Sténoses carotides: chirurgie, stenting ou traitement médical seul?

Pr. JL Mas

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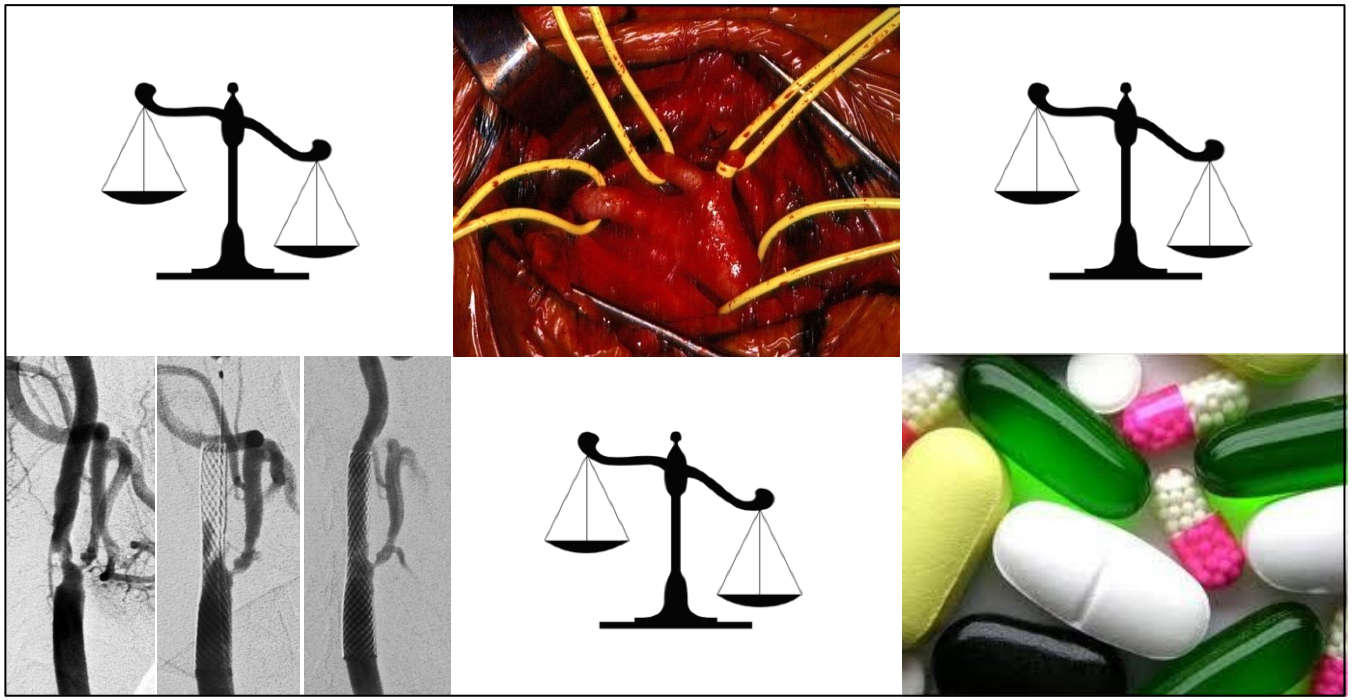


Eur J Vasc Endovasc Surg (2011) 41, 150–152

EDITORIAL

Just When We Thought We Knew All the Answers, Someone Changed the Questions!

AR Naylor

"The purpose of art is to lay bare the questions that have been hidden by the answers"

James Baldwin (1924-1987)

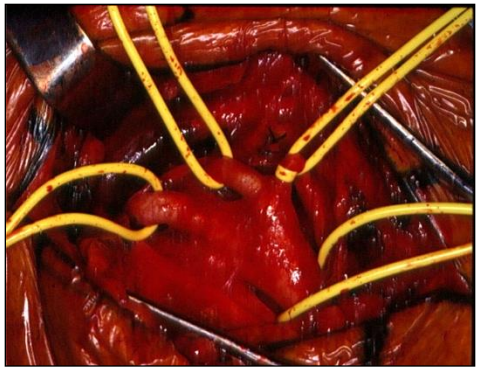
Cas 1

- Monsieur N., 65 ans, consulte pour la survenue soudaine d'une faiblesse de la main gauche et d'une asymétrie faciale, pendant 1h 30mn
- Facteurs de risque vasculaire: HTA non traitée, 1 paquet de cigarettes par jour, alcool: 5 verres standards par jour
- IRM avec séquence de diffusion: petite lésion ischémique correspondant à la clinique
- ED TSA et ARM : sténose >70% NASCET ACI droite. Plaque non sténosante de l'ACI gauche.
- ECG, échographie cardiaque: pas de cardiopathie emboligène
- PA 150/90 mm Hg à plusieurs reprises
- Glycémie à jeun normale, LDL cholestérol 1,2 g/L

Questions

- Quel traitement proposez-vous ?
  - Chirurgie carotide
  - Angioplastie carotide
  - Traitement médical seul

- Si vous proposez une revascularisation, dans quel délai pensez-vous qu'il doit être réalisé?
  - Le plus tôt possible, < 2 semaines
  - Environ 1 mois après l'infarctus
  - Le délai n'a pas une grande importance



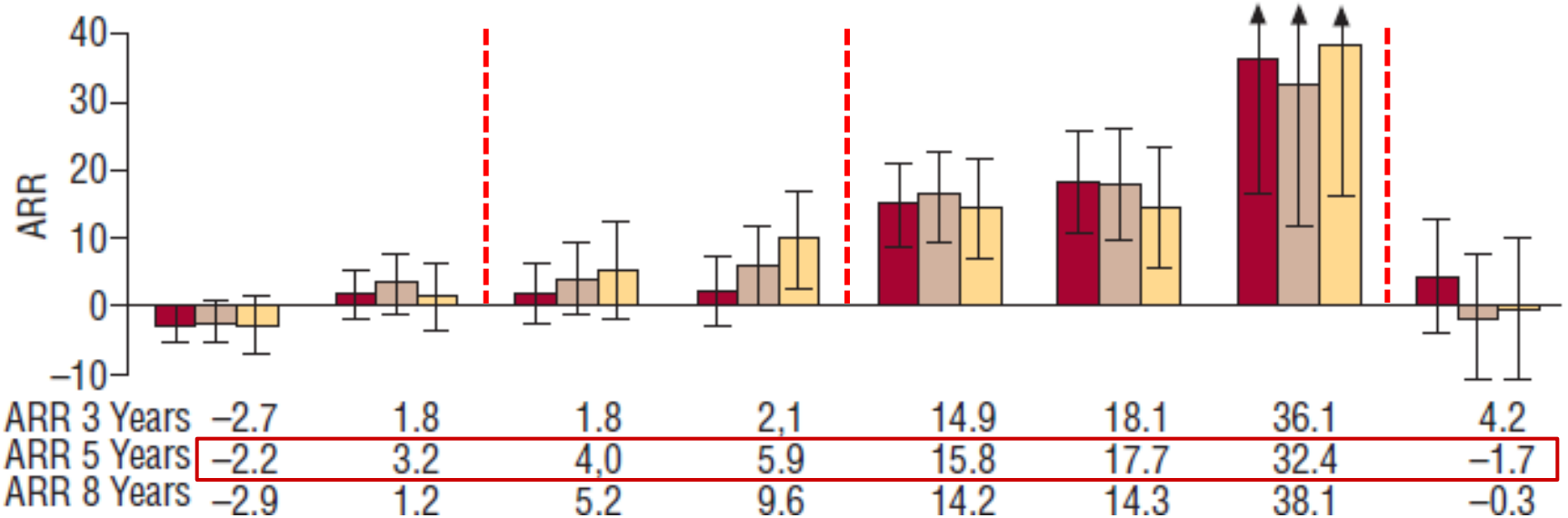
Sténose carotide symptomatique

Chirurgie carotide vs. Traitement médical seul

Rothwell et al, Lancet 2003

Meta-analysis of individual patients' data from ECST, NASCET, and VA309, n = 6092 patients

Ipsilateral ischemic stroke and any operative stroke or death



ARR 3 Years	–2.7	1.8	1.8	2,1	14.9	18.1	36.1	4.2
ARR 5 Years	–2.2	3.2	4,0	5.9	15.8	17.7	32.4	–1.7
ARR 8 Years	–2.9	1.2	5.2	9.6	14.2	14.3	38.1	–0.3
Stenosis*	**<30%**	**30-49%**	**50-59%**	**60-69%**	**70-79%**	**80-89%**	**90-99%**	**Near Occl.**

* measured according to the NASCET method

Sténose carotide symptomatique

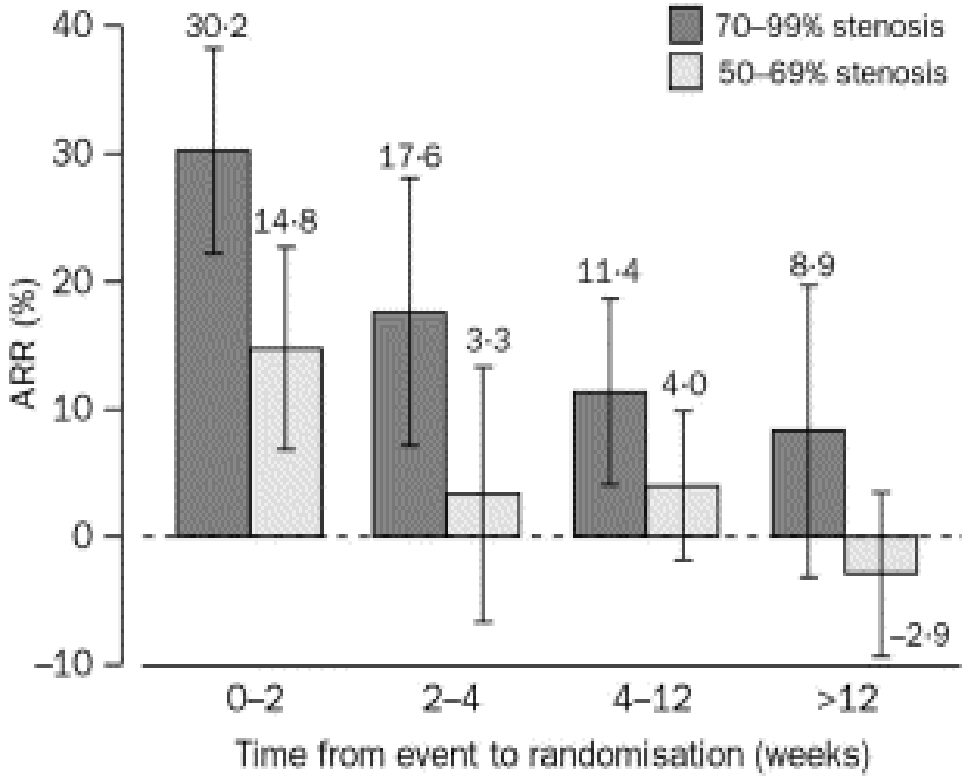
Chirurgie carotide vs. Traitement médical seul

Rothwell et al, Lancet 2004

Pooled analysis from ECST and NASCET, 5893 patients

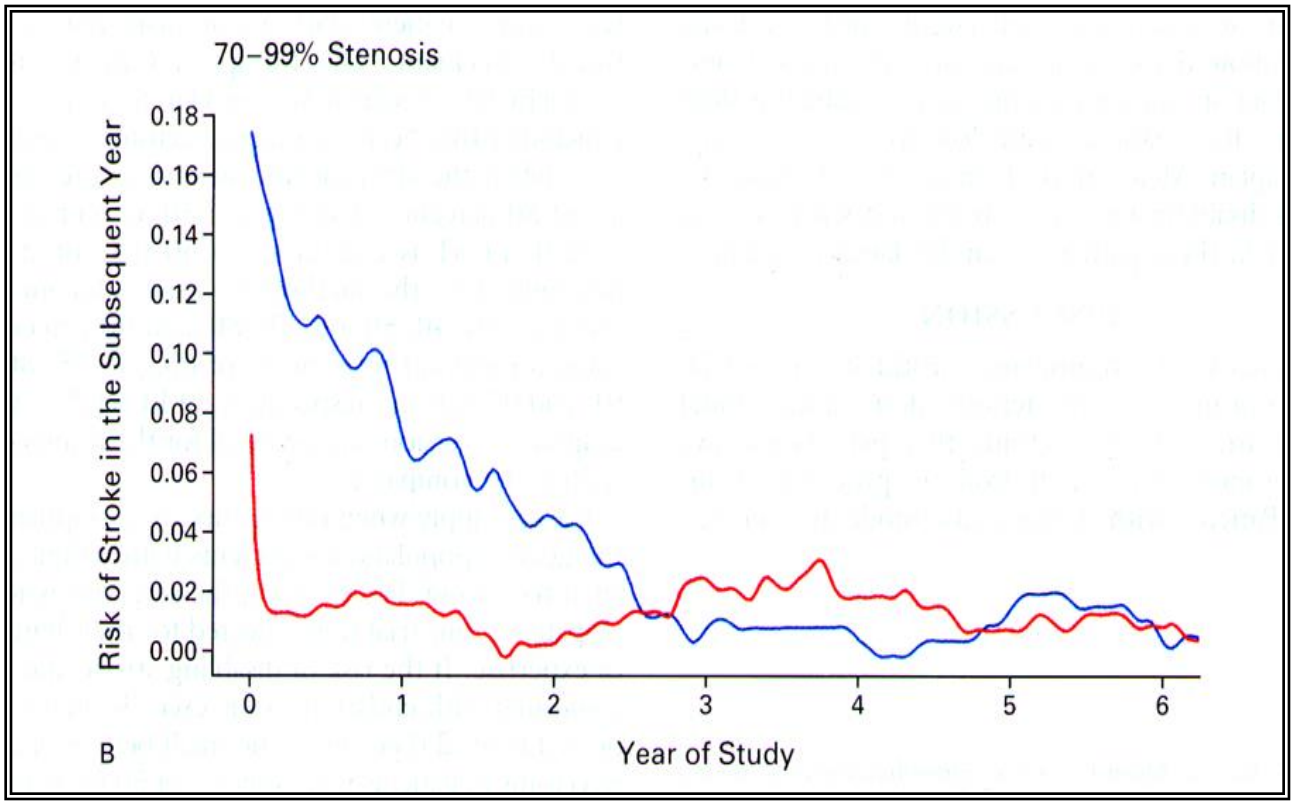
N patients with >=50% stenosis needed to treat to prevent 1 ipsilateral stroke in 5 years

- Men : 9
  Women : 36
  (p = 0.003)
- > 75 years : 5
  < 65 years : 18
  (p = 0.03)
- R < 2 weeks : 5
  R > 12 weeks : 125
  (p = 0.009)



Sténose carotide symptomatique

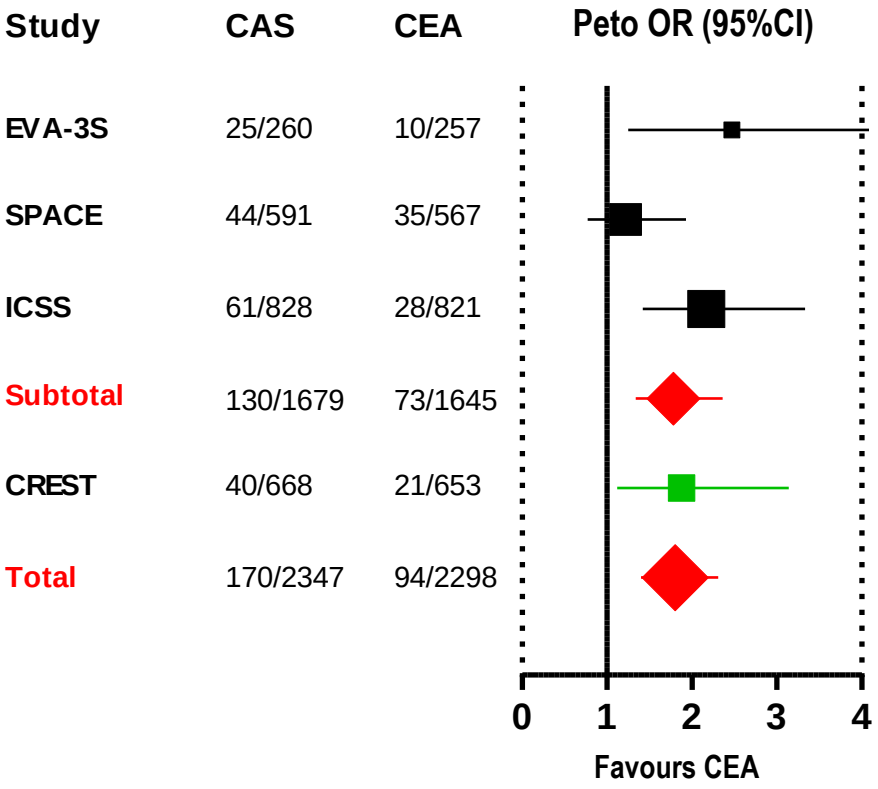
Barnett et al, NEJM 1998



Sténose carotide symptomatique

Stenting vs. Chirurgie: risques des procédures

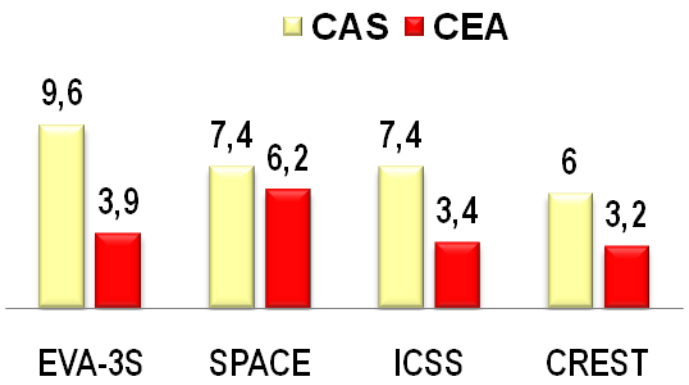
Stroke or death within 30 days of treatment (per protocol analysis)



OR (Fixed) = 1.80 (1.40 – 2.31), p = 0.000

Heterogeneity p = 0.23

Absolute risks



EVA-3S, Mas et al, NEJM 2006
SPACE Collaborative group, Lancet 2006
ICSS investigators, Lancet 2010
CREST, Brott et al, NEJM 2010

Sténose carotide symptomatique

Stenting vs. Chirurgie: risques des procédures

Brott et al, NEJM 2010

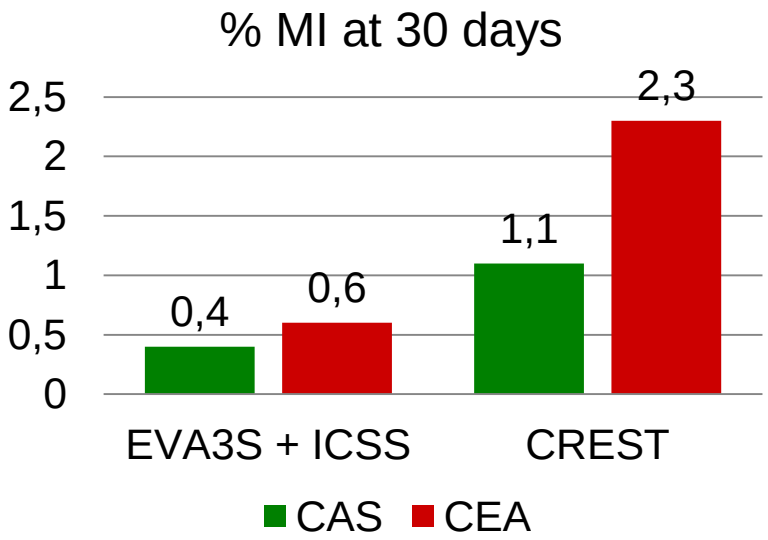
CREST

- 1321 patients with symptomatic carotid stenosis
- ≥ 50% by angiography; ≥ 70% by US or >= 70% by CTA or MRA if US 50-69%

Within 30 days after the procedure	CAS	CEA	HR (95%CI)
Any stroke, MI or death	**6.7%**	**5.4%**	**1.26 (0.81 - 1.96)**
Any stroke or death	**6.0%**	**3.2%**	**1.89 (1.11 - 3.21)**
Any stroke	5.5%	3.2%	1.74 (1.02 - 2.98)
MI	1.0%	2.3%	0.45 (0.18 – 1.11)

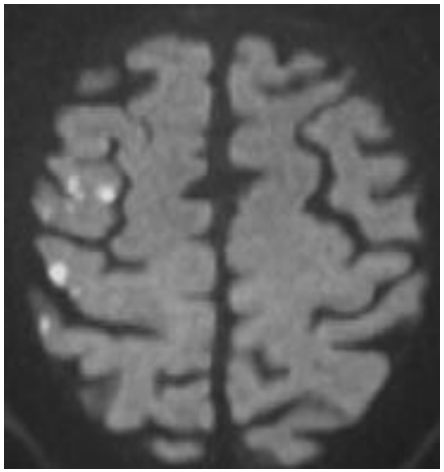
Sténose carotide symptomatique

Stenting vs. Chirurgie: infarctus du myocarde



Definition of MI in CREST

- Clinical symptoms or ECG evidence of ischemia + elevation of CK-MB or troponin
- 40% clinically asymptomatic



ICSS substudy
Bonati et al, Lancet Neurol 2010

DWI MRI	CAS (n=124)	CEA (n=107)
>= 1 new lesion	62 (50%)	18 (17%)

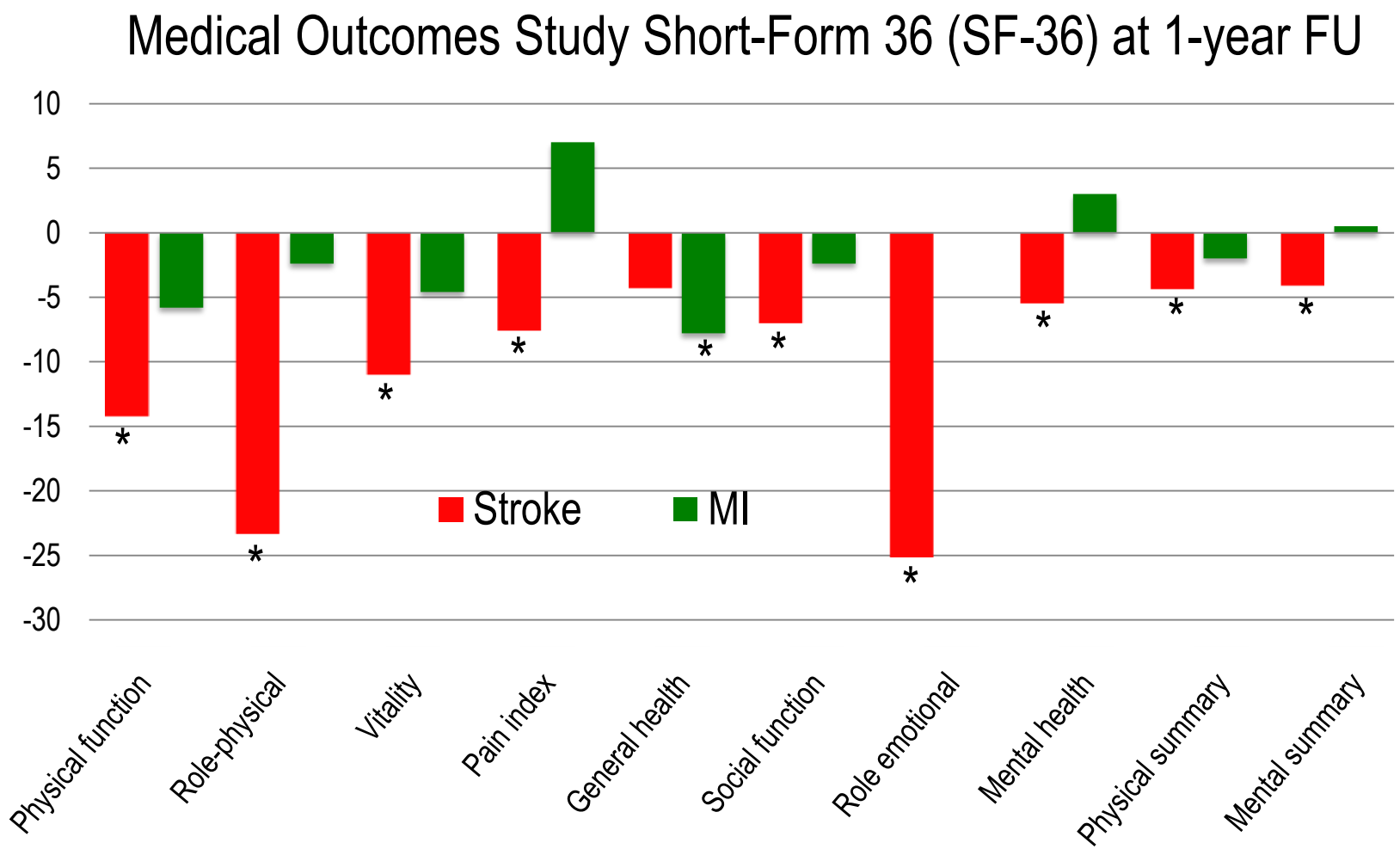
OR = 4.94 (2.67 – 9.16)

Sténose carotide symptomatique

Stenting vs. Chirurgie: infarctus du myocarde

Cohen et al, JACC 2011

CREST

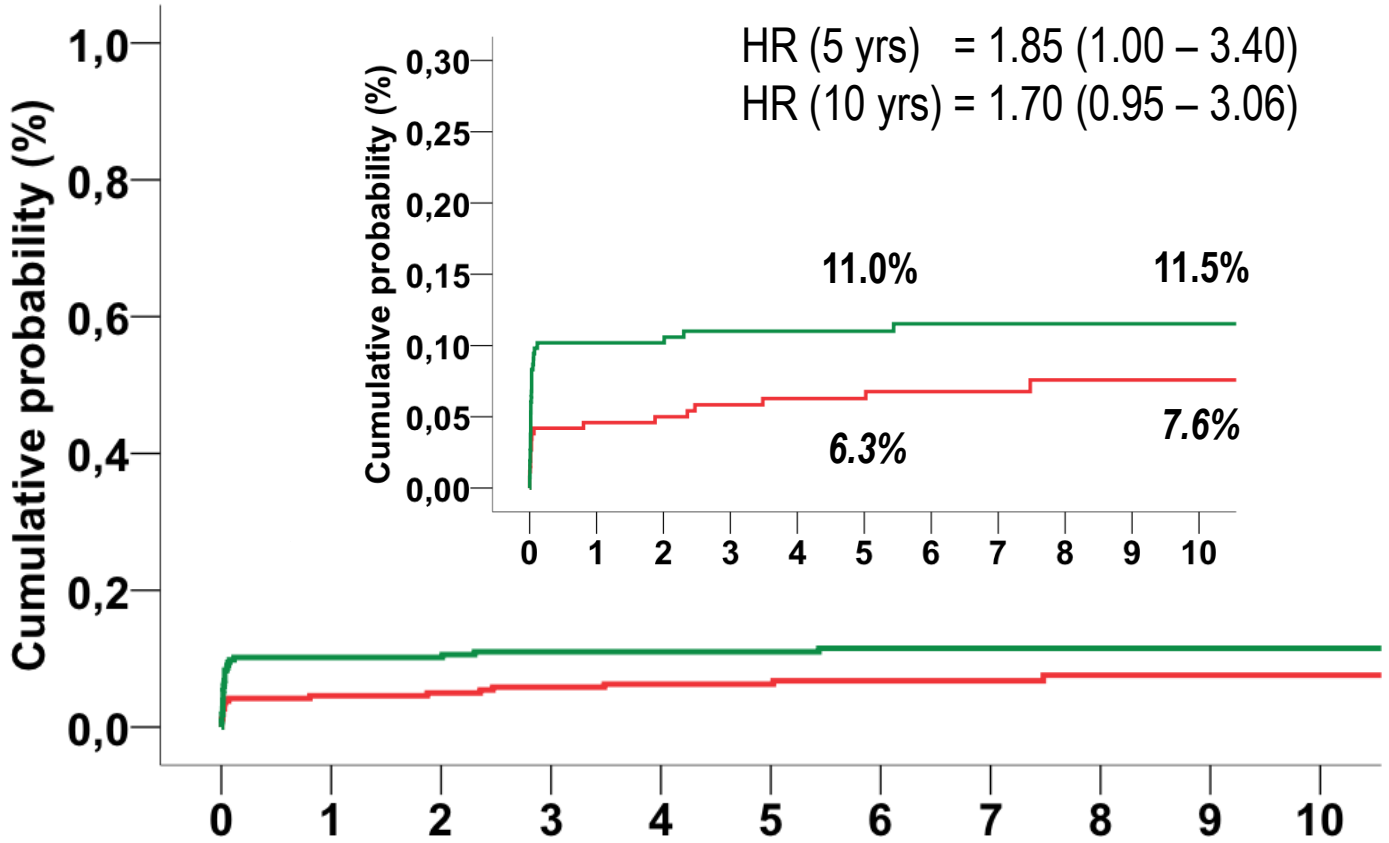


Sténose carotide symptomatique

Stenting vs. Chirurgie: prévention des récidives

Mas et al, Lancet Neurol 2008, Stroke 2014

EVA3S



CAS	265	231	222	209	196	181	168	128	90	58	24
CEA	262	241	232	222	208	194	174	137	84	54	28

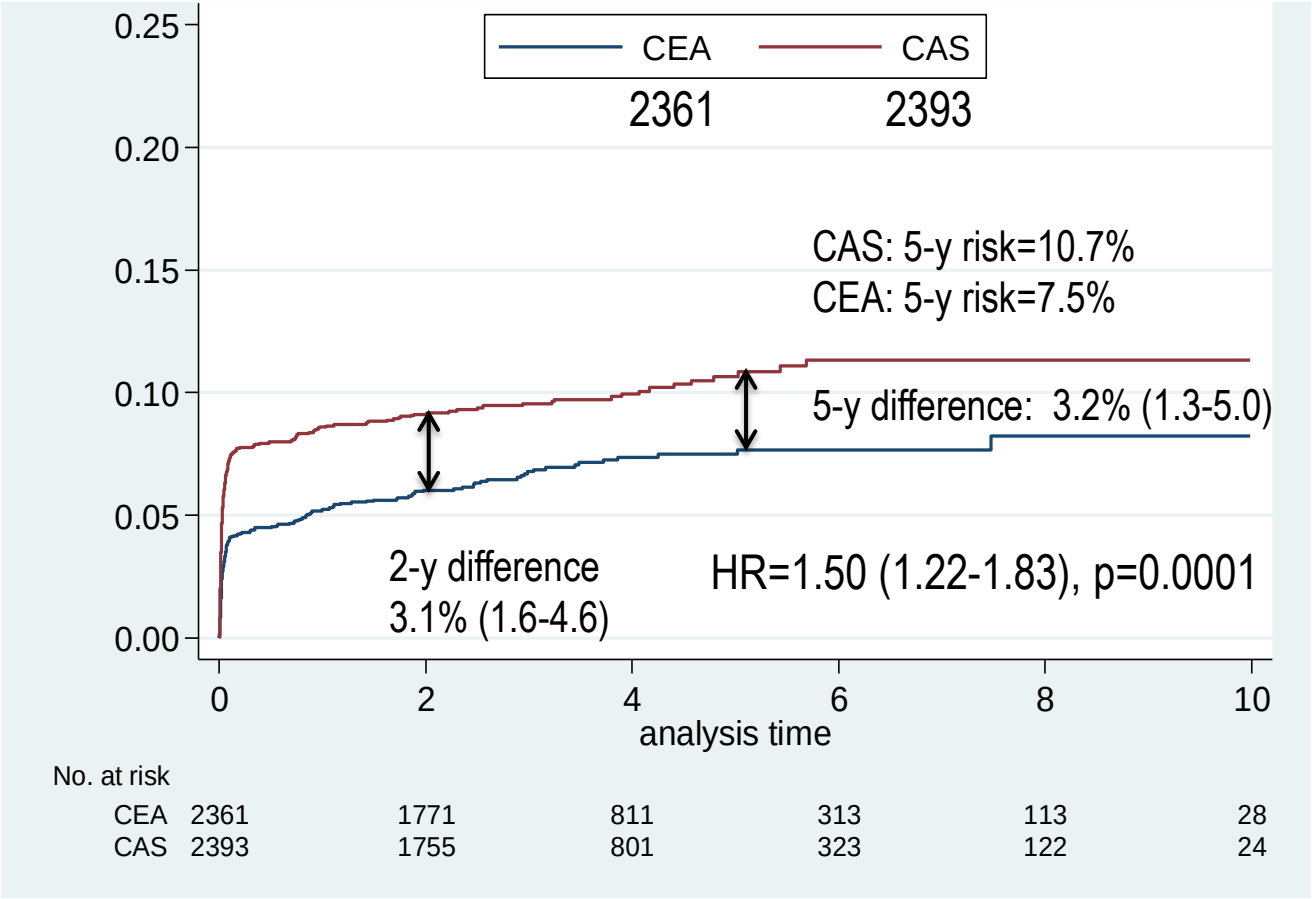
Sténose carotide symptomatique

Stenting vs. Chirurgie: prévention des récidives

Calvet et al, ESC Nice, 2014

CSCT

Primary outcome event: Intention to treat analysis

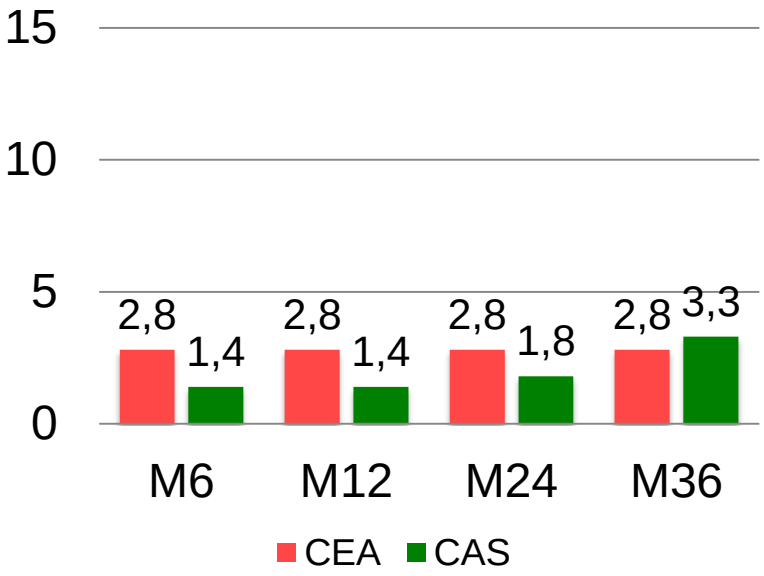


Sténose carotide symptomatique

Stenting vs. Chirurgie: resténose carotide

EVAS 3S (Arquizan et al, Stroke 2011)

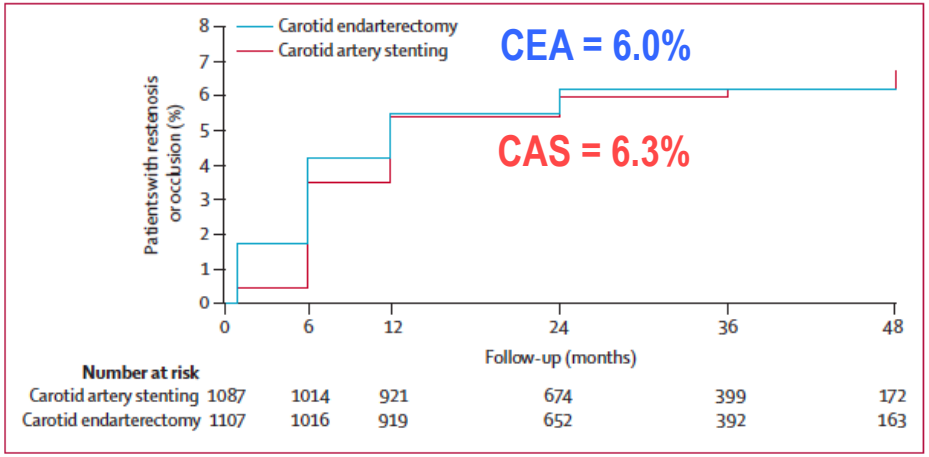
Restenosis >= 70%
or occlusion



Restenosis 50% - 70% : B-mode imaging, NASCET.
Restenosis > 70% : B-mode imaging, NASCET or PSV > 210 (CEA), > 300 cm/sec. (CAS)

CREST (Lal et al, Lancet Neurol 2012)

Restenosis >= 70%
or occlusion



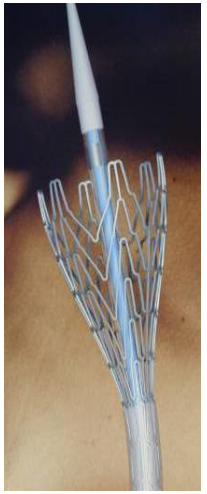
Restenosis > 70% (PSV > 300 cm/sec.)

HR = 0.90 (0.63 - 1.29; p=0.58)

Stenting carotide

Facteurs de risque d'AVC péri-opératoire

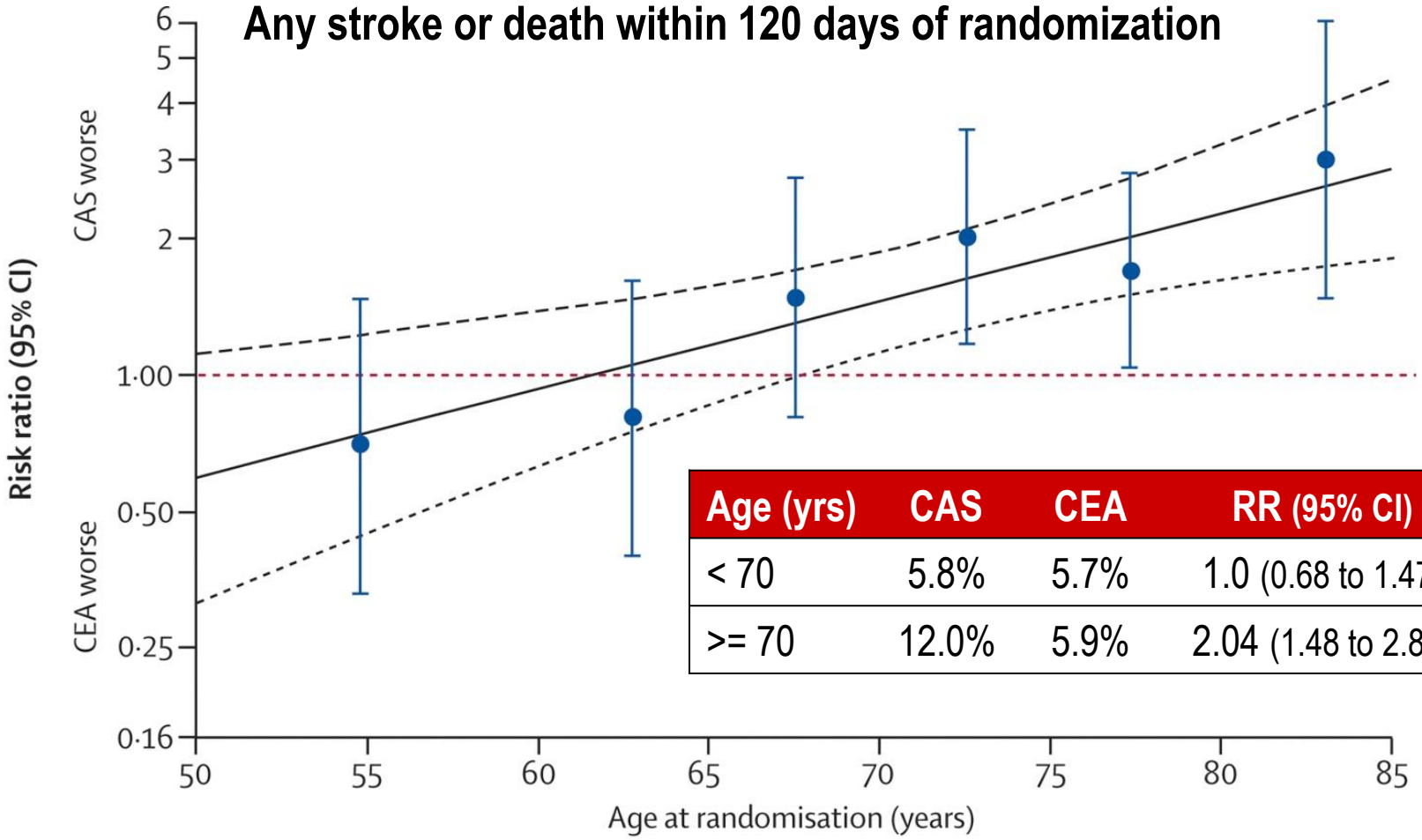
- **Patient**
  - Age (> 70 ans), anomalies de la substance blanche à l'IRM
  - Facteurs anatomiques: ACI-ACC > 60° , sténose carotide longue
- **Procédure**
  - Type de stent (cellules ouvertes vs. cellules fermées)
  - Expérience de l'opérateur : < 6 angioplasties carotides /an
  - *Timing de la procédure*



Sténose carotide symptomatique

Stenting vs. Chirurgie: âge

Carotid Stenting Trialists' Collaboration, Lancet 2010



Age (yrs)	CAS	CEA	RR (95% CI)
< 70	5.8%	5.7%	1.0 (0.68 to 1.47)
>= 70	12.0%	5.9%	2.04 (1.48 to 2.82)

Sténose carotide symptomatique

Stenting vs. Chirurgie: hypersignaux de la SB

Ederle et al, Lancet Neurol 2013

- ICSS. 1036 patients had baseline imaging data.
- Carotid stenting was associated with a higher risk of stroke compared with carotid endarterectomy in patients with an ARWMC score >= 7, but there was no risk difference in patients with an ARWMC score < 7.

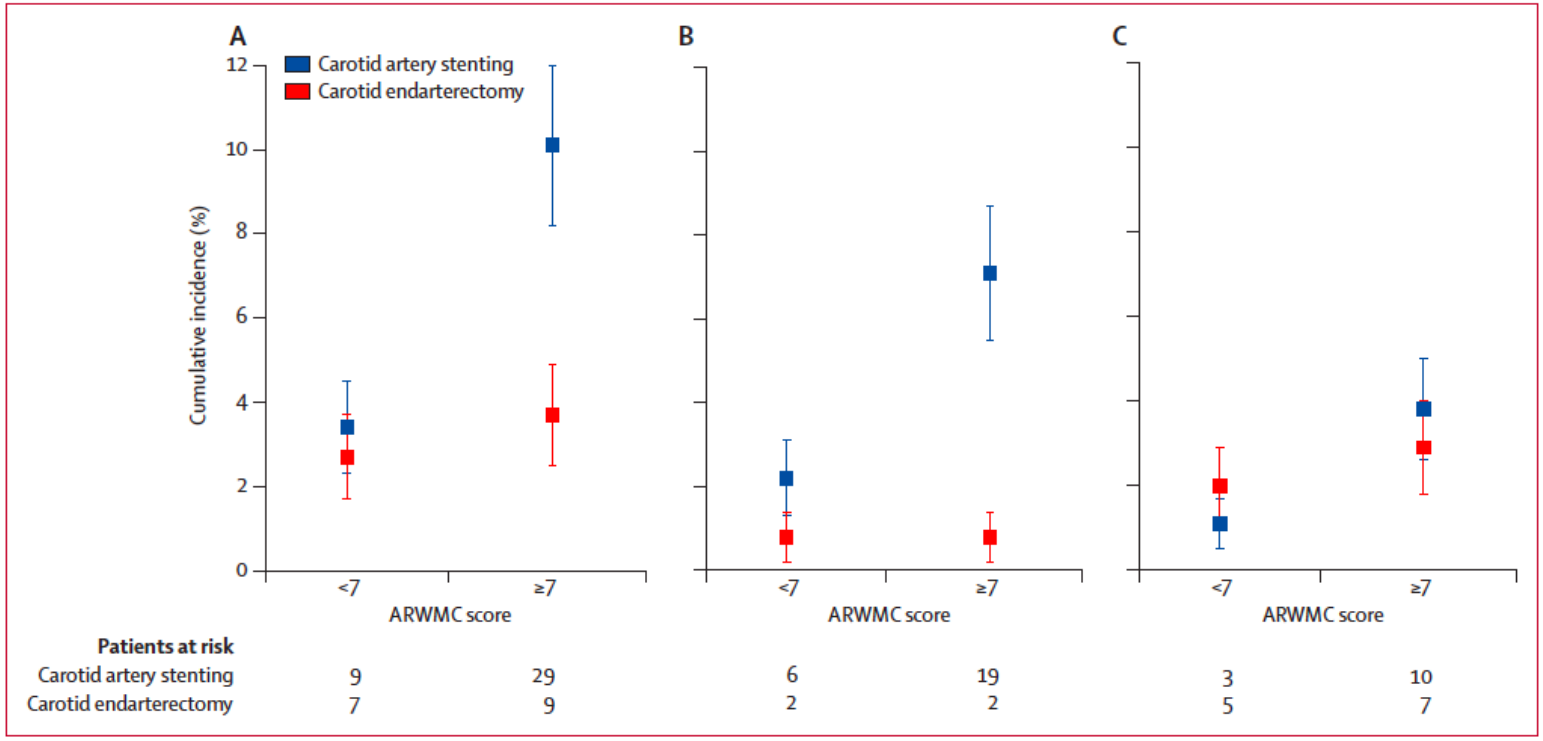


Figure 2: 30-day cumulative incidence of stroke by severity of white-matter lesions
(A) any stroke, (B) non-disabling stroke, (C) fatal or disabling stroke. ARWMC=age-related white-matter changes. Error bars are SDs.

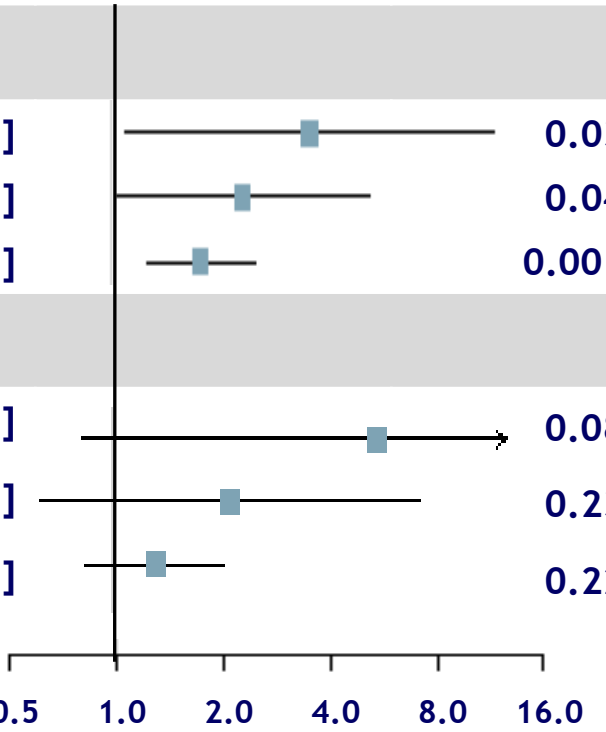
Sténose carotide symptomatique

Stenting vs. Chirurgie: timing de la procédure

CSCT

Rantner et al, J Vasc Surg 2013

	CEA Risk	CAS Risk	RR	P-value
Stroke or Death				
≤ 7 days	3 (2.8%)	13 (9.4%)	3.79 [1.1-13.1]	0.03
8-14 days	7 (3.4%)	19 (8.1%)	2.42 [1.0-5.7]	0.04
> 14 days	44 (4.0%)	78 (7.3%)	1.82 [1.3-2.6]	0.001
Disabling Stroke				
≤ 7 days	1 (0.9%)	7 (5.1%)	6.40 [0.8-51.0]	0.08
8-14 days	3 (1.4%)	7 (3.0%)	2.28 [0.6-8.7]	0.23
> 14 days	28 (2.6%)	34 (3.5%)	1.35 [0.8-2.2]	0.22



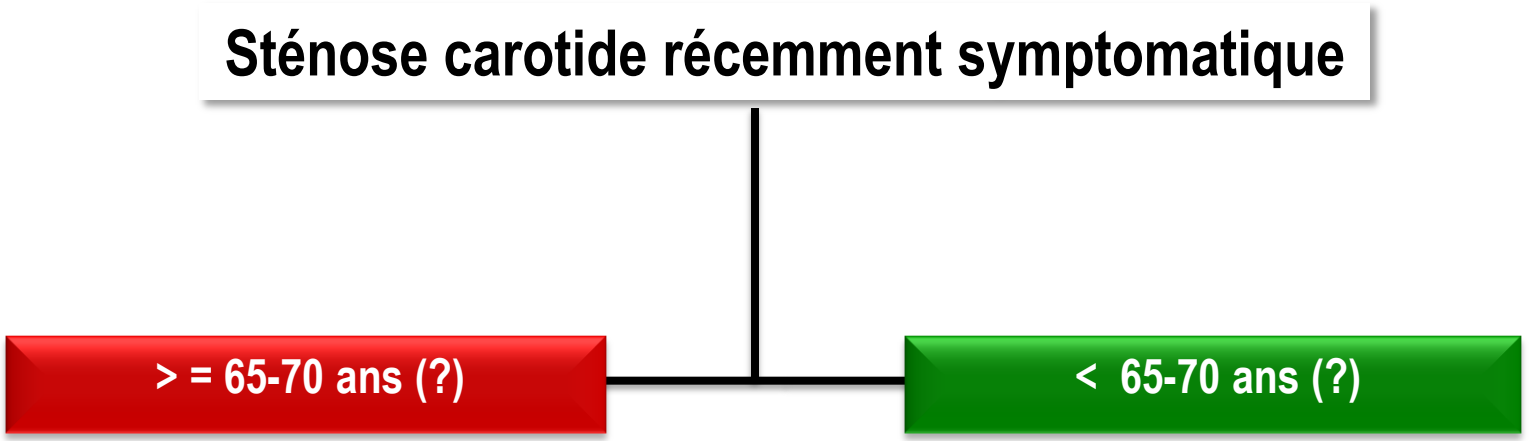
Binominal regression analysis

Sténose carotide symptomatique
Conclusions

- La chirurgie reste le traitement de référence des sténoses carotides symptomatiques.
- Comparé à la chirurgie, le stenting carotide comporte un risque plus élevé d''AVC périprocédural et un risque plus faible d'infarctus du myocarde periprocédural.
- Le stenting semble aussi durable que la chirurgie en termes de prévention à long-terme des infarctus ipsilatéraux et de risque de resténose carotide.

Sténose carotide symptomatique

De nouvelles recommandations?



- Chirurgie
- Stenting
  - CI Chirurgie
  - Sténose radique
  - Resténose après chir.
  - Sténose inaccessible

- Chirurgie ou stenting
  - Anatomie vasculaire
  - Risque coronaire
  - Préférence du patient

Cas 2

- Madame AS…, 75 ans, a eu un EDTSA car elle a des facteurs de risque vasculaire: surpoids (hypertension artérielle, hypercholestérolémie; tabac, 10 cigarettes par jour « depuis toujours ». L'observance de son traitement n'est pas optimale. Sa pression artérielle est à 150/90 mm Hg à plusieurs reprises; le LDL cholestérol à 1.40 g/L.
- Cet examen montre une sténose de l'ACI droite, estimée à environ 60%. Pas d'autre sténose. Pas de retentissement hémodynamique au DTC. Elle a un angioscanner (ci-contre) pour confirmer.
- Elle a vu un chirurgien vasculaire, qui pense qu'il faut l'opérer, pour « diminuer de moitié son risque d'infarctus »

Questions

- **Quel est le niveau de risque d'infarctus cérébral homolatéral ?**
  - 0.5 à 1 % par an
  - ≅ 2% par an
  - > 5% par an
- **Quel(s) traitement(s) proposez-vous ?**
  - Traitement médical seul et surveillance ?
  - Chirurgie carotide ?
  - Angioplastie ?
- **Quelles autres explications et conseils lui donnez-vous ?**

Sténose carotide asymptomatique

Chirurgie carotide vs. Traitement médical seul

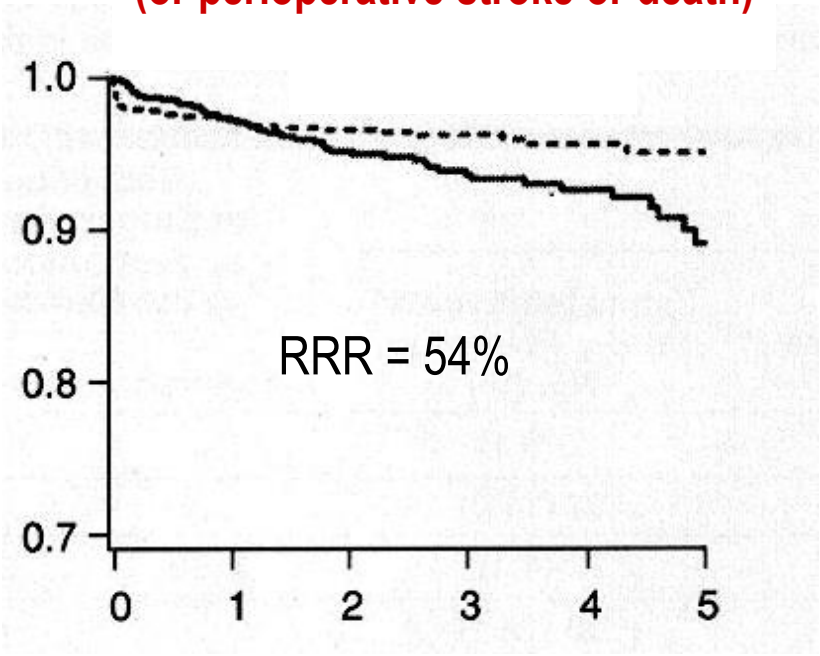
Asymptomatic Carotid Atherosclerosis Study JAMA 1995

- 1662 patients, 40-79 years, ACS > 60%
- Operative risk = 2.3%

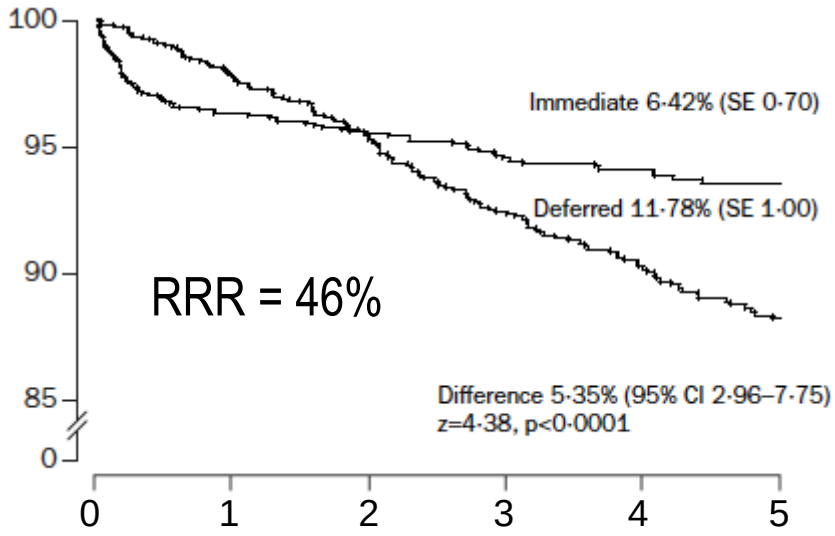
Asymptomatic Carotid Surgery Trial
Lancet 2004, 2010

- 3120 patients, ACS > 60%
- Operative risk = 2.8%

Ipsilateral stroke
(or perioperative stroke or death)



Any stroke
(or perioperative stroke or death)



Sténose carotide asymptomatique

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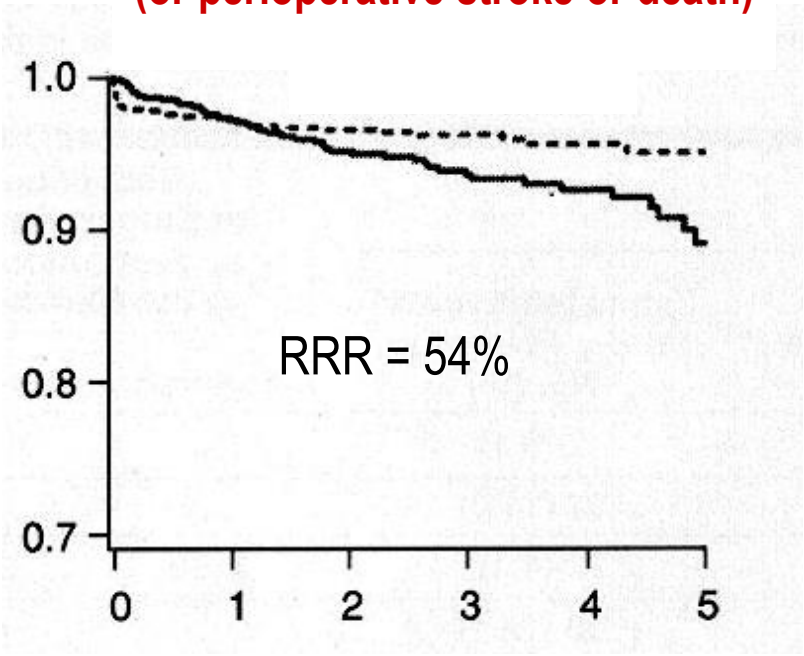

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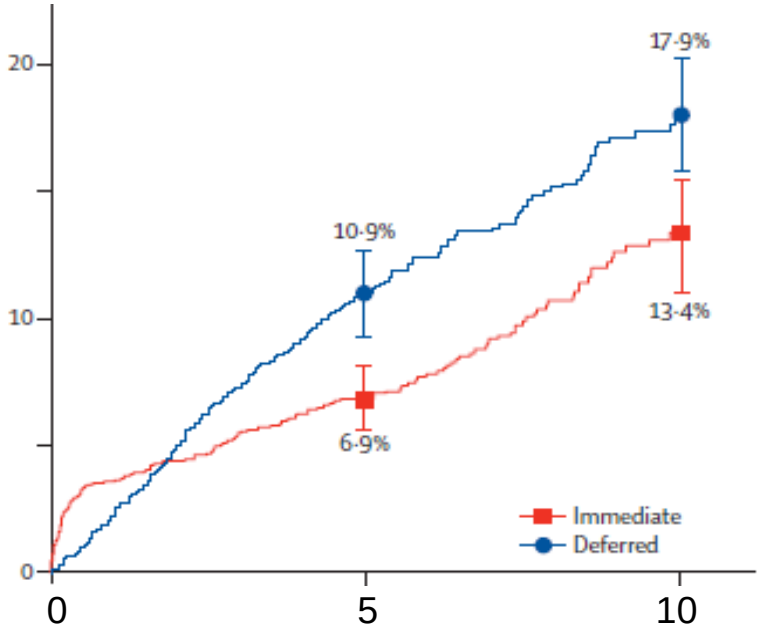
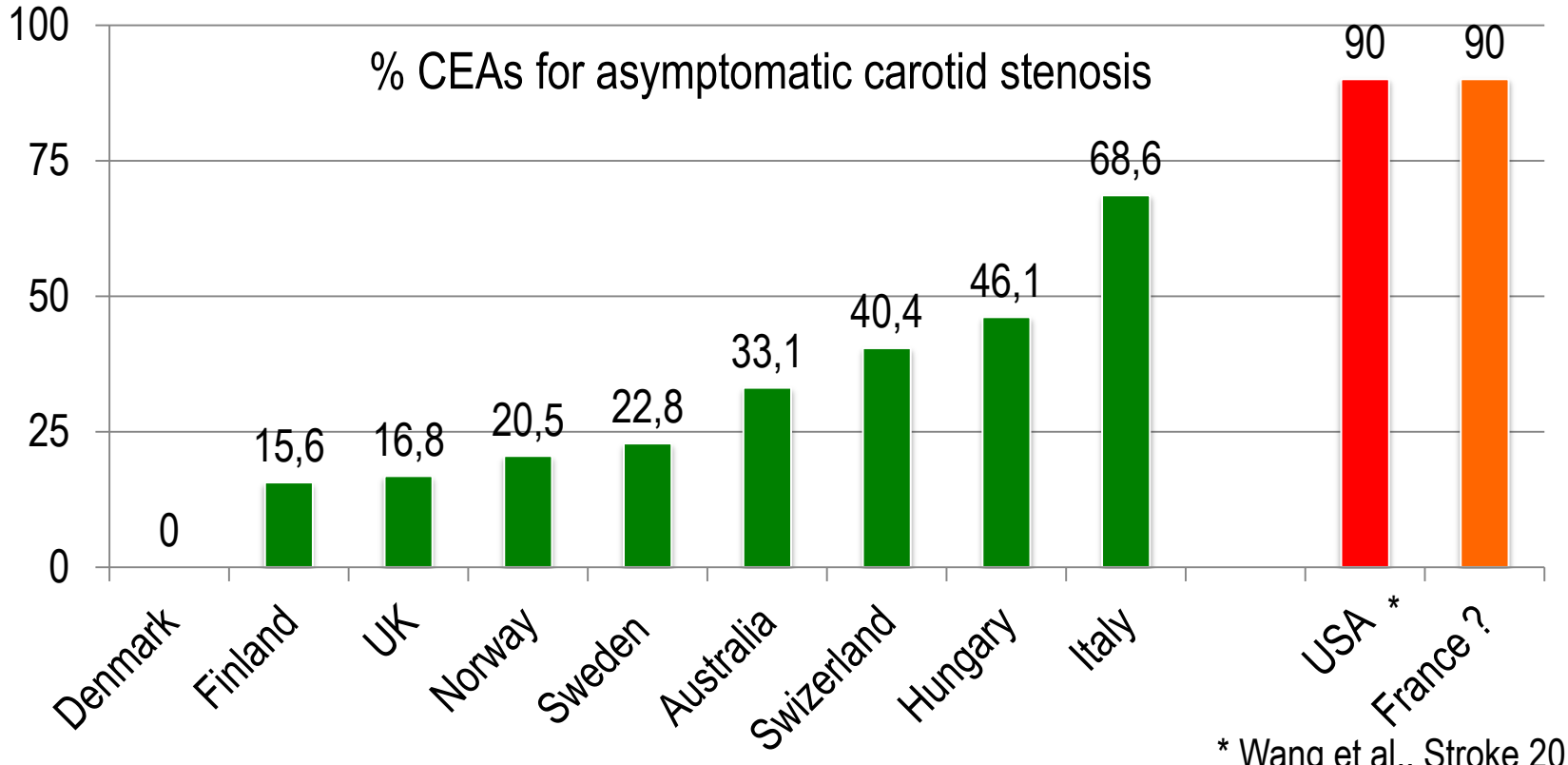


Sténose carotide asymptomatique

Des indications très variables

Vikatmaa et al, EJVES 2012

- VASCUNET: vascular registries from Europe and Australasia
- 48,185 CEAs, 4602 CAS



* Wang et al., Stroke 2011

Sténose carotide asymptomatique

Chirurgie carotide vs. Traitement médical seul

5-year outcomes

Trial	n	Operative risk (%)	Risk of stroke with MT (%)	Risk of stroke with CEA (%)	RRR with CEA (%)	ARR with CEA (%)
ACAS	1,662	2.3	11.0*	5.1*	54	5.9
ACST	3,120	2.8	11.8	6.4	46	5.4

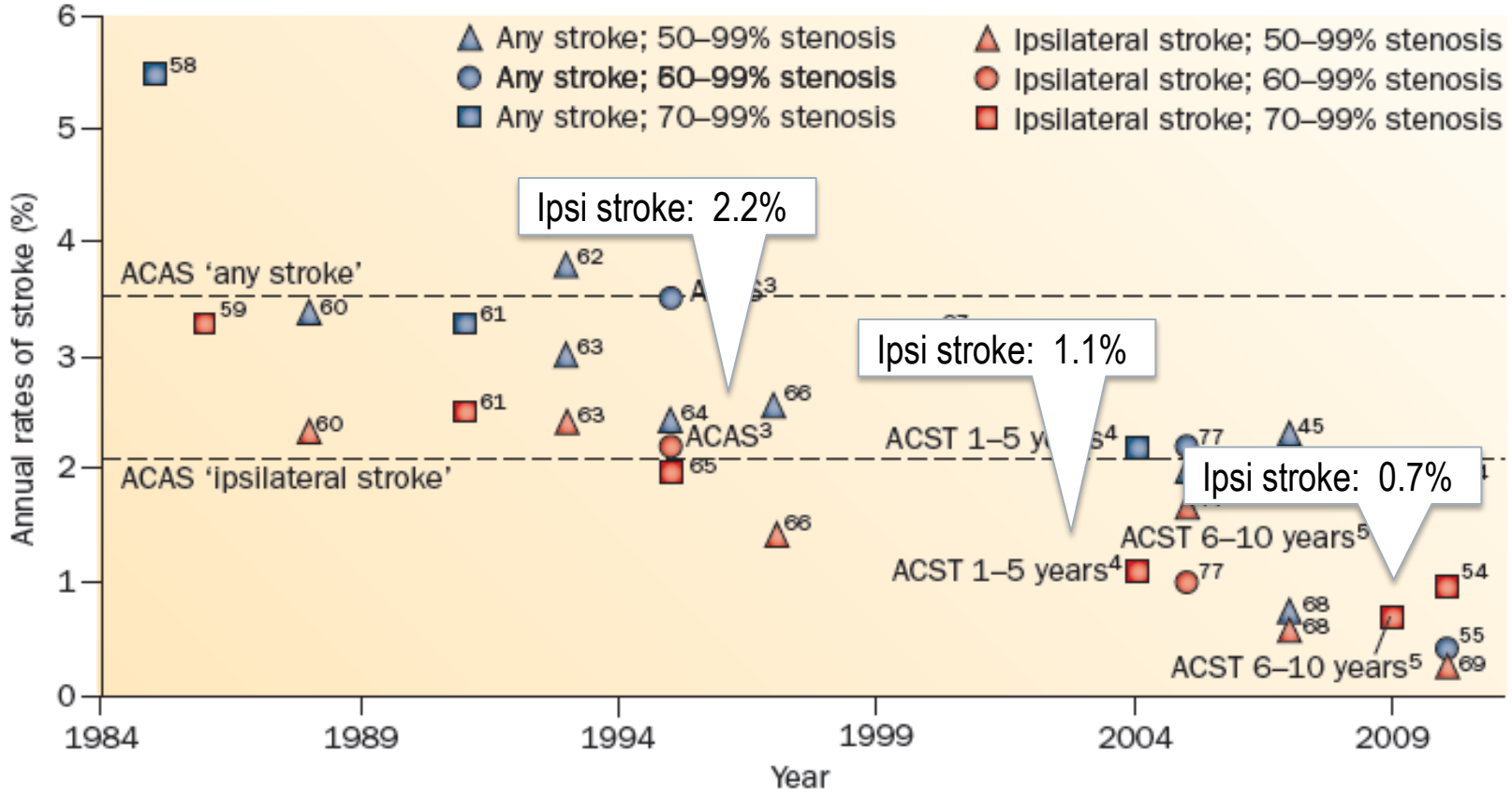
* ipsilateral stroke

- **Low absolute risk reduction of ipsilateral stroke**
  - ARR ≈ 1% /year, Number Needed to Treat to prevent 1 stroke in 1 year ≈ 100
  - ≈ 60 strokes prevented at 5 years for every 1,000 CEAs
- **Low population-attributable risk**
  - Could only prevent <= 4% of all strokes

Sténose carotide asymptomatique

Risque d'AVC sous traitement médical

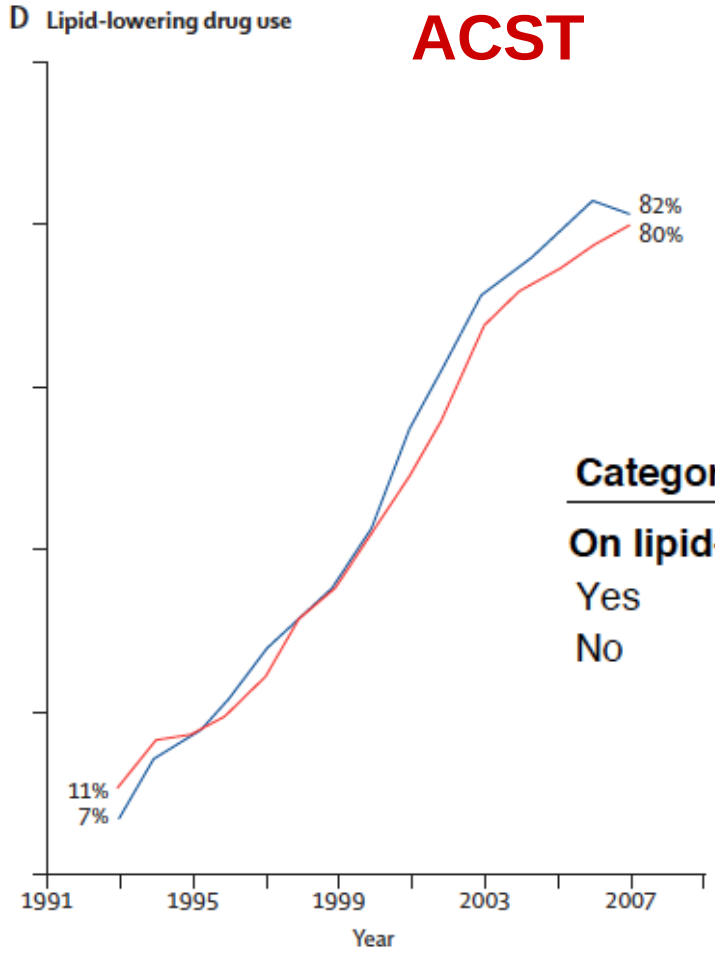
Naylor, Stroke 2011



Sténose carotide asymptomatique

Traitement hypolémiant

Halliday et al, Lancet 2010



ACST

Category	Events/person-years and annual event rate (%)	
	Immediate CEA	Deferral
On lipid-lowering therapy before any stroke?		
Yes	45/6623 (0.7%)	88/6568 (1.3%)
No	54/2959 (1.8%)	100/2988 (3.3%)

Sténose carotide asymptomatique

Stenting vs. chirurgie: CREST

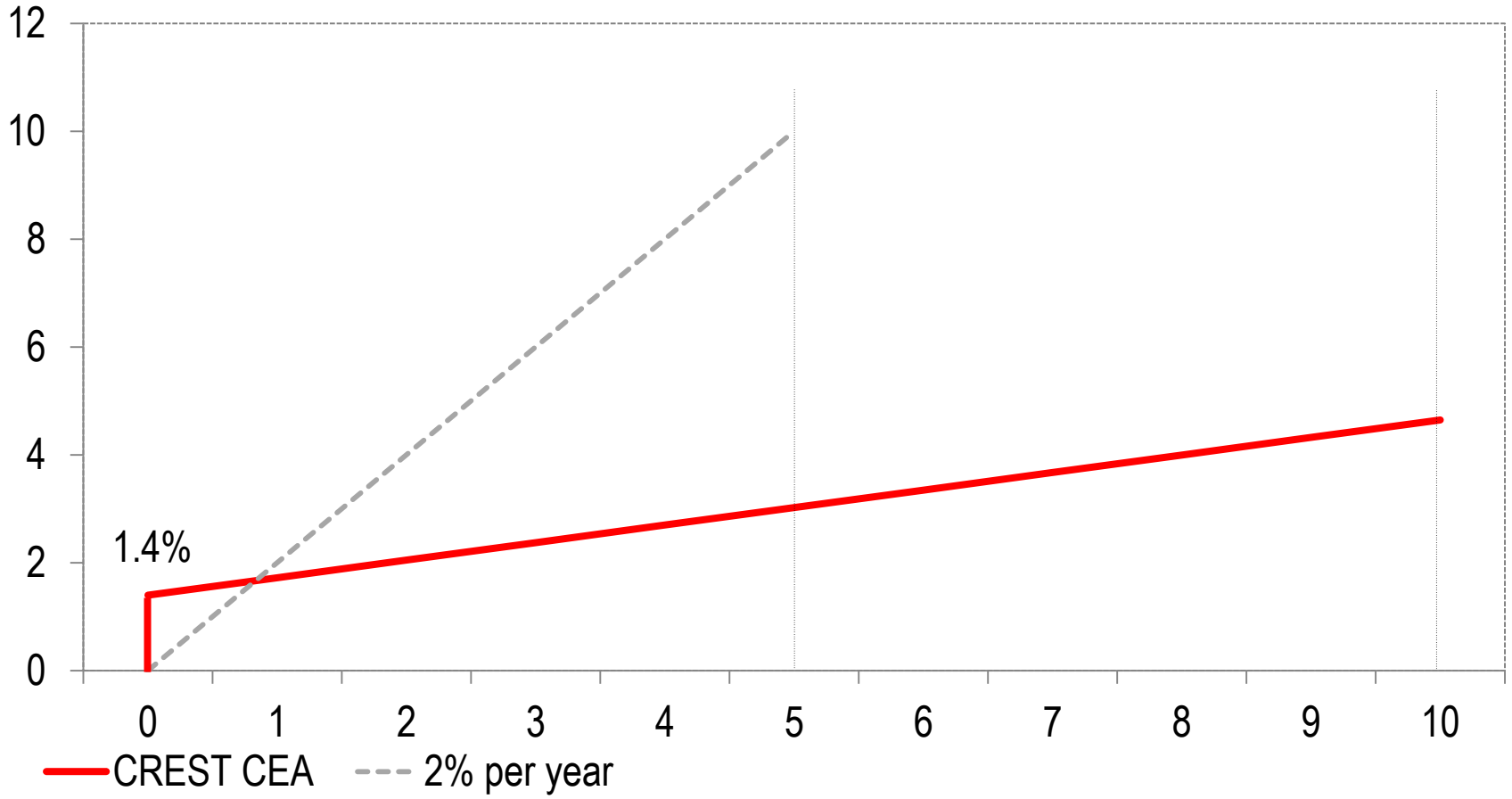
Brott et al, NEJM 2010

- N = 1181 patients with asymptomatic carotid stenosis
- ≥ 60% by angiography, ≥ 70% by US, or > 80% by CTA or MRA if US 50-69%

J30	Stenting	Chirurgie	HR (95%CI)
Any stroke, MI or death	**3.5%**	**3.6%**	**1.02 (0.55 - 1.86)**
Any stroke or death	**2.5%**	**1.4%**	**1.88 (0.79 – 4.42)**
Any stroke	2.5%	1.4%	1.88 (0.79 – 4.42)
MI	1.2%	2.2%	0.55 (0.22 – 1.38)

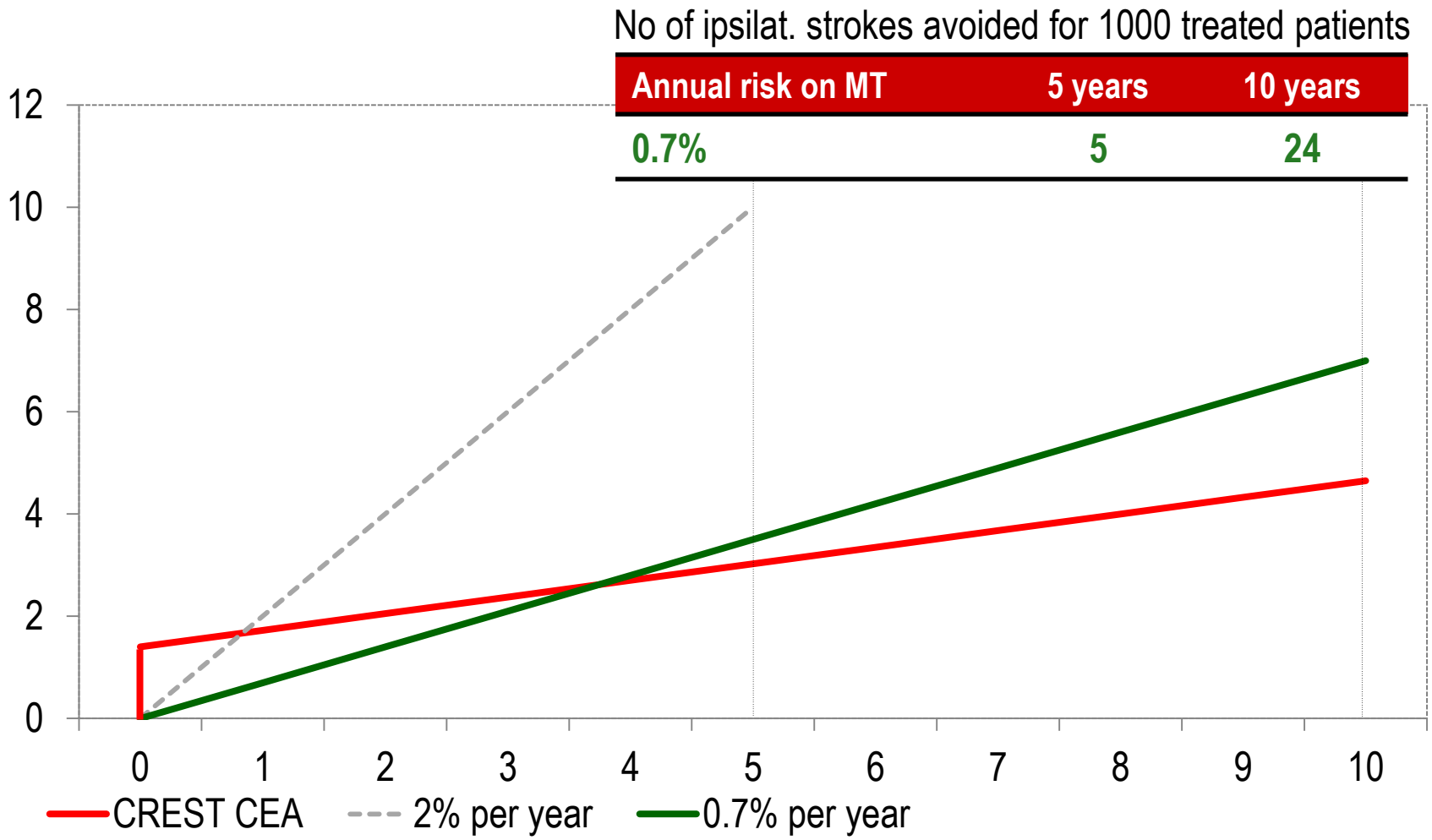
Sténose carotide asymptomatique

Chirurgie vs. Traitement médical seul



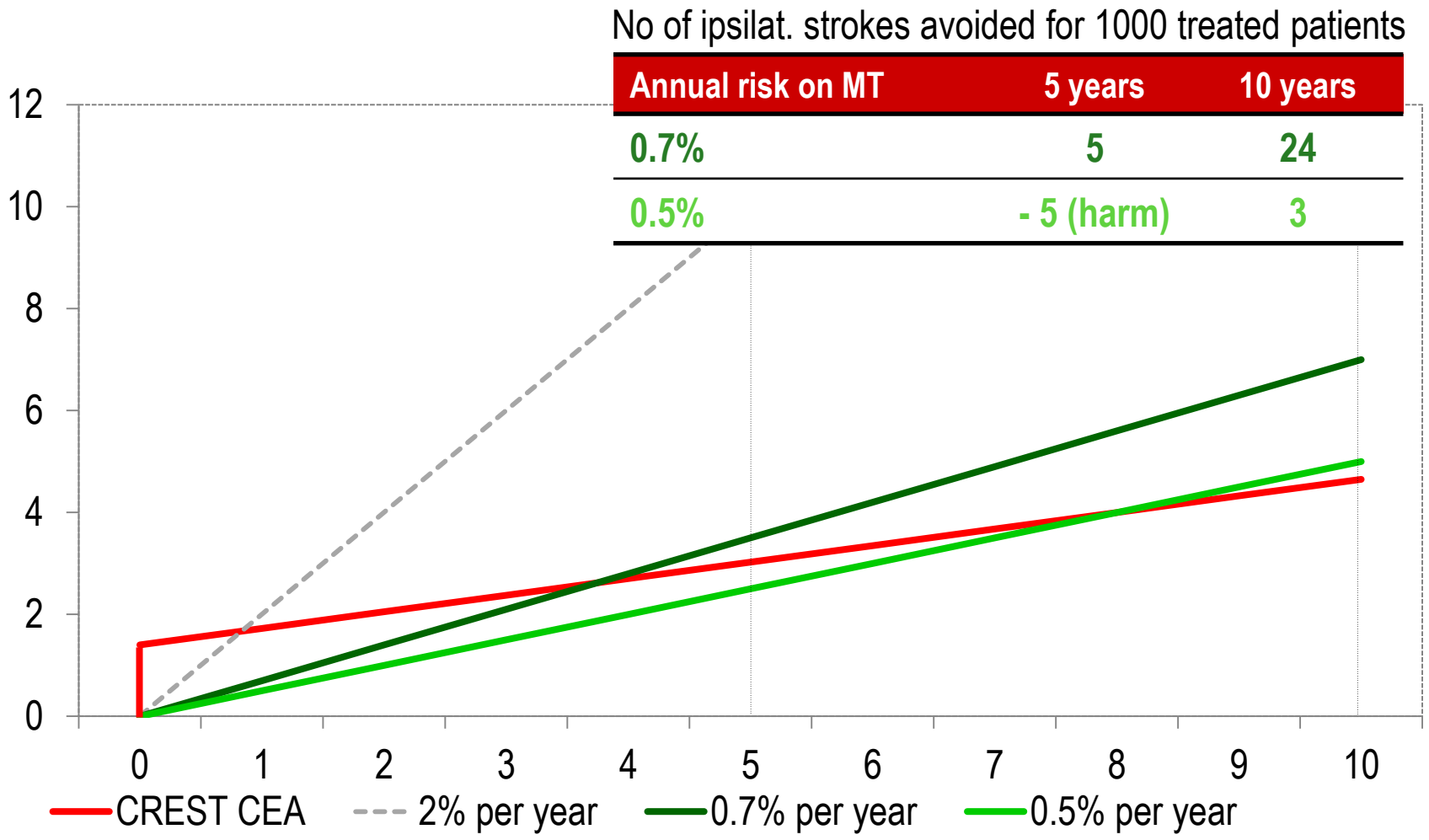
Sténose carotide asymptomatique

Chirurgie vs. Traitement médical seul



Sténose carotide asymptomatique

Chirurgie vs. Traitement médical seul

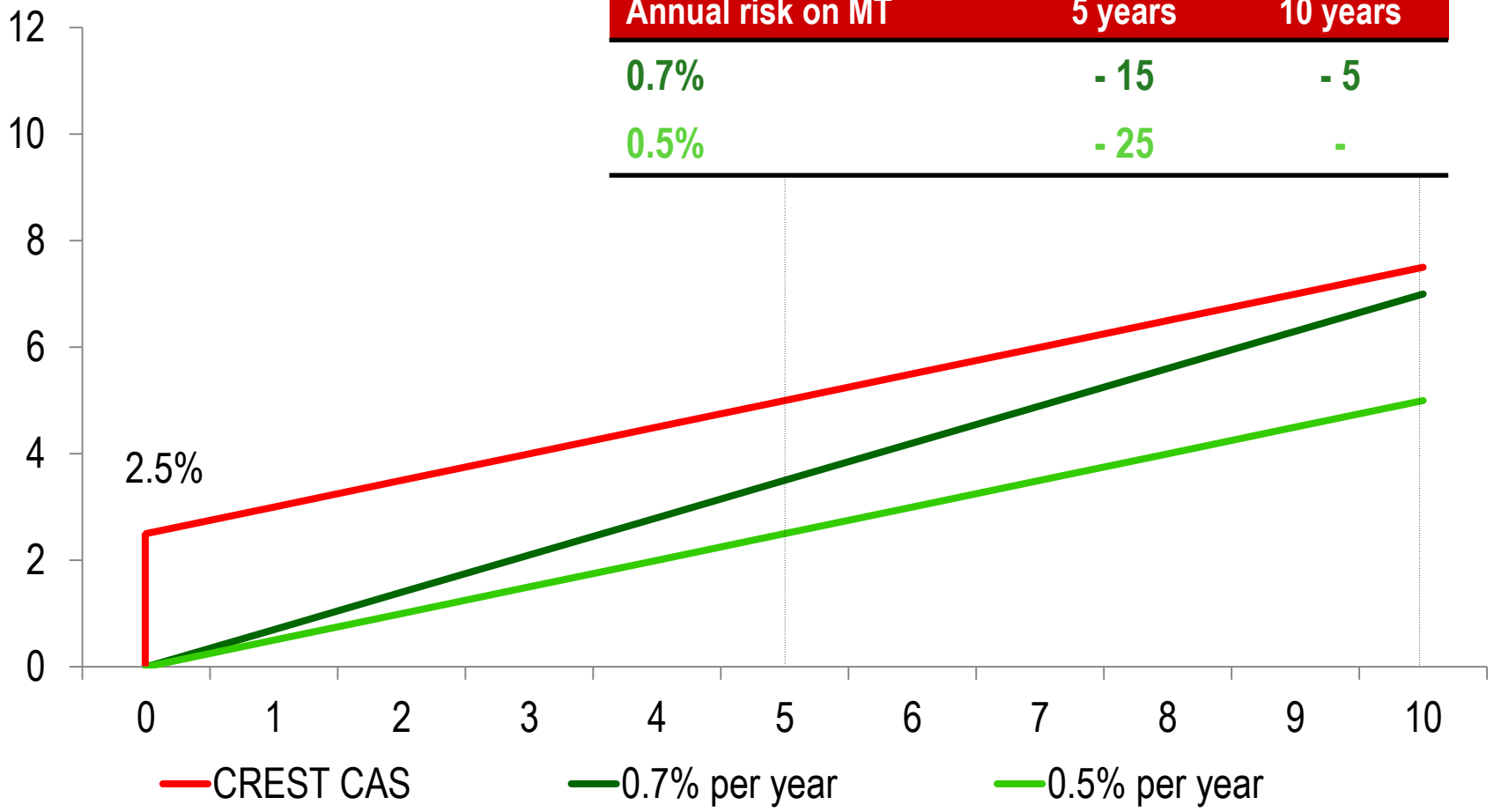


Sténose carotide asymptomatique

Stenting vs. Traitement médical seul

No of ipsilat. strokes avoided for 1000 treated patients

Annual risk on MT	5 years	10 years
0.7%	- 15	- 5
0.5%	- 25	-



Sténose carotide asymptomatique

Pour quels patients?

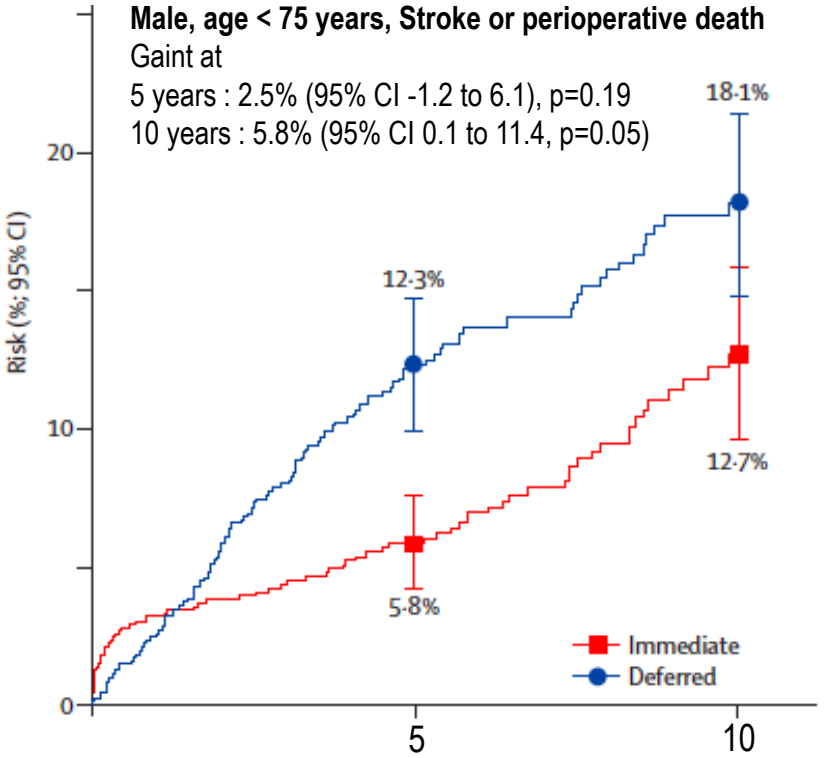
- < 75 ans, **espérance de vie > 5-10 ans**
- Homme > Femme
- Infarctus cérébral ipsilatéral silencieux (type embolique)
- **Diminution de la réserve circulatoire cérébrale**
- **Progression de la sténose**
- **Signaux micro-emboliques au DTC**
- **Structure de la plaque : IRM**, ultrasons, PET, …
- Biomarqueurs circulants

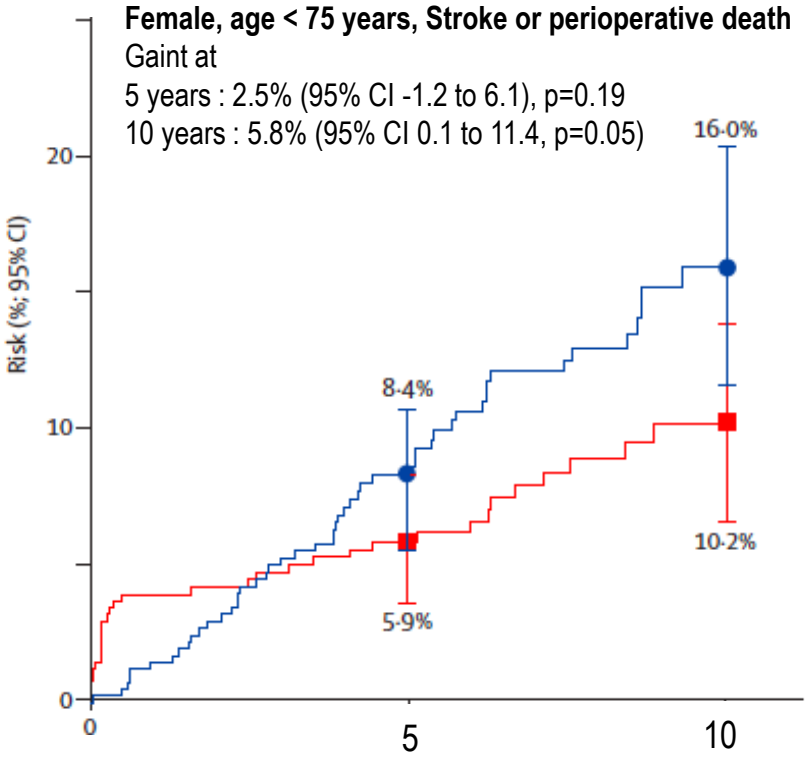
Sténose carotide asymptomatique

Age, sexe

Non-operative stroke
ACST, Lancet 2010

Category	Events/person-years and annual event rate (%) Immediate CEA	Deferral	Ratio of annual event rates Immediate CEA:Deferral [95% CI]
Men < 75	53/5272 (1.0%)	105/5063 (2.1%)	0.50 [0.33-0.75]
Women < 75	16/2658 (0.6%)	45/2792 (1.6%)	0.41 [0.21-0.79]
Men ≥ 75	13/965 (1.3%)	22/1024 (2.1%)	0.63 [0.26-1.50]
Women ≥ 75	17/687 (2.5%)	16/677 (2.4%)	1.03 [0.42-2.53]

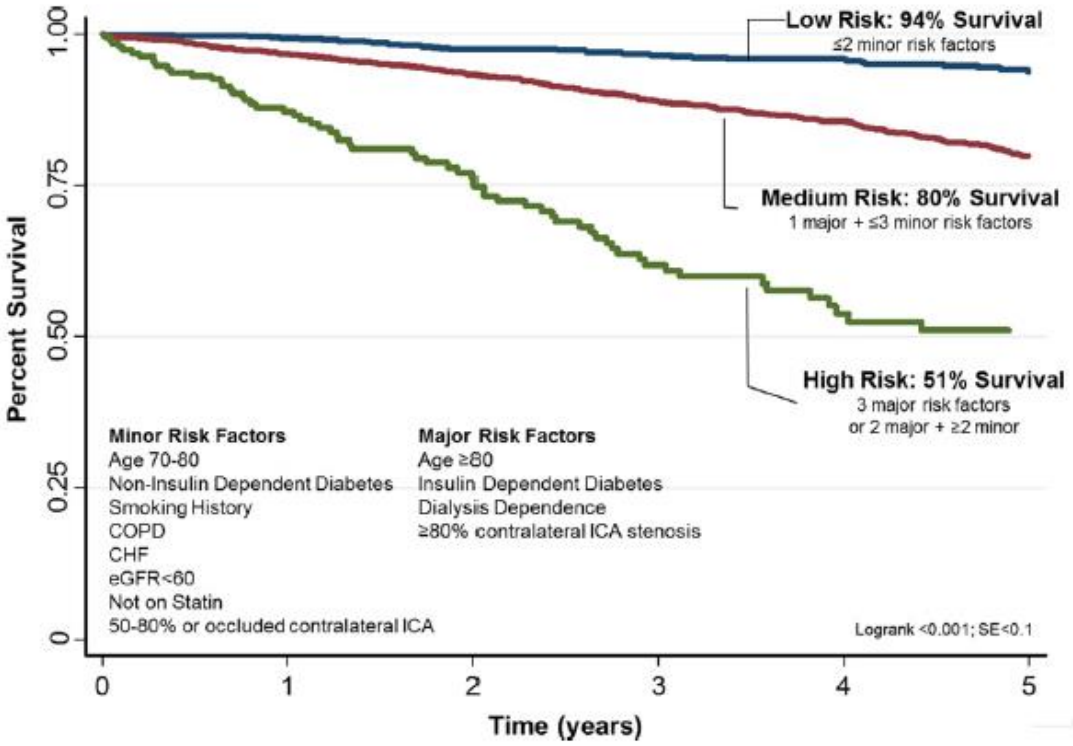




Sténose carotide asymptomatique
Espérance de vie

Wallaert et al, JVS 2013

- 4114 isolated CEAs performed for asymptomatic stenosis across 24 centers in the Vascular Study Group of New England between 2003 and 2011
- To examine factors associated with 5-year survival following CEA in patients with asymptomatic internal carotid artery (ICA) stenosis.



Sténose carotide asymptomatique

Pour quels patients?

- < 75 ans, **espérance de vie > 5-10 ans**
- Homme > Femme
- Infarctus cérébral ipsilatéral silencieux (type embolique)
- **Diminution de la réserve circulatoire cérébrale**
- **Progression de la sténose**
- **Signaux micro-emboliques au DTC**
- **Structure de la plaque : IRM**, ultrasons, PET, …
- Biomarqueurs circulants

Sténose carotide asymptomatique

Progression de la sténose

Hirt et al, Stroke 2014

- 1469 patients included in the medical (deferred endarterectomy) arm of the Asymptomatic Carotid Surgery Trial. Carotid US follow-up >= 5 years.

- 244 had ipsilateral events
- 240 had ipsilateral carotid surgery
- 370 died from nonstroke causes
- 82 had an asymptomatic carotid occlusion
- Categories of progression: < 50%, 50% to 69%, 70% to 89%, 90% to 99%, and 100%
- Annual incidence of progression: 5.2%
- Progression over 1 year of:
  - 1 cat.: 463 patients; 29 (6.3%) had an event
  - 2 cat.: 50 patients; 9 (18%) had an event
  - 3 cat.: 10 patients; 2 (20%) had an event

Table 3. Multivarate Poisson Regression With Ipsilateral Neurological Events as the Dependent Variable

Independent Variables	IRR	*P* Value	95%	CI
Diabetes	**1.150***	**0.020**	**1.090**	**2.130**
Prior contralateral symptoms	**1.500**	**0.010**	**1.110**	**2.020**
Systolic blood pressure	1.000	0.320	1.000	1.010
Diastolic blood pressure	1.010	0.070	1.000	1.030
Carotid luminal narrowing	0.990	0.900	0.800	1.210
Yearly rate of change	**1.660**	**0.000**	**1.270**	**2.170**
–2 or –3 categories	4.63E-006	0.990	4.80E-002	4.50E+209
-1 category	0.780	0.440	0.420	1.470
+1 categories	1.410	0.150	0.890	2.220
+2 categories	**4.030**	**0.000**	**1.820**	8.930
+3 categories	**7.560**	**0.010**	**1.810**	**31.560**

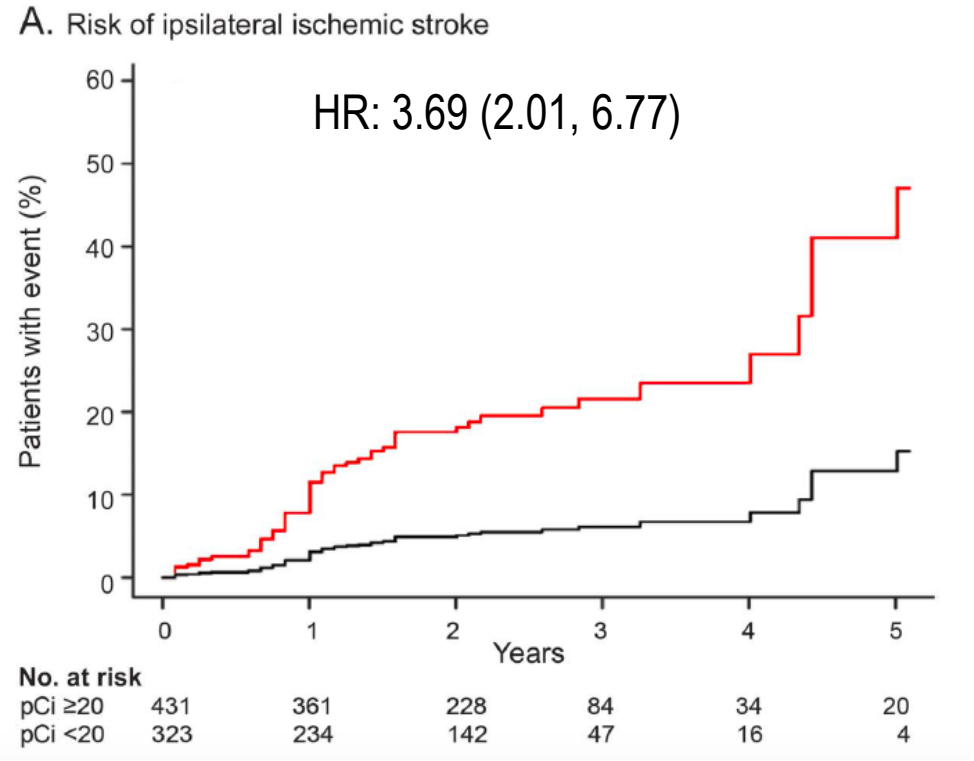
CI indicates confidence interval; and IRR, incidence rate ratio.
*Boldface indicates statistically significant results.

Sténose carotide asymptomatique

Retentissement hémodynamique

Reinhard et al, Neurology 2014

- Méta-analysis: Individual data from 754 patients from 9 studies were included.

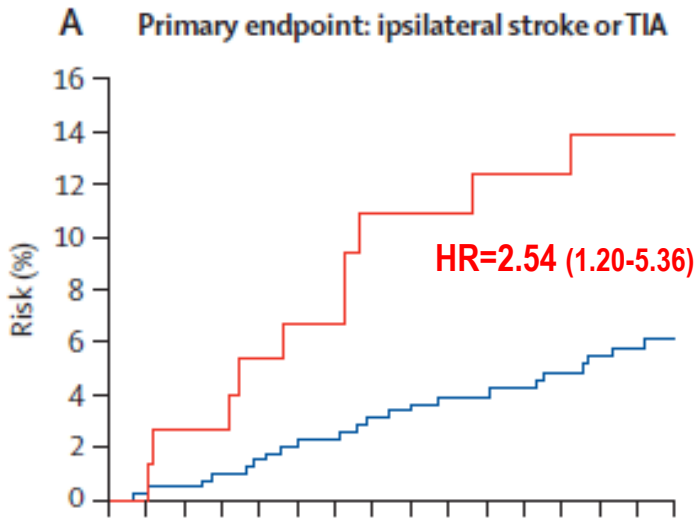


Sténose carotide asymptomatique

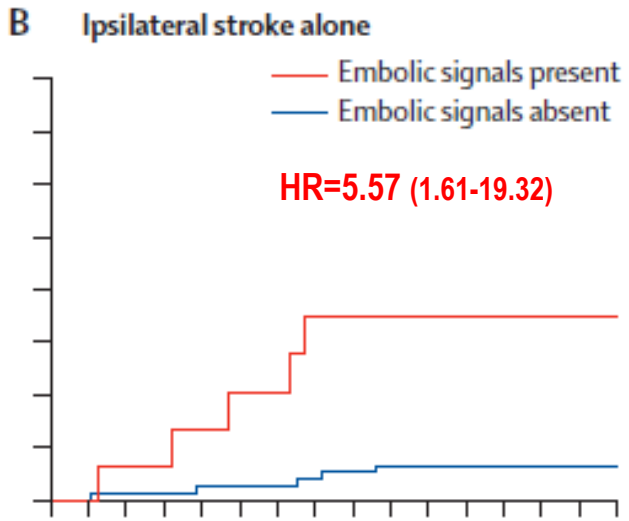
Microsignaux emboliques au DTC

Markus et al, Lancet Neurol 2010

- 482 patients with >=70% asymptomatic carotid stenosis
- 1 h TCD recordings from the ipsilateral MCA at baseline and at 6,12, and 18 months.
- Follow-up 2 years
- Embolic signals in 77 of 467 (16.5%) patients at baseline.



- Absolute annual risk
  - ES + = 7·13%
  - ES - = 3·04%

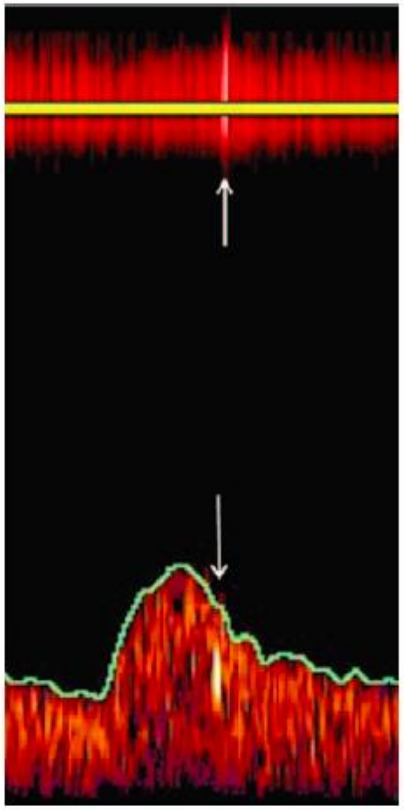


- Absolute annual risk
  - ES + = 3.62%
  - ES - = 0.70%

Sténose carotide asymptomatique

Microsignaux emboliques au DTC

Markus et al, Lancet Neurol 2010



	Embolic signals present	Embolic signals absent	Weight (%)	Odds ratio (95% CI)
Ipsilateral stroke				
Abbott[16]	2/60	4/171	20·2%	1·44 (0·26–8·07)
Molloy[21]	1/12	0/30	6·3%	7·96 (0·30–209·70)
Orlandi[22]	3/6	0/15	6·7%	31·00 (1·29–747·03)
Siebler[23]	1/8	1/56	8·1%	7·86 (0·44–140·14)
Spence[15]	5/32	3/287	25·8%	17·53 (3·97–77·38)
Subtotal	**12/118**	**8/559**	**67·0%**	**7·46 (2·24–24·89)**
Heterogeneity: τ^2=0·54; χ^2=6·62, df=4 (p=0·23); I^2=29%				
Test for overall effect: Z=3·27 (p=0·001)				
ACES	5/77	5/390	33·0%	5·35 (1·51–18·94)
Total	**17/195**	**13/949**	**100·0%**	**6·63 (2·85–15·44)**
Heterogeneity: τ^2=0·15; χ^2=5·74, df=5 (p=0·33); I^2=13%				
Test for overall effect: Z=4·38 (p<0·0001)				

0·001 0·1 1 10 1000

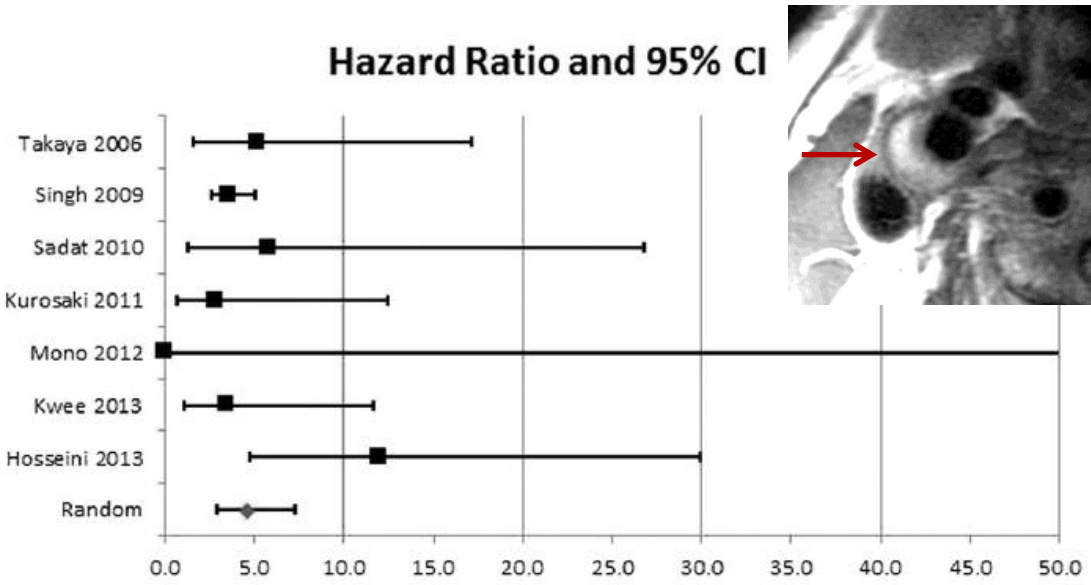
Sténose carotide asymptomatique

Hémorragie intraplaque en IRM-HR

Gupta et al, Stroke 2013

- Meta-analysis: 7 studies, 678 patients, 702 carotid arteries, mean follow-up of 20.2 months

	Study Name	HR	Lower Limit	Upper Limit	P-Value
All IPH Studies	Takaya 2006	5.20	1.581	17.153	0.007
	Singh 2009	3.59	2.561	5.05	<0.01
	Sadat 2010	5.85	1.286	26.794	0.022
	Kurosaki 2011	2.83	0.644	12.425	0.168
	Kwee 2013	3.50	1.043	11.684	0.043
	Hosseini 2013	12.00	4.762	29.943	<0.01
	Mono 2013	0.03	0.000	86.6	0.999
	Random	**4.59**	**2.92**	**7.24**	**<0.01**



Sténose carotide asymptomatique
Conclusions

- Le risque d'infarctus cérébral chez les patients ayant une sténose carotide asymptomatique traitée médicalement a diminué au cours des 20 dernières années. Il est actuellement beaucoup plus faible que celui observé dans les essais cliniques randomisés.
- La question de la valeur ajoutée d'une revascularisation carotide chez les patients recevant un traitement médical optimal doit être résolue par de nouveaux essais randomisés comparant les patients recevant un traitement optimal seul à ceux ayant en plus une revascularisation carotide.
- En attendant les résultats de ces essais, la décision d'une revascularisation carotide doit être individualisé et prendre en compte la présence de facteurs de risque d'infarctus cérébral ipsilatéral, l'espérance de vie du patient, le risque d'AVC périprocédural et les préférences du patient.

Sténose carotide asymptomatique

Une revascularisation carotide est-elle plus efficace qu'un traitement médical optimal?

→ **Essais thérapeutiques en cours**

Si une revascularisation est jugée nécessaire

- Chirurgie : meilleure option dans la majorité des cas

- Homme > femme
- < 75 ans, espérance de vie > 5-10 ans
- Progression de la sténose > degré de sténose
- Diminution de la réserve circulatoire
- Infarctus silencieux
- Signaux microemboliques au DTC
- Composition de la plaque (IRM,US, …)

ACTRIS

ENDARTERECTOMY COMBINED WITH OPTIMAL MEDICAL THERAPY

VERSUS OPTIMAL MEDICAL THERAPY ALONE

IN PATIENTS WITH **A**SYMPTOMATIC SEVERE ATHEROSCLEROTIC

CAROTID ARTERY S**T**ENOSIS

AT HIGH **R**ISK OF **I**PSILATERAL **S**TROKE

ACTRIS
Objectives

- **Primary objective**
  - To assess whether carotid endarterectomy combined with optimal medical therapy improves long-term survival free of ipsilateral stroke (or periprocedural stroke or death) when compared with optimal medical therapy alone.
- **Secondary objectives**
  - To assess differences between groups with regard to risks of any stroke (or periprocedural death), any disabling or fatal stroke (or periprocedural death), any stroke or death, myocardial infarction, cardiovascular death, symptomatic and asymptomatic lesions on brain MRI at 2 years, disability, cognitive impairment, health-related quality of life and depression.
  - To assess to what extent medical treatment objectives can be achieved and identify factors associated with goals achievement.

ACTRIS

Main inclusion criteria

- Age 50 years or over
- No ipsilateral stroke or TIA within 180 days of randomisation
- Atherosclerotic carotid stenosis between 60 and 99% (NASCET method)
- At least one of the following:
  - TCD-detected microembolic signals
  - Impairment of TCD-measured cerebral vasomotor reserve
  - Intraplaque haemorrhage on magnetic resonance imaging
  - Rapid stenosis progression
- High probability to live at least 5 years

Eur J Vasc Endovasc Surg (2011) 41, 150–152

EDITORIAL

Just When We Thought We Knew All the Answers, Someone Changed the Questions!

AR Naylor

"The purpose of art is to lay bare the questions that have been hidden by the answers"

James Baldwin (1924-1987)