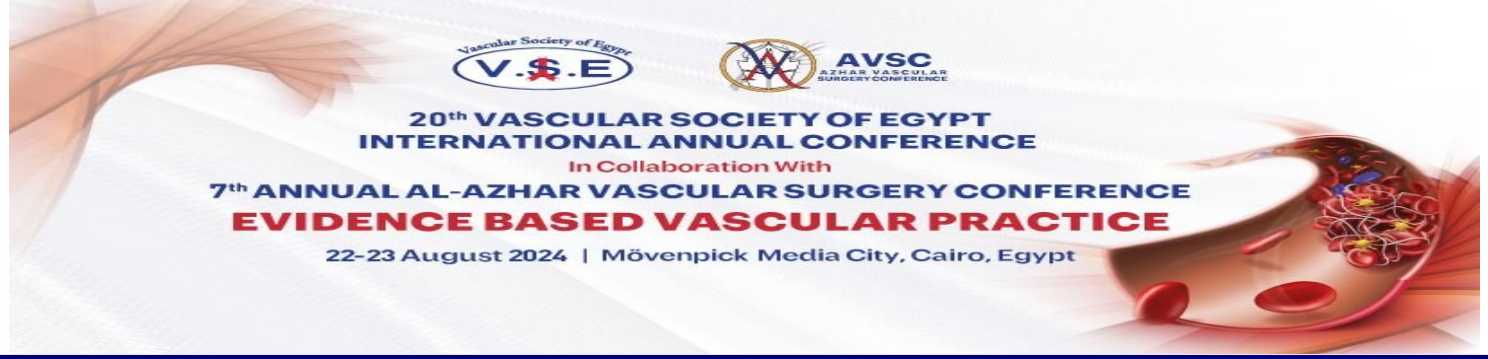

Is Intervention In Asymptomatic Carotid Stenosis Justified: Review Of Current Evidence

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WORLD NEUROSURGERY :JULY 2016

Natural History of Asymptomatic Moderate Carotid Artery Stenosis in the Era of Medical Therapy

Yang-Jin Park[1,4], Dong-Ik Kim[1,4], Gyeong-Moon Kim[2,4], Duk-Kyung Kim[3,4], Young-wook Kim[1,4]

OBJECTIVE: **To determine the incidence and risk factors of carotid stenosis progression in patients with asymptomatic moderate carotid artery stenosis (CAS).**

METHODS: **Patients with asymptomatic moderate CAS in duplex ultrasound (DUS) were identified from 2003 to 2008, and only those with more than 1 DUS were included during a**

carotid stenosis progression and development of INS were 63.5% ± 5.3% and 98.1% ± 1.4%, respectively, with no difference from those of statin. There was no significant predictor of carotid stenosis progression, and it was not significantly associated with development of INS. The 5-year actuarial patient survival and symptom-free survival were 95.3% ± 2.7 and 93.4% ± 3.0%, respectively, with no difference from those of statin. The only independent predictor of death and INS/death was a remote history of INS (hazard ratio 18.166, $P = 0.021$, hazard ratio 4.840, $P = 0.046$).

CONCLUSIONS: **The incidence of carotid stenosis progression in asymptomatic moderate CAS was high even in popular use of aspirin and statin. Although development of INS was not associated with carotid stenosis progression, it was a risk factor of long-term morbidity and survival.**

CONCLUSIONS: The incidence of carotid stenosis progression in asymptomatic moderate CAS was high even in use of aspirin and statin.

…se of CAS) …rtant …een a …s an …ears.[3] …s not … the prevalence of asymptomatic, moderate-to-severe CAS (50%–99%) was 3.1% for patients aged ≥65 years participating in a health-screening program and 14.7% for patients with peripheral vascular disease.[4,5]

In contemporary practice, the practice guidelines currently support carotid endarterectomy (CEA) as the treatment in asymptomatic CAS patients with a severity greater than 70%, who demonstrate an estimated perioperative morbidity and mortality risk of 3%.[6,7] Recently, there is emerging evidence in favor of aggressive medical management that reduces the compelling indications for CEA/stenting in asymptomatic populations.[8] The best medical therapy includes smoking cessation, antiplatelet therapy, control of hypertension and diabetes, and lipid reduction with statin.[6] Although there is no current guideline

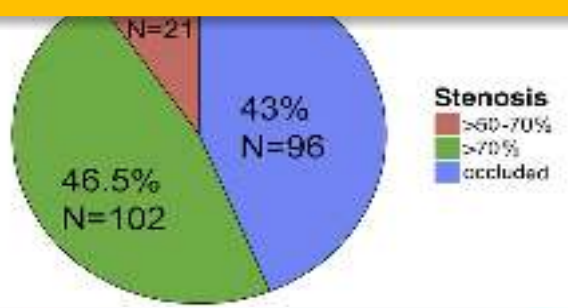
Previously Asymptomatic Patients Presenting with Carotid-Related Stroke

Retrospective, single center study

219 patients

7%

219 of 3382 stroke patients had previously



Medical Therapy on Admission

35% **Both**

Conclusion

Asymptomatic patients on medical

- are still at risk of having carotid related stroke

Conclusion: medical therapy alone is unlikely to be sufficient stroke prevention for patients with significant asymptomatic carotid stenosis

JVS Journal of Vascular Surgery
Official Publication of the Society for Vascular Surgery

Klarin et al. *J Vasc Surg November 2018*

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J Vasc Sur; 2020

Asymptomatic carotid stenosis is associated with mobility and cognitive dysfunction and heightens falls in older adults

Vicki L. Gray, PhD,[a] Andrew P. Goldberg, MD,[b] Mark W. Rogers, PhD,[a] Laila Anthony, BS,[c,d] Michael L. Terrin, MD, CM, MPH,[e] Jack M. Guralnik, MD, PhD,[f] William C. Blackwelder, PhD,[g] Diana F. H. Lam, PhD,[f] Siddhartha Sikdar, PhD,[h] *and* Brajesh K. Lal, MD,[c,d] *Baltimore, Md; and Fairfax, Va*

Conclusion: ACAS is associated with impaired mobility and cognition that are accompanied with increased fall risk. These impairments increased with increase severity of ICA stenosis.

State Examination). Falls were recorded for the past 6 months. Standardized carotid ultrasound examination classified participants into no stenosis (<50% diameter reduction) (n = 54), moderate stenosis (50%-69%) (n = 17), and high-grade stenosis (70%-99%) (n = 9) groups. Linear and logistic regression analyses determined the associations between these measures and the degree of stenosis (three groups).

Results: Logistic regression analysis showed their degree of stenosis was associated with reductions in mobility (Short Physical Performance Battery [$P = .008$], Berg Balance Scale [$P = .0008$], Four Square Step Test [$P = .005$], DGI [$P = .0001$], TUG [$P = .0004$], gait speed [$P = .02$]), perceived physical function (ABC [$P < .0001$], SF-12 Physical Function Component [$P < .0001$]), and cognition (MMSE [$P = .003$]). Adults with moderate- and high-grade stenosis had a greater incidence of falls compared with those without stenosis (relative risk, 2.86; $P = .01$). Results remained unchanged after adjustment for age, sex and cardiovascular risk factors.

Conclusions: ACAS is associated with impaired mobility and cognition that are accompanied with increased fall risk. These impairments increased with worsening severity. (J Vasc Surg 2020;71:1930-7.)

Guidelines

- Europian society of vascular surgery (ESVS): 2017/2023

Management of Atherosclerotic Carotid and Vertebral Artery Disease: 2017 Clinical Practice Guidelines of the European Society for Vascular Surgery (ESVS)

Writing Group [a], A.R. Naylor, J.-B. Ricco, G.J. de Borst, S. Debus, J. de Haro, A. Halliday, G. Hamilton, J. Kakisis, S. Kakkos, S. Lepidi, H.S. Markus, D.J. McCabe, J. Roy, H. Sillesen, J.C. van den Berg, F. Vermassen, ESVS Guidelines Committee [b], P. Kolh, N. Chakfe, R.J. Hinchliffe, I. Koncar, J.S. Lindholt, M. Vega de Ceniga, F. Verzini, ESVS Guideline Reviewers [c], J. Archie, S. Bellmunt, A. Chaudhuri, M. Koelemay, A.-K. Lindahl, F. Padberg, M. Venermo

Keywords: Carotid, Vertebral, Stroke, Transient ischaemic attack, Endarterectomy, Stenting, Medical therapy, Screening, Dementia, Asymptomatic, Symptomatic, Thrombolysis, Imaging, Bypass, Surgical techniques, Complications, Patch infection, Restenosis

- Society For Vascular Surgery: 2022

Society for Vascular Surgery clinical practice guidelines for management of extracranial cerebrovascular disease

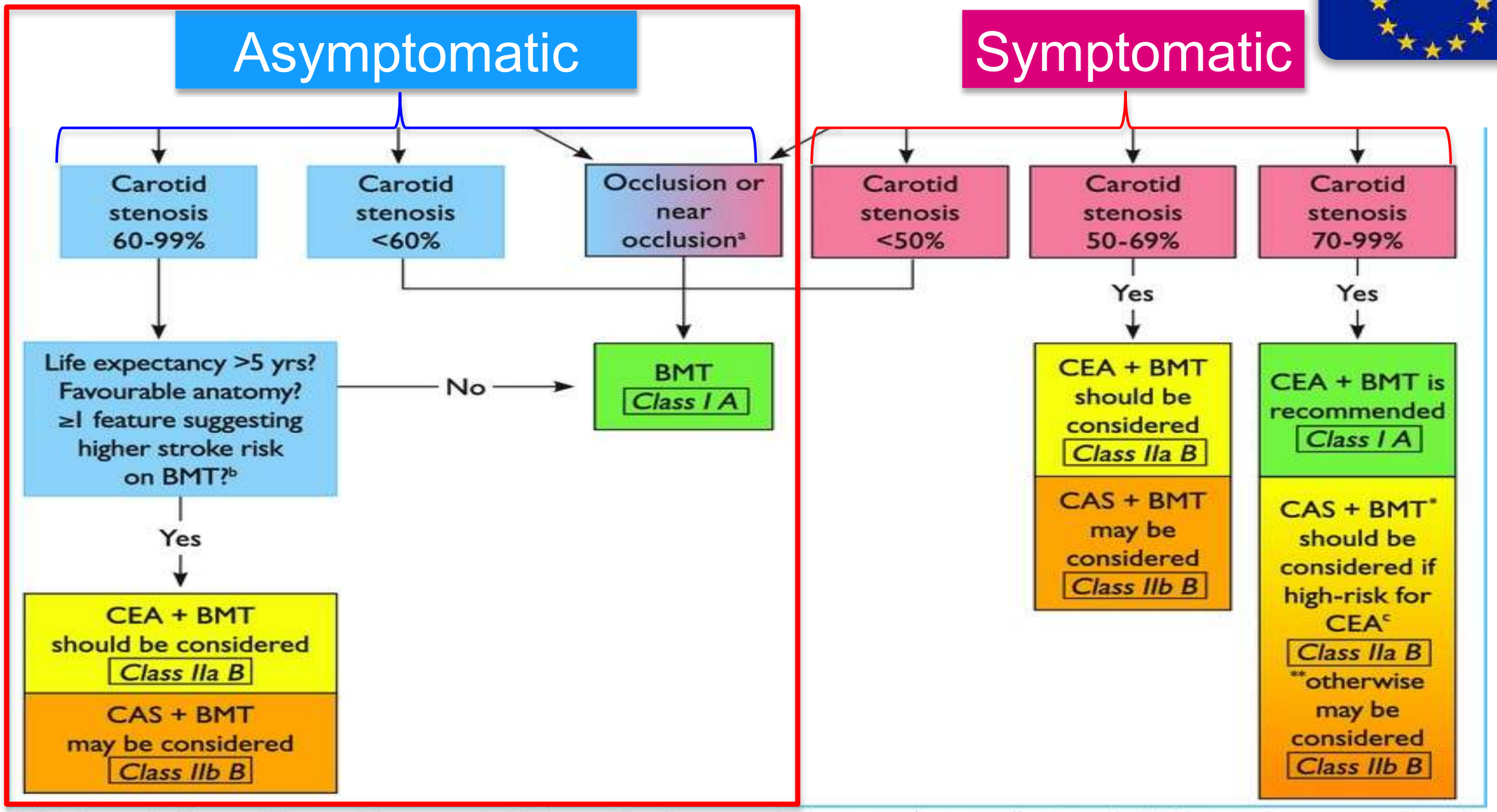
Ali F. AbuRahma, MD,[a] Efthymios D. Avgerinos, MD, PhD,[b] Robert W. Chang, MD,[c] R. Clement Darling III, MD,[d] Audra A. Duncan, MD,[e] Thomas L. Forbes, MD,[f] Mahmoud B. Malas, MD, MHS,[g] Mohammad Hassan Murad, MD, MPH,[h] Bruce Alan Perler, MD, MBA,[i] Richard J. Powell, MD,[j] Caron B. Rockman, MD,[k] and Wei Zhou, MD,[l] *Charleston, WVa; Pittsburgh, Pa; San Francisco and La Jolla, Calif; Albany and New York, NY; London and Toronto, Ontario, Canada; Rochester, Minn; Baltimore, Md; Lebanon, NH; and Tucson, Ariz*

ABSTRACT

Management of carotid bifurcation stenosis in stroke prevention has been the subject of extensive investigations, including multiple randomized controlled trials. The proper treatment of patients with carotid bifurcation disease is of major interest to vascular surgeons and other vascular specialists. In 2011, the Society for Vascular Surgery published guidelines for the treatment of carotid artery disease. At the time, several randomized trials, comparing carotid endarterectomy (CEA) and carotid artery stenting (CAS), were reported. Since the 2011 guidelines, several studies and a few systematic reviews comparing CEA and CAS have been reported, and the role of medical management has been reemphasized. In the present publication, we have updated and expanded on the 2011 guidelines with specific emphasis on five areas: (1) is CEA recommended over maximal medical therapy for low-risk patients; (2) is CEA recommended over transfemoral CAS for low surgical risk patients with symptomatic carotid artery stenosis of >50%; (3) the timing of carotid intervention for patients presenting with acute stroke; (4) screening for carotid artery stenosis in asymptomatic patients; and (5) the optimal sequence of intervention for patients with combined carotid and coronary artery disease.

A separate implementation document will address other important clinical issues in extracranial cerebrovascular disease. Recommendations are made using the GRADE (grades of recommendation assessment, development, and evaluation) approach, as was used for other Society for Vascular Surgery guidelines. The committee recommends CEA as the first-line treatment for symptomatic low-risk surgical patients with stenosis of 50% to 99% and asymptomatic

(ESVS) 2017/2023



Features associated with increased risk of stroke in patients with ACS treated medically

Clinical[a]	• Contralateral TIA/stroke[121]
Cerebral imaging	• Ipsilateral silent infarction[122]
Ultrasound imaging	• Stenosis progression (> 20%)[123] • Spontaneous embolization on transcranial Doppler (HITS)[124] • Impaired cerebral vascular reserve[125] • Large plaques[b][126] • Echolucent plaques[96] • Increased juxta-luminal black (hypoechogenic) area[127]
MRA	• Intraplaque haemorrhage[128] • Lipid-rich necrotic core

J Vasc Surg 2022

Society for Vascular Surgery clinical practice guidelines for management of extracranial cerebrovascular disease

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A separate implementation document will address other important clinical issues in extracranial cerebrovascu disease. Recommendations are made using the GRADE (grades of recommendation assessment, development, a evaluation) approach, as was used for other Society for Vascular Surgery guidelines. The committee recommends C as the first-line treatment for symptomatic low-risk surgical patients with stenosis of 50% to 99% and asymptoma patients with stenosis of 70% to 99%. The perioperative risk of stroke and death in asymptomatic patients must be <3 to ensure benefit for the patient. In patients with recent stable stroke (modified Rankin scale score, 0-2), caro revascularization is considered appropriate for symptomatic patients with >50% stenosis and should be performed soon as the patient is neurologically stable after 48 hours but definitely <14 days after symptom onset. In the gene population, screening for clinically asymptomatic carotid artery stenosis in patients without cerebrovascular sympto or significant risk factors for carotid artery disease is not recommended. In selected asymptomatic patients with increased risk of carotid stenosis, we suggest screening for clinically asymptomatic carotid artery stenosis as long as t patients would potentially be fit for and willing to consider carotid intervention if significant stenosis is discovered. F patients with symptomatic carotid stenosis of 50% to 99%, who require both CEA and coronary artery bypass grafti we suggest CEA before, or concomitant with, coronary artery bypass grafting to potentially reduce the risk of stro and stroke/death. The sequencing of the intervention depends on the clinical presentation and institutio experience. (J Vasc Surg 2022;75:4S-22S.)

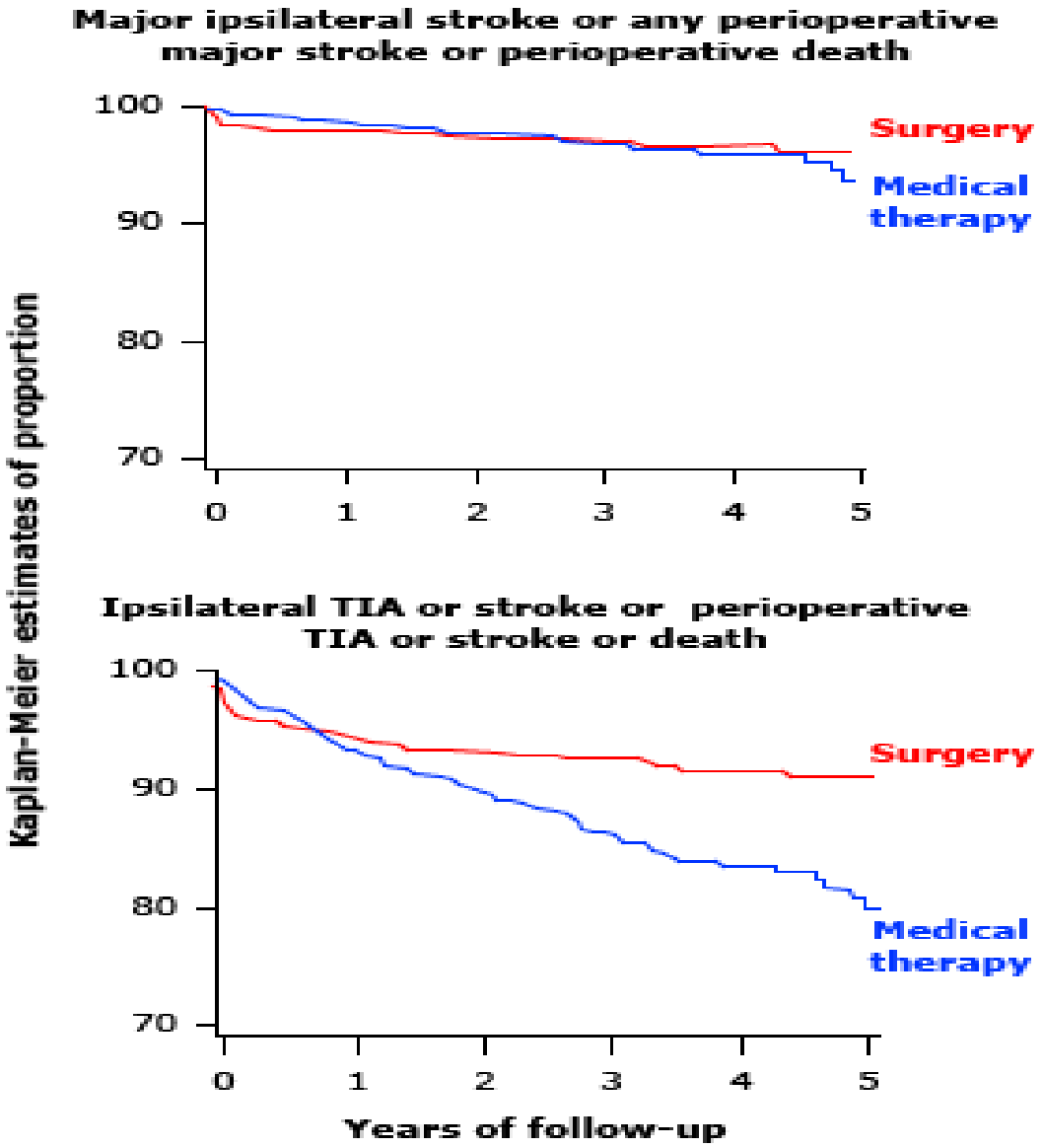
Two Main RCT for CEA vs Medical for Asymptomatic ICA

- Asymptomatic Carotid Artery Study (ACAS) 1995 with update 2004

- Asymptomatic Carotid Surgery Trial (ACST) & (ACST1)

ACAS, 1995

- Asymptomatic Carotid Artery Study
  - ✓ Prospective randomized trial
  - ✓ 39 sites in the US and Canada
  - ✓ 5 years follow up (1987-1993)
  - ✓ 1662 patients with asymptomatic carotid artery stenosis 60% or greater
  - ✓ Daily aspirin administration and medical risk factor management for all patients
  - ✓ Medical vs. carotid endarterectomy



There was no difference between the two groups in the incidence of major stroke or death

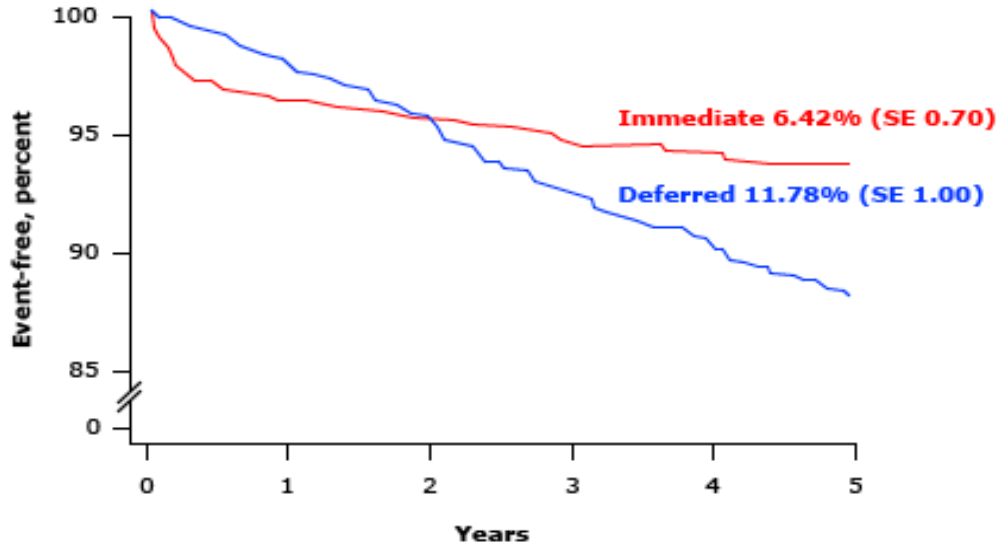
The incidence of any ipsilateral TIA or stroke or death was lower in the surgical group ($p = 0.004$)

Conclusion

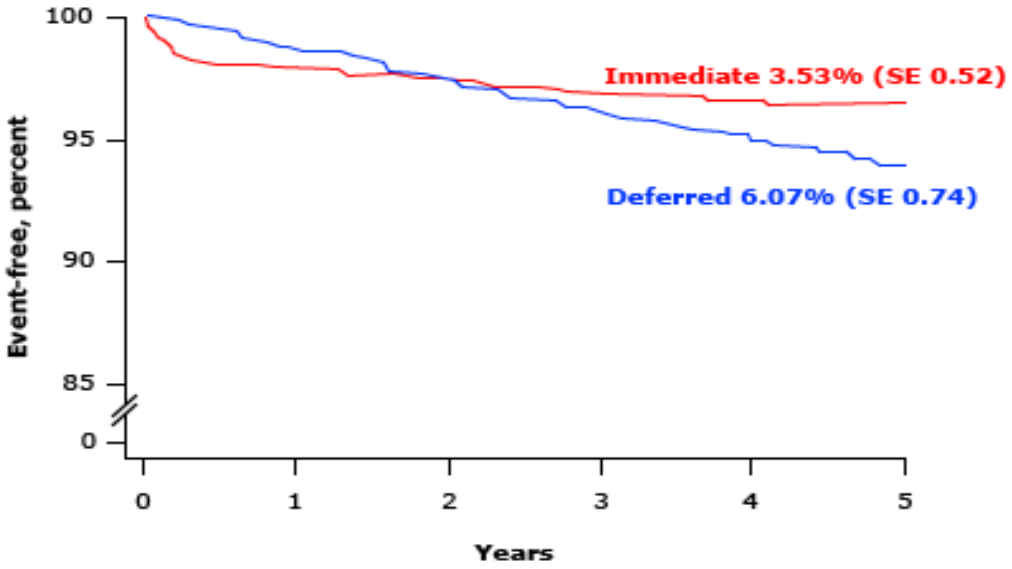
- CEA reduces the risk of any stroke or death from 11% to 5% at five years in patients with asymptomatic stenosis of ≥ 60% . Reduction 53%
- The ACAS recommended CEA for patients aged <80 years as long as the expected combined stroke and mortality rate for the individual surgeon <3%.

ACST Trial

- RCT assigned 3120 patients with ≥60 percent asymptomatic carotid stenosis to immediate CEA vs medical therapy.
- 5 years of follow-up (1993 and 1998)
- That trial also showed an advantage in limiting stroke and death at 5 years for CEA compared with maximal medical therapy (4.1% vs 10.0%)



5 years risk for all strokes in the CEA group was reduced by half compared with the CEA deferral group



5 years risk for fatal or disabling strokes in the CEA group was reduced by half compared with the CEA deferral group

Lancet , 2010

10-year stroke prevention after successful carotid endarterectomy for asymptomatic stenosis (ACST-1): a multicentre randomised trial

*Alison Halliday, Michael Harrison, Elizabeth Hayter, Xiangling Kong, Averil Mansfield, Joanna Marro, Hongchao Pan, Richard Peto, John Potter, Kazem Rahimi, Angela Rau, Steven Robertson, Jonathan Streifler, Dafydd Thomas, on behalf of the Asymptomatic Carotid Surgery Trial (ACST) Collaborative Group**

Summary

Conclusions:

- CEA for asymptomatic patients reduces 10-year stroke risks (17.9% vs 13.3%, gain 4·6%).
- Half this reduction is in disabling or fatal strokes.

…gical …long- …ually, …finite …years …) and …This …The proportions operated on while still asymptomatic were 89·7% versus 4·8% at 1 year (and 92·1% *vs* 16·5% at 5 years). Perioperative risk of stroke or death within 30 days was 3·0% (95% CI 2·4–3·9; 26 non-disabling strokes plus 34 disabling or fatal perioperative events in 1979 CEAs). Excluding perioperative events and non-stroke mortality, stroke risks (immediate *vs* deferred CEA) were 4·1% versus 10·0% at 5 years (gain 5·9%, 95% CI 4·0–7·8) and 10·8% versus 16·9% at 10 years (gain 6·1%, 2·7–9·4); ratio of stroke incidence rates 0·54, 95% CI 0·43–0·68, p<0·0001. 62 versus 104 had a disabling or fatal stroke, and 37 versus 84 others had a non-disabling stroke. Combining perioperative events and strokes, net risks were 6·9% versus 10·9% at 5 years (gain 4·1%, 2·0–6·2) and 13·4% versus 17·9% at 10 years (gain 4·6%, 1·2–7·9). Medication was similar in both groups; throughout the study, most were on antithrombotic and antihypertensive therapy. Net benefits were significant both for those on lipid-lowering therapy and for those not, and both for men and for women up to 75 years of age at entry (although not for older patients).

Interpretation Successful CEA for asymptomatic patients younger than 75 years of age reduces 10-year stroke risks. Half this reduction is in disabling or fatal strokes. Net benefit in future patients will depend on their risks from unoperated carotid lesions (which will be reduced by medication), on future surgical risks (which might differ from those in trials), and on whether life expectancy exceeds 10 years.

What about lipid-lowering medication

- The strength of these conclusions has been questioned that the medical therapy arm did not reflect contemporary medical management (statin)
- ACST-1 showed that the stroke risk with CEA plus MT was nearly half that of MT alone, irrespective of whether patients were receiving lipid-lowering drugs or not.
  - ✓ 0.7% vs 1.3% annually, (P < .0001) for those on lipid-lowering drugs
  - ✓ 1.8% vs 3.3% annually (P < .0001) for those not on lipid lowering drugs.

Best medical treatment alone may not be adequate for all patients with asymptomatic carotid artery stenosis

Kosmas I. Paraskevas, MD, PhD,[a] Frank J. Veith, MD, FACS,[b,c] *and* Jean-Baptiste Ricco, MD, PhD, FEBVS,[d]
London, United Kingdom; New York, NY; Cleveland, Ohio; and Poitiers, France

Journal of Vascular Surgery, 2018

- Not all pts with ACS carry the same risk of stroke.
- Not all "Asymptomatic" patients are truly asymptomatic
  - ✓ patient suffering TIA while asleep may have no symptoms the following day and will be considered asymptomatic
  - ✓ ACS is associated with cognitive decline:
    - There is evidence that cognitive function improves after CEA or CAS, whereas there is no improvement with MT

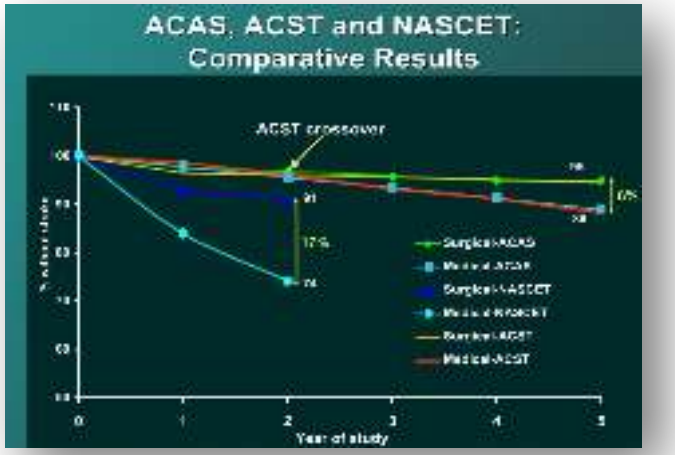
Society for Vascular Surgery clinical practice guidelines 2022

- In low surgical risk patients with asymptomatic carotid bifurcation atherosclerosis and stenosis of >70% , we recommend CEA with best medical therapy over maximal medical therapy alone for the long-term prevention of stroke and death

(grade IB)

Factors influencing outcome

- Delay to benefit :
  - ✓ long-term investment , approximately two years after surgery.
- Perioperative complications
  - ✓ The perioperative stroke and death rate is <3 percent.
- Sex : Male get better benefit ?



The 10-year data from ACST-1 found a similar benefit for the outcome of any stroke or perioperative death for males and females <75 years of age (males: ARR 5.5 %; females: ARR 5.8%).

Still in Doubt ????

patients with ACS who have a high risk of ischemic stroke :

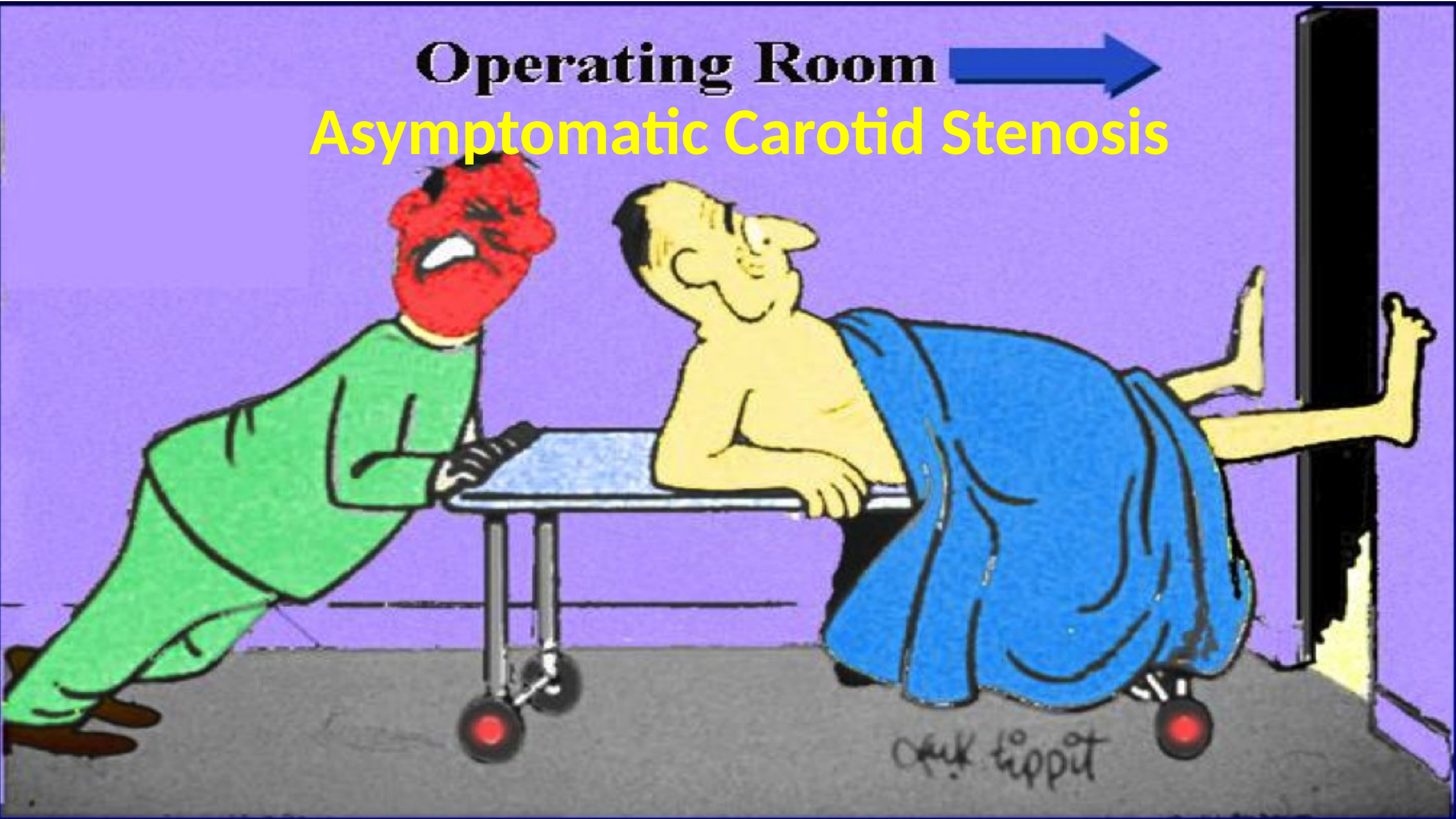
- Severe carotid stenosis >80%
- Progression of the carotid stenosis (twice the risk)
- Asymptomatic embolism detected on transcranial Doppler ultrasound(TCD)
- Ipsilateral silent embolic infarcts on CTA / MRI
- Carotid plaque morphology
  - ✓ Carotid plaque ulceration : > 3 increase the risk of stroke at 3 years
  - ✓ Large plaque area
  - ✓ Plaque echolucency or hypoechoic on US
  - ✓ Intraplaque hemorrhage on MRI
- Reduced cerebral blood flow reserve

Patients unlikely to benefit from revascularization

- Severe comorbidity due to other medical or surgical illnesses that increase their perioperative risk
- Limited life expectancy
- Prior disabling ipsilateral stroke
- Patients with total occlusion of the internal carotid artery

Conclusion

- Patient with >70% asymptomatic carotid stenosis should be considered for CEA, TCAR, or TF-CAS to decrease long-term risk of stoke
  - ✓ Patient has 3-5 yers life expectency
  - ✓ Periop stroke / Death rates < 3%
- Determination which technique based on presence / absence of high risk criteria for CEA, TCAR, or TF-CAS
- Upcoming randomized trials to answer role of modern pharmacological RX in management of Asx carotid stenosis:
  - ✓ SPACE-II
  - ✓ CREST 2


Operating Room
Asymptomatic Carotid Stenosis


Thank You For Your
Attention