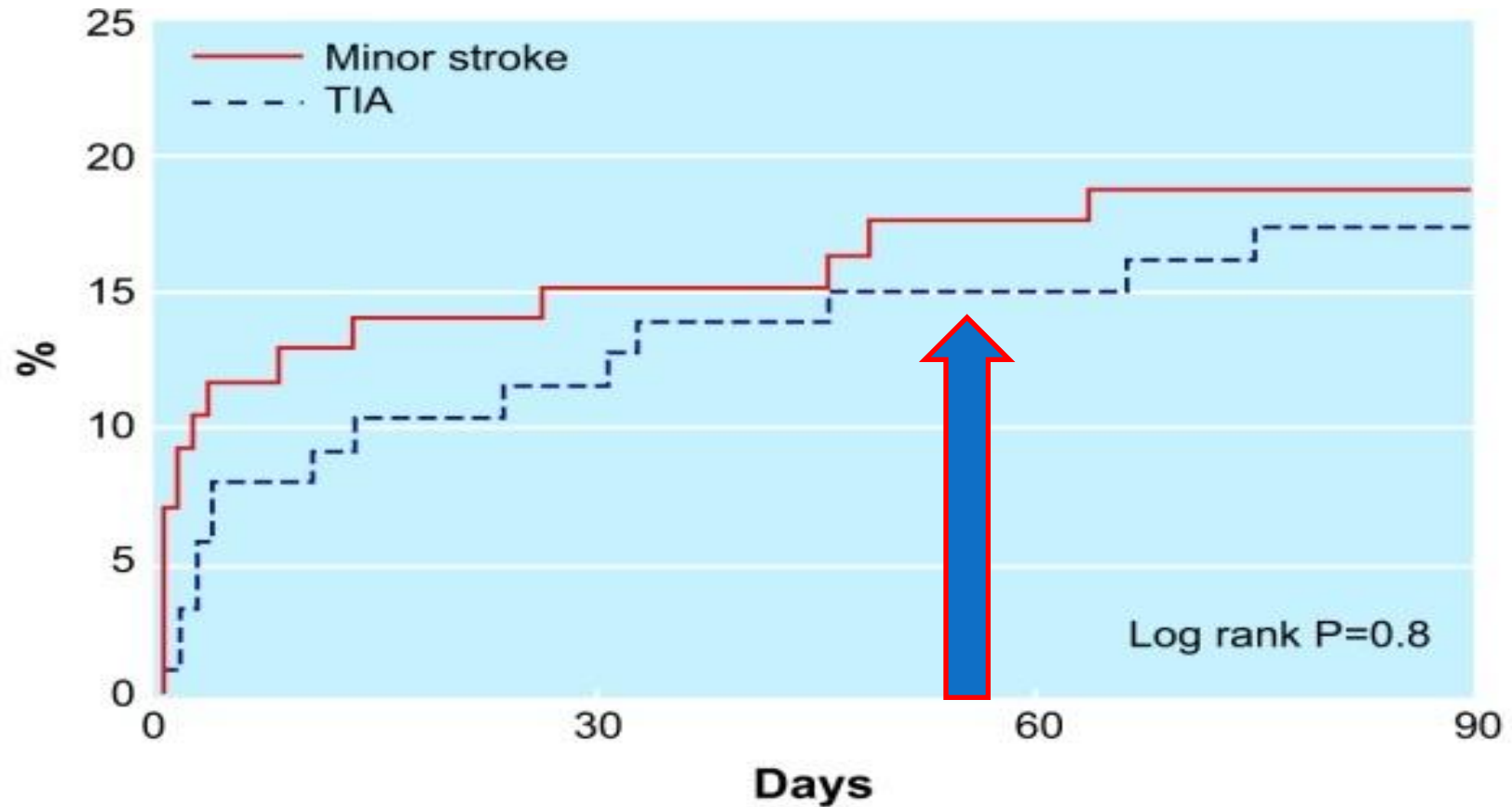
Risico op 2^e (ernstiger) infarct

TABLE 3: RISK OF STROKE AFTER TIA OR MINOR STROKE

Author	Year	5 days	7 days	30 days
Eliasziw (27)	2000	5.5%		
Johnstone (28)	2000	5.2%		
Lovett (29)	2003	5.1%	8.6%	12.0%
Coull (30)	2005		8.0%	11.5%

- “Old school” : 1 - 2^o risico op CVA na 7 dgn
2 - 4^o risico op CVA na 30 dgn
- Realiteit : Hoogste risico in eerste week 5% na 5 dgn

Cumulatief risico op CVA na doorgemaakte TIA versus minor stroke



Coull et al. BMJ 2004; 328: 326-328

Invloed van timing op uitkomsten gerandomiseerde trials

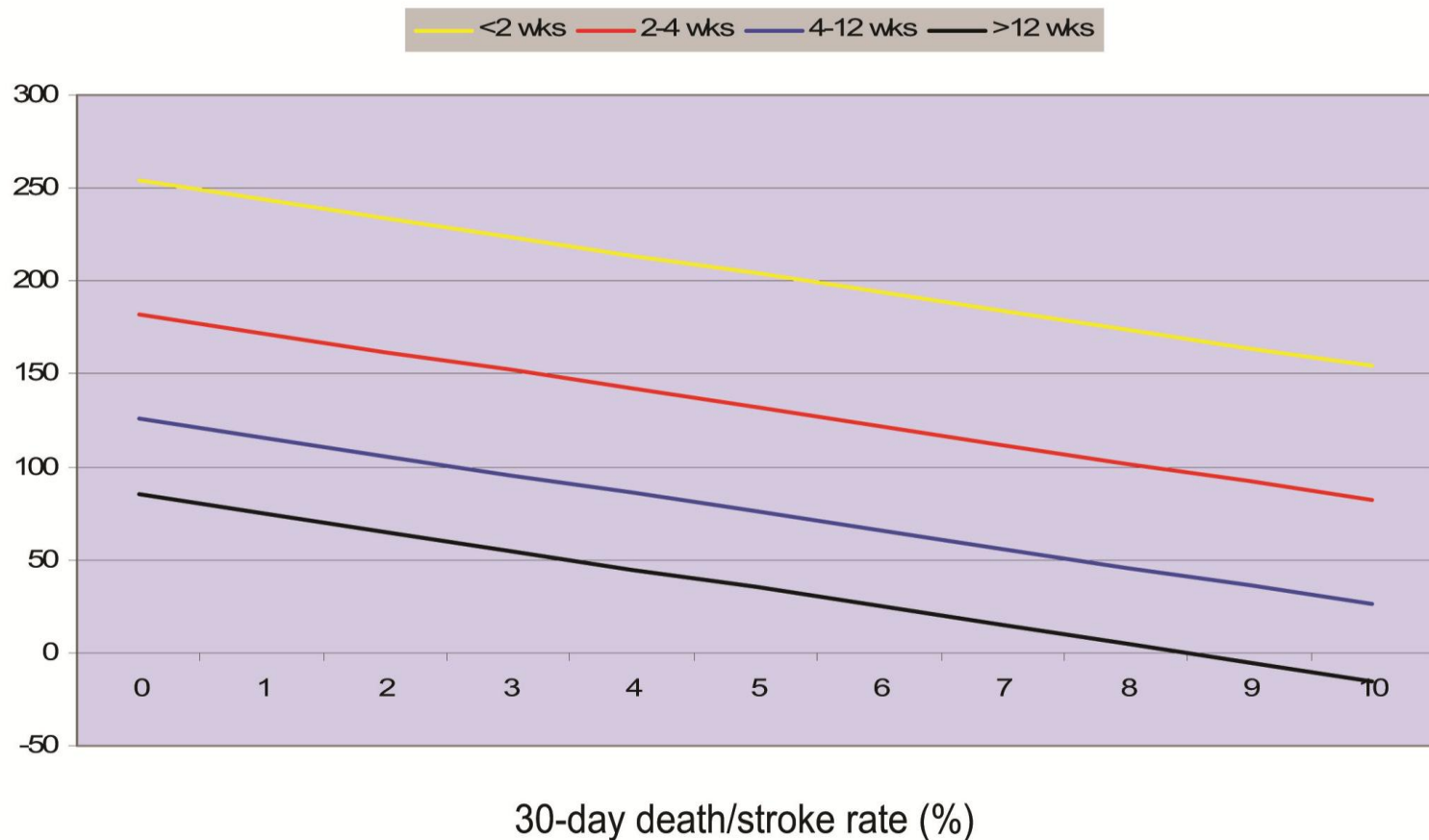
Table 4. Absolute risk reduction conferred by CEA in the 5 year cumulative risk of ipsilateral carotid territory ischaemic stroke (including the peri-operative risk) in patients with a NASCET 50–99% stenosis, stratified for delay from index event to randomisation*

Time since randomisation	50–69% stenoses			70–99% stenoses			ALL 50–99% stenoses		
	ARR	NNT	CVA/1000	ARR	NNT	CVA/1000	ARR	NNT	CVA/1000
< 2 weeks	14.8	7	148	23.0	4	230	18.5	5	185
2–4 weeks	3.3	30	33	15.9	6	159	9.8	10	98
4–12 weeks	4.0	25	40	7.9	13	79	5.5	18	55
>12 weeks	-2.9	nil	nil	7.4	14	74	0.8	125	8

CETC data herberekend naar tijd tussen event en randomisatie. Naylor EJVES 2008

Preventie van CVA/1000 CEA/5 yr

afhankelijk van 1) delay; 2) operatie risico

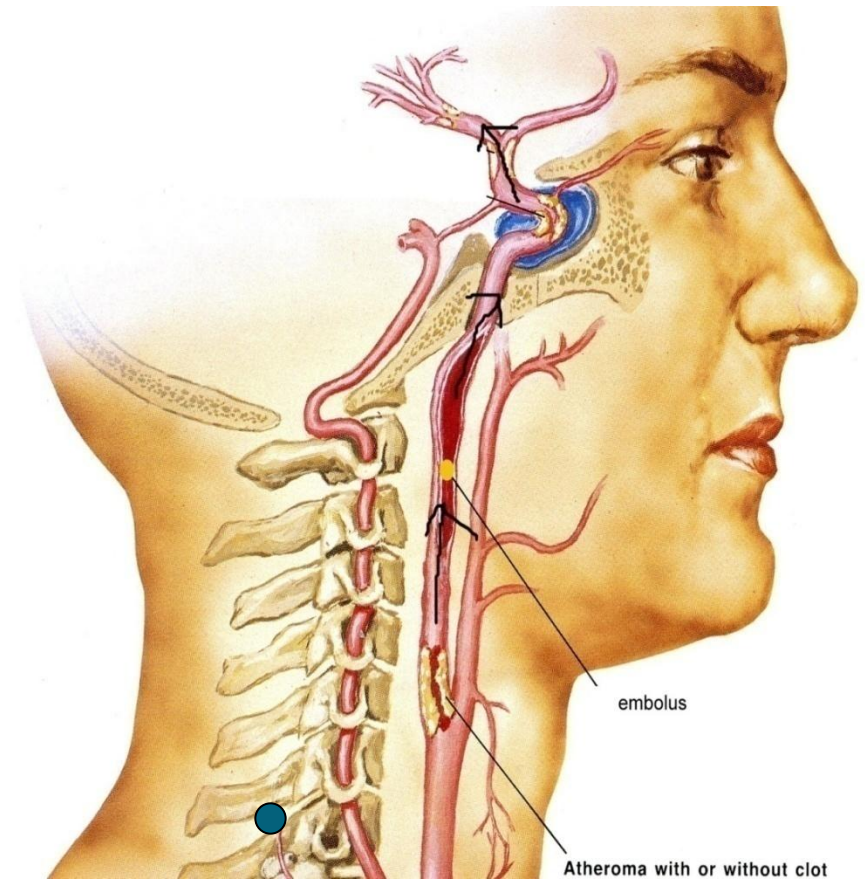


Doel van carotis interventie

Preventie van CVA !

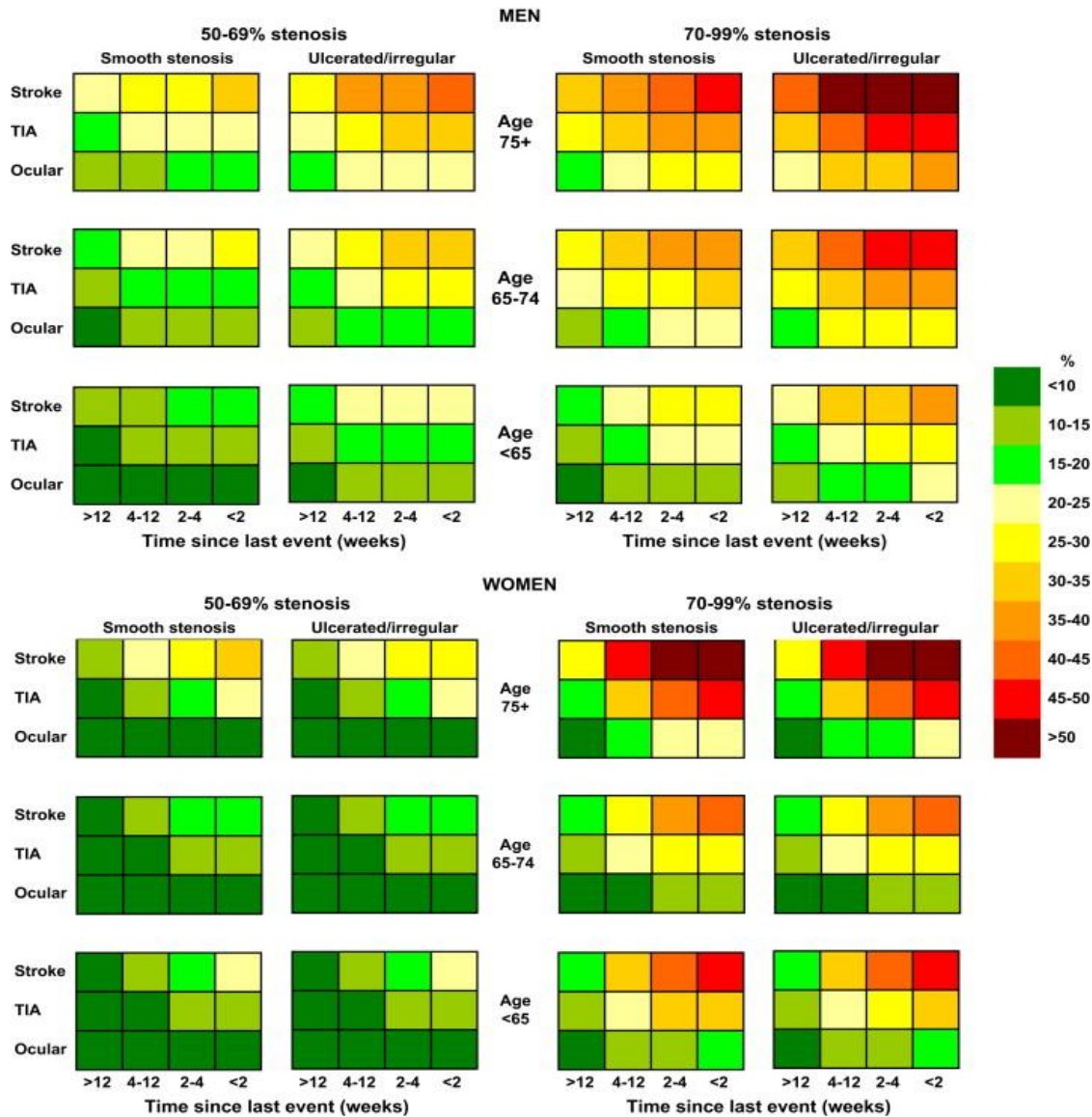
Behandel de patient met het hoogste risico op het ontwikkelen van een CVA !

Niet excellente individuele operatieve track records !



Treating the Individual ?





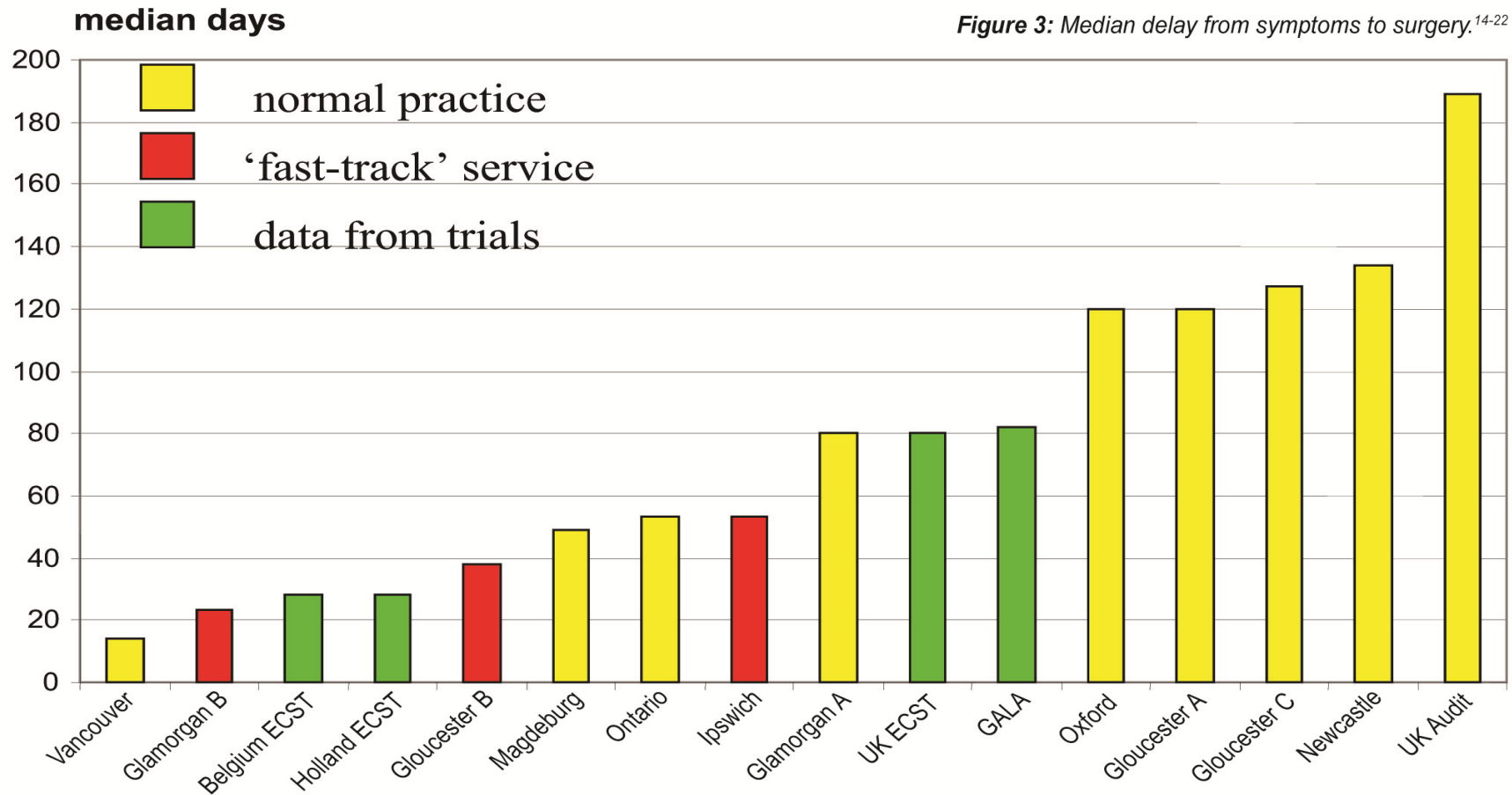
Hoe snel kunnen we handelen ?



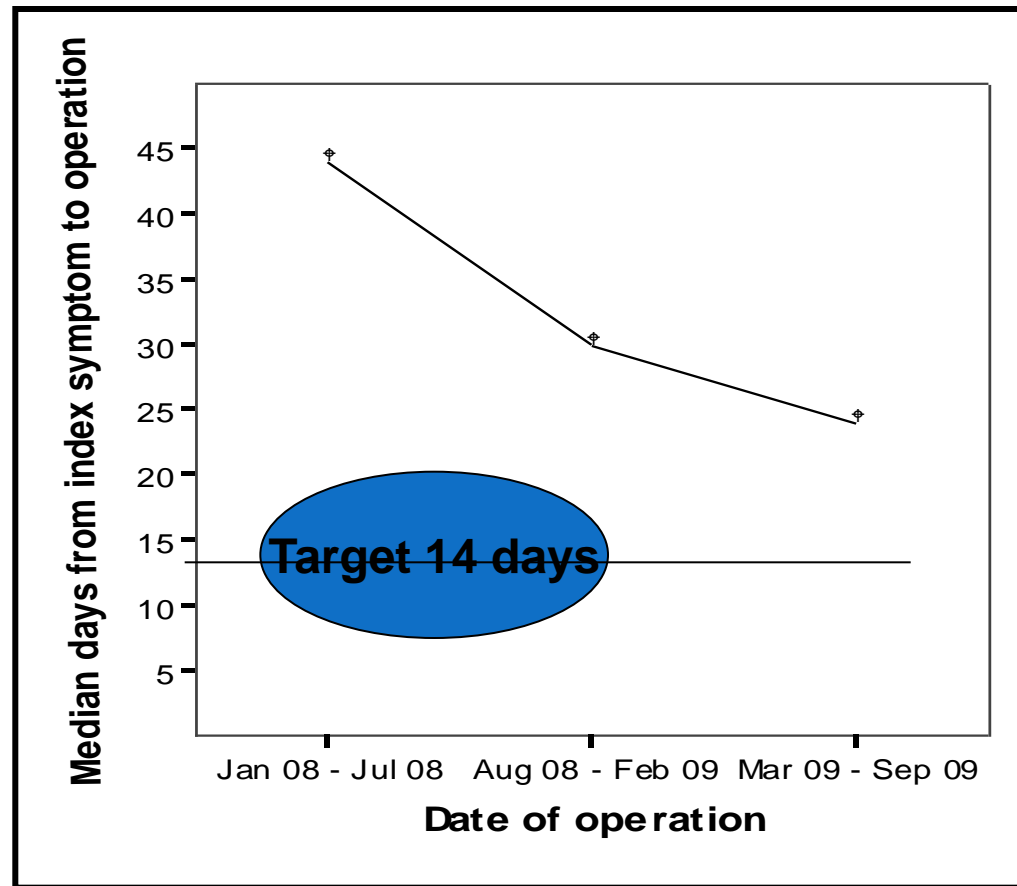
Tijd tot interventie in recente carotis trials

	CAVATAS	EVA-3S	SPACE	ICSS	CREST
Inclusion	Sx / 6 mths	Sx > 60/4m	Sx >70%	Sx >50% /12m	Sx/6 mths
Time from <u>randomisation</u> to treatment	CAS 20 (8-32) CEA 27 (13-41)	NR	CAS 4(2-6) CEA 5(2-7)	CAS 9(5-17) < 14d: 70% CEA 11 (5-24) < 14d: 57%	CAS 4 CEA 5
Time from <u>qualifying event</u> to treatment	NA	< 14d CAS 20% < 14d CEA 16%	NR	CAS 35 (15-82) < 14d: 25% CEA 40(18-87) < 14d: 18%	CAS 36.3 +- 39.6 CEA 40.9 +- 43

Realiteit



Tijd tussen index symptoom en operatie

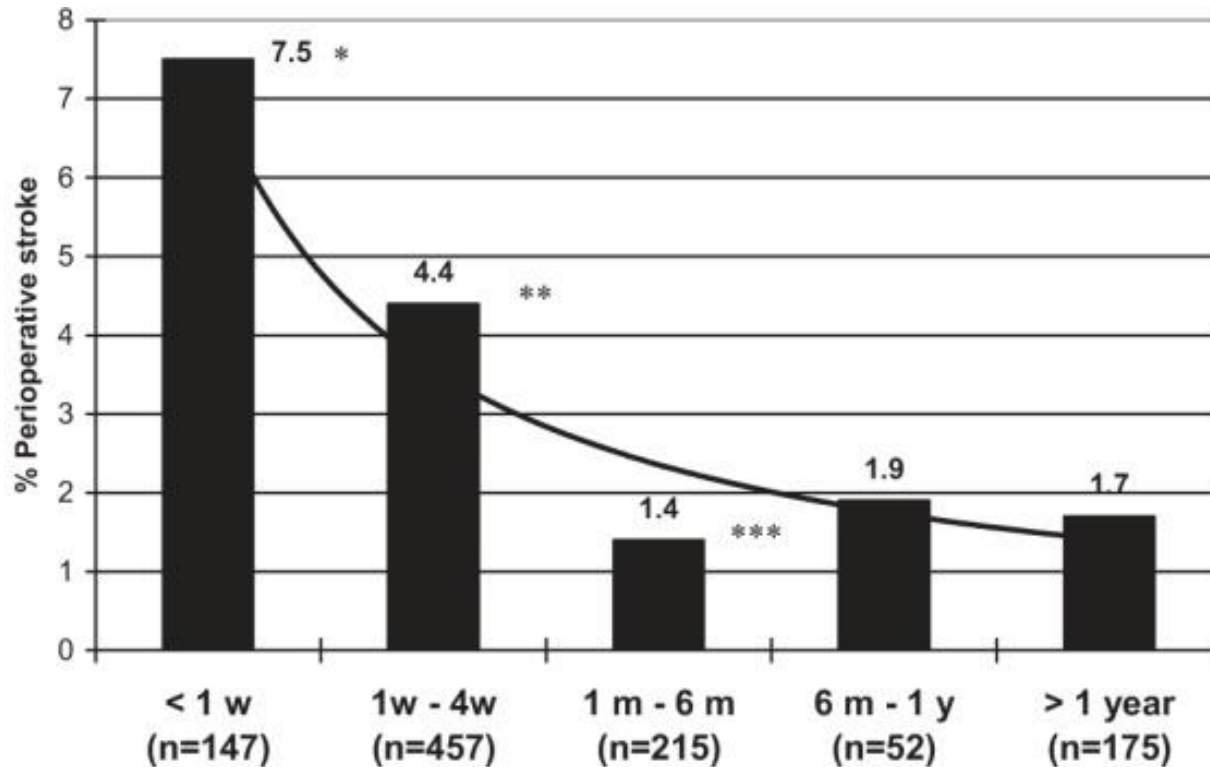


- Halliday A. Steering Committee, UK CEA Audit period 2008 and 2009, presented at *CX Symposium, April 10th 2010*

Is vroege CEA geassocieerd met slechtere perioperatieve resultaten ?



Timing en risico op perioperatief CVA



Rockman CB. J Vasc Surg 2006; 44: 480-7.

Subgroepen met zeer hoog risico op perioperatief CVA

1. Recente carotis occlusie
2. Rankin score ≥ 3
3. Ischaemisch infarct $> 2/3$ van ACM territory
4. Geen neurologisch “plateau”
5. Fluctuerend bewustzijns niveau
6. ICH op CT scan

Conclusies

- Symptomatische Carotis stenose = “urgent”
- Individuele therapy strategie
- Logistiek ?
- Meer perioperatieve CVAs om meer CVAs te voorkomen ?



Time changes everything ...or not ?



1910 - 1915



1915 - 1925



1925 - 1946



1946 - 1972



1972 - 1999

Exclusion /high risk criteria carotid trials

Anatomic criteria	Medical co-morbidities
Lesion at C2 or higher	Age > 80 years
Lesion below clavicle	Class III/IV congestive HF
Prior radical neck surgery or radiation	Class III/IV angina pectoris
Contralateral carotid occlusion	Left main/ >2 vessel coronary disease
Prior ipsilateral CEA	Urgent heart surgery
Contralateral laryngeal nerve palsy	LV ejection fraction < 30%
Tracheostomy	Recent < 30d myocard infarction
	Severe chronic lung disease
	Severe renal disease

Indications

- Neurological symptomatology
- Degree of stenosis
- Timing
- Medical co-morbidities
- Vascular and local anatomical features
- Carotid plaque morphology

High risk period/patient/procedure?

Exclusion Criteria for Major Carotid Stenosis Trials

	NASCET	ACAS	SAPPHIRE
Age	≥80	<40 or ≥80	>80
Anatomy	<30% stenosis	<60% stenosis	-
	Ipsilateral occlusion	Ipsilateral occlusion	Contralateral occlusion
	Tandem lesion	Tandem lesion	-
	Unsuitable for CEA	Unsuitable for CEA	-
History	Stroke in evolution	Stroke in evolution	Acute stroke ≤48 hr
	Prior ipsilateral CEA	Prior ipsilateral CEA	Prior ipsilateral CEA
	Recent contralateral CEA	-	Recent contralateral CEA
	Prior CVA with major deficit	Prior CVA with major deficit	
	Major surgery <1 month	Major surgery <1 month	Synchronous operation
	Atrial fibrillation	Atrial fibrillation	-
	Valvular disease	Valvular disease	-
	Renal failure	Renal failure	-
	Pulmonary failure	Pulmonary failure	-
	Heart failure	Heart failure	Heart failure
	Liver failure	Liver failure	-
	Unstable angina	Unstable angina	Unstable angina
	MI < 6 months	-	MI < 4 weeks
	-	-	Positive stress test
	-	Neck radiation	Neck radiation
	-	-	Intracranial pathology
	-	-	Contralateral laryngeal nerve palsy

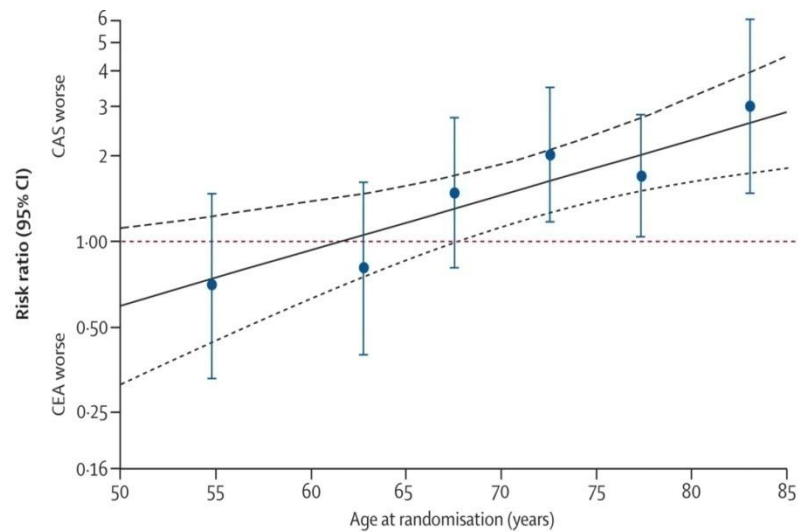
Abbreviations: NASCET, North American Symptomatic Carotid Endarterectomy Trial; ACAS, Asymptomatic Carotid Atherosclerosis; CEA, carotid endarterectomy; CVA, cerebrovascular accident; MI, myocardial infarction.

ESVS guidelines: Treatment options according to vascular and local anatomical features:

- CAS is indicated in contralateral laryngeal nerve palsy, previous radical neck dissection, cervical irradiation, prior CEA (restenosis), high bifurcation or intracranial extension of the carotid lesion... provided that the per-interventional stroke or death rate is acceptable... [C]
- CAS is not advisable in patients with extensive aortic and supra-aortic vessel plaques, calcification and tortuosity, unless performed in high volume centres with documented low peri-procedural stroke and death rate [C].

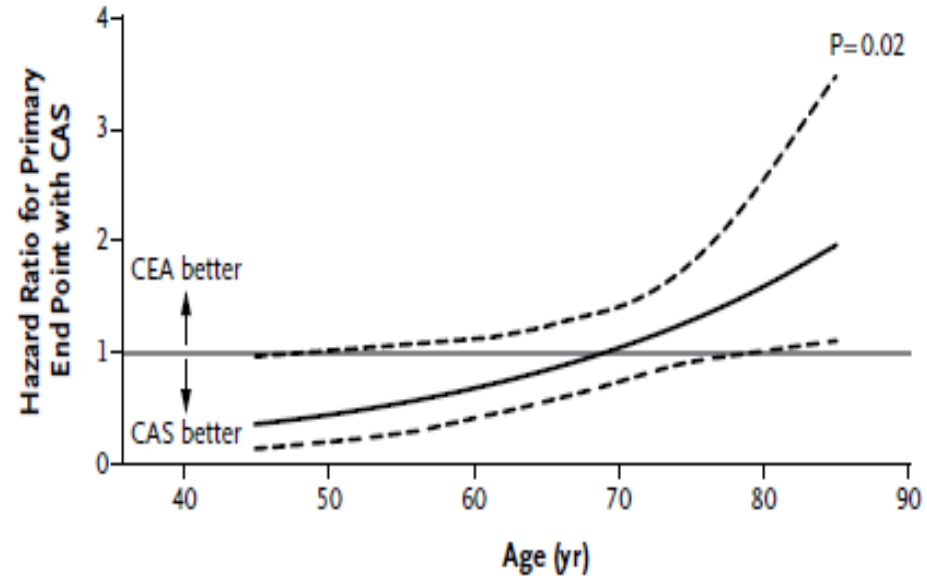
High risk Age ?

Meta-analysis EVA-3S,SPACE,ICSS



Bonati et al Lancet. 2010

Interim analysis CREST



Brott. et al. N Engl J Med. 2010
Voeks et al. Stroke 2011 (online only)

Previous cervical irradiation: < 30 days

Fokkema Stroke 2012

	N	Sx (%)	Stroke (n)	TIA (n)	CNP t/p (n)
CAS	315	64	8*	4	NR
CEA	145	65	1	2	13/1

*non-disabling (3), disabling, fatal (1), CNP t/p: cranial nerve palsy; temporary (< 30 days) or permanent .



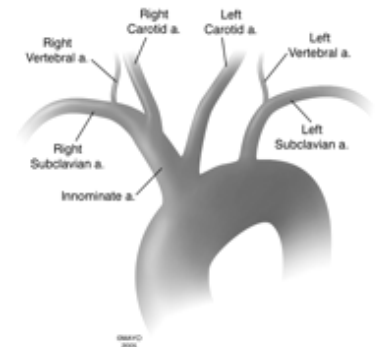
	CAS	CEA	Significance
Risk for CVE % (95% CI)	2.4 (0 - 6)*	0.8 (1 - 4)	p = 0.75 (-0.12 - 0.09)**
Risk for CNP % (95% CI)	NA	6.2 (1 - 15)	NA

CVE: Cerebrovasculair event (TIA + Stroke),

“High risk CAS” I: anatomical considerations

Predictors of increased Risk for ipsilateral stroke :

- Calcifications arcus aortae
- Concentric calcification carotid bifurcation
- Tortuosity of the carotid artery
(≥ 2 90° bends within a 5 cm segment
spanning a lesion)



“High risk CAS” II: anatomical considerations

“Delphi Carotid Stenting Consensus panel”

Scoring system for anatomic suitability: to grade *expected* difficulty

- Tortuosity
- Calcification
- Type III arch
- Arch atheroma

Regression Model With Interactions-Predicted Mean Level of Difficulty of CAS (SD)

	Regression Model With Interactions-Predicted Mean Level of Difficulty of CAS (SD)																	
	No arch disease				Arch atheroma				Diseased CCA									
	Normal access		Angulated target vessel		ECA problem		Angulated distal ICA		Diseased CCA		Normal access		Angulated target vessel		ECA problem		Angulated distal ICA	
Normal arch	Standard	3.4 (0.4)	3.3 (1.2)	3.3 (1.2)	4.3 (1.2)	3.7 (1.3)	4.3 (1.4)	4.3 (1.9)	5.1 (1.7)	5.3 (1.8)	6.3 (1.7)	5.0 (2.2)	5.9 (1.9)					
	Pinhole	3.6 (1.2)	3.8 (1.2)	3.9 (0.9)	4.3 (1.0)	4.1 (1.7)	5.0 (1.3)	4.7 (1.0)	5.6 (1.5)	5.8 (1.6)	6.6 (1.6)	5.5 (2.2)	6.4 (1.8)					
	stennis																	
Bifurc arch	Standard	3.6 (1.4)	4.3 (1.2)	4.3 (1.6)	5.5 (1.1)	4.0 (1.4)	5.7 (1.0)	5.0 (1.9)	5.9 (1.3)	6.0 (1.4)	6.9 (1.3)	5.8 (1.8)	6.7 (1.6)					
	Pinhole	4.1 (1.2)	5.0 (1.3)	5.1 (1.6)	6.0 (0.7)	5.3 (1.4)	6.2 (1.2)	5.5 (1.5)	6.3 (1.4)	6.5 (1.4)	7.4 (0.9)	6.3 (1.6)	7.1 (1.0)					
	stennis																	
Type III arch	Standard	4.0 (1.6)	5.5 (1.0)	5.7 (1.3)	6.5 (1.2)	5.9 (1.4)	6.7 (0.9)	6.0 (1.4)	6.8 (1.2)	7.0 (0.9)	7.8 (0.9)	6.9 (1.6)	7.9 (1.1)					
	Pinhole	5.1 (1.3)	6.0 (0.9)	6.1 (1.4)	7.3 (0.2)	6.3 (1.4)	7.2 (0.2)	6.4 (1.6)	7.5 (0.9)	7.4 (1.1)	8.5 (0.9)	7.2 (1.2)	8.1 (0.9)					
	stennis																	
Bifurc arch & Type III arch	Standard	5.5 (1.4)	6.3 (1.2)	6.5 (1.4)	7.1 (1.1)	6.7 (1.4)	7.6 (1.1)	6.4 (1.3)	7.5 (1.3)	7.3 (1.1)	8.5 (0.9)	7.5 (1.2)	8.4 (0.9)					
	Pinhole	6.0 (1.4)	6.8 (1.3)	7.0 (1.5)	7.8 (0.9)	7.2 (1.5)	8.0 (0.9)	6.8 (1.7)	7.7 (1.3)	7.9 (1.1)	9.0 (0.9)	7.6 (1.2)	8.5 (0.9)					
	stennis																	

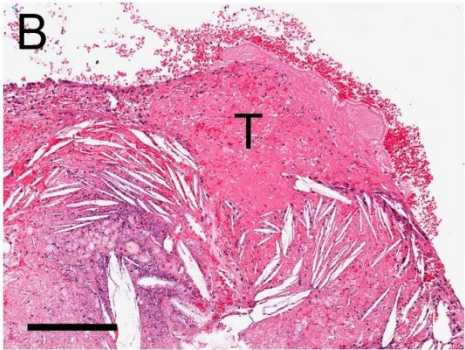
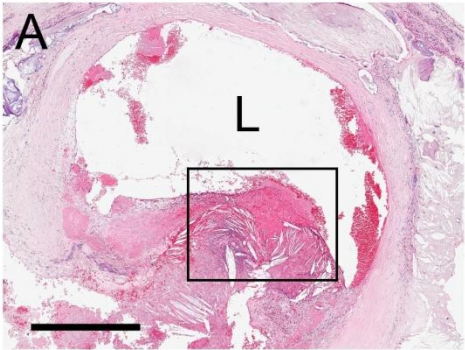
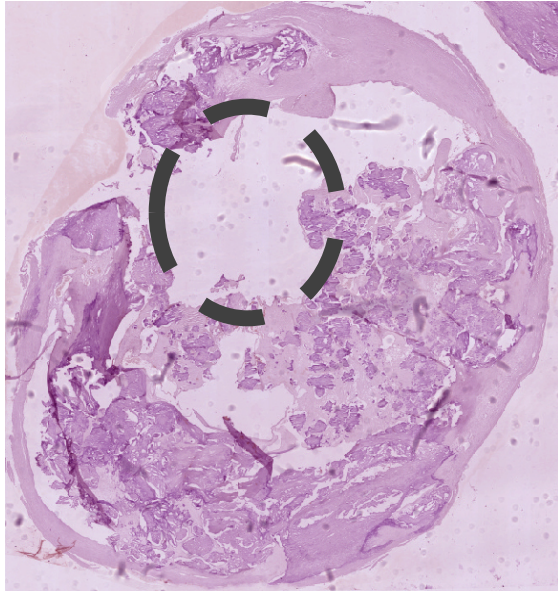
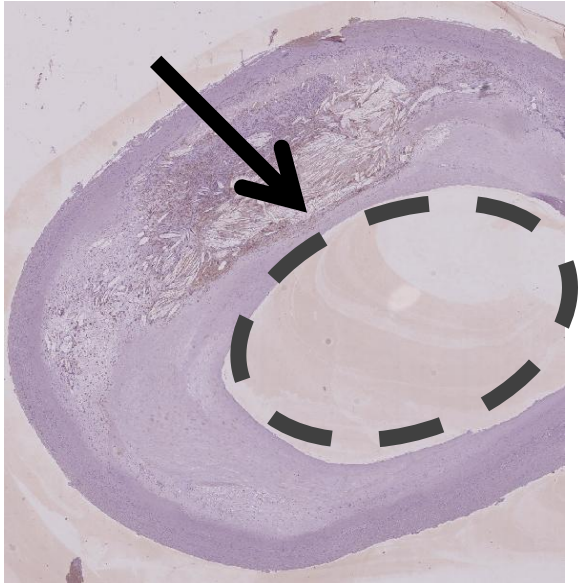
Legend: ≤4.9 (Green), 5.0-5.9 (Yellow), 6.0-6.9 (Orange), ≥7.0 (Red)

Predicted mean level of difficulty for CAS in each specified combination anatomy from the regression model (with interactions). Standard deviations are given in parentheses. The mean cutting score differentiating a “yes” response from a “no” response across the panelists was 5 with a mean score of 7 for a “no” response and a mean score of 4 for a “yes” response. The scores in Table 4 were therefore presented as traffic light colors; red for particularly difficult anatomy, a broad amber band (pale and dark allowing for the minor degree of uncertainty amongst panelists) representing moderate difficulty and green representing lesser difficulty.

Indications

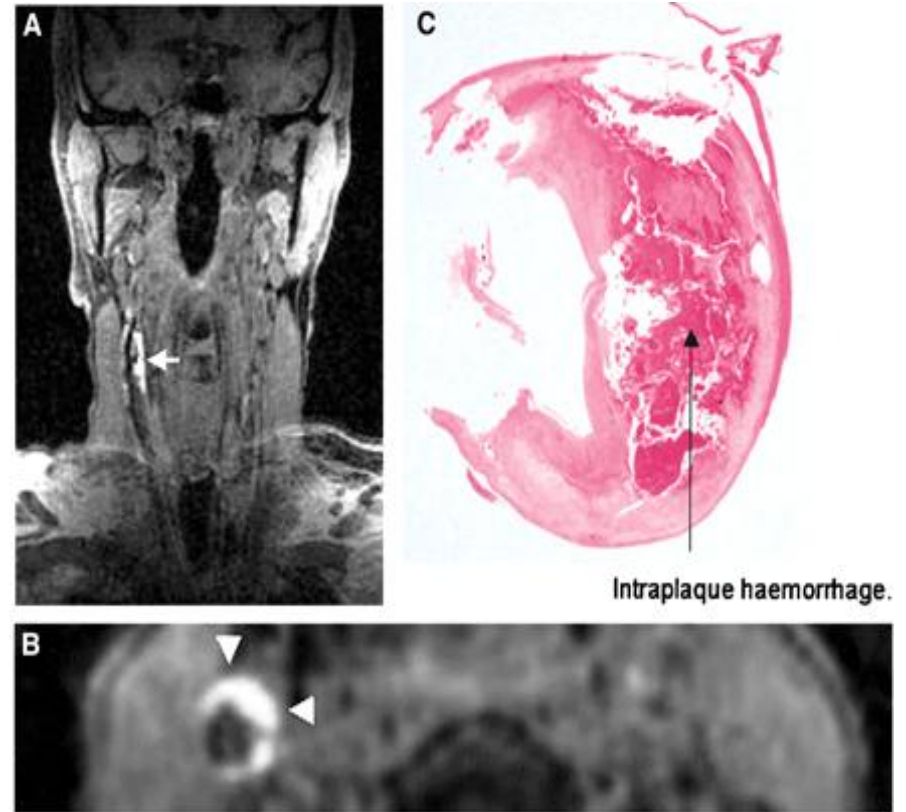
- Neurological symptomatology
- Degree of stenosis
- Timing
- Medical co-morbidities
- Vascular and local anatomical features
- Carotid plaque morphology

Plaque compositie & pitfalls CAS



Plaque imaging

- Echo lucency
- CTA (calcium)
- MR (fibrous cap ?/intra-plaque haemorrhage/thrombus)
- FDG PET
- OCT



Conclusions

- Symptomatic status and degree of stenosis !
- Rapid treatment of symptomatic patients
- Clinical and anatomic characteristics of the individual patients dictate which of treatment options should be chosen.
- CEA remains the gold standard for carotid revascularisation. In subgroups, there will be a complementary role for CEA and CAS

