2017 MID-ATLANTIC
CONFERENCE

7th ANNUAL CURRENT CONCEPTS IN
VASCULAR THERAPIES

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65 yo Man With High Grade, Asymptomatic Carotid Stenosis: The Case for CEA

CEA vs CAS

- No disclosures

Current Concepts in Vascular Therapies 2017

- The given Scenario:
  - 65 yo Male presents to your primary care office with no symptoms of any adverse neurologic sequelae, but on routine exam you find a carotid bruit.
  - Has htn, chol, prior smoker. Appropriate screening study is ordered: Carotid Duplex
  - This shows 80% right ica stenosis; what now?

Why worry about ICA stenoses and its role in stroke?

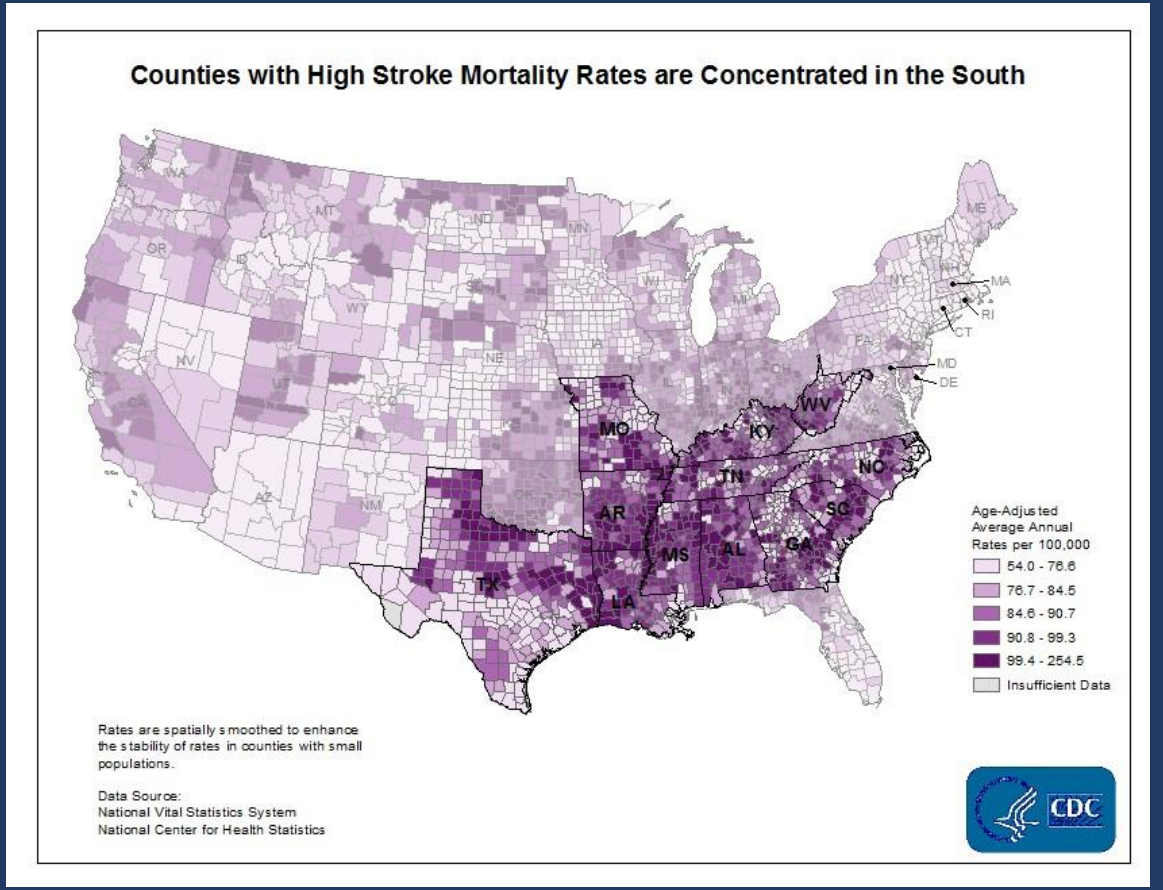
- Historical perspective on stroke:

Stroke kills >170K Americans each year (5th leading cause of death)

- 87% of all strokes are ischemic (up to 20% ICA etiology)

795K strokes annually in the U.S.. . 610K of these are first time strokes

- Stroke costs the U.S. an estimated 41$ billion annually



Internal Carotid Artery Stenosis

- Natural History of ICA stenosis:
  - Asymptomatic: Annual rate of unheralded stroke ipsilateral to hemodynamically significant (>50%) extracranial carotid artery stenosis: 1-2%[1]
  - Symptomatic: For patients enrolled in NASCET (659 pts, hemispheric tia or retinal event/nondisabling cva and stenosis >70%, ipsilateral), 2 yr stroke risk was 26% in the medical arm (i.e. natural history)
  - This is the history behind and impetus provided to act to avoid a preventable catastrophic event; the vascular surgery version of primary care/prevention

1) Inzitari D. The causes and risk of stroke in patients with asymptomatic internal carotid artery stenosis. NASCET collaborators, NEJM 2000; 342:1693.

Carotid Stenosis: Incidence

- Prevalence of carotid atherosclerosis:
  - Incidence of ipsilateral stroke in the presence of >50% ICA stenosis is approximately 0.5-1%/yr[1]
  - Incidence of >50% luminal compromise by age and sex[2]
    - <50 yo: men 0.2% women 0%
    - >80 yo: men 7.5% women 5%
  - the number of Americans >65yo :
    - By 2016: 46 million
    - By 2060: 98 million

1) Spence, JD, et al. Management of asymptomatic carotid stenosis. Neurol Clin 2015; 33:443.
2) de Weerd. et al. Prevalence of asymptomatic carotid artery stenosis in the general population: an individual participant data meta-analysis. Stroke 2010; 41:1294.

Therapeutic Options

- Treatment options:
  - Optimal Medical therapy (OMT): statins, htn control, asa, DM control, tobacco cessation, lifestyle changes, etc..
  - Surgical therapy:
    - Carotid endarterectomy (CEA)
    - Carotid stent (CAS)

CEA: A Historical Perspective

- A Brief History of CEA and its role in stroke risk reduction:
  - First done in the U.S. by Dr. Michael Debakey, 1953, Methodist Hospital, Houston.
  - No trial for years positively established the role of surgical intervention vs. best medical therapy until NASCET, August 1991.
  - NASCET: a RCT, best medical therapy (ASA) vs. CEA for patients with symptomatic event and angiographically confirmed high grade (70-99%) ica stenosis.
  - Demonstrated a highly beneficial effect of CEA for patients with 70-99% stenosis, modest benefit for patients 50-69% stenosis

CEA (for symptomatic patients)

- NASCET results:
  - Reduction in cumulative risk of any ipsilateral stroke at two years from 26% in the medical arm (n=331), down to 9% in the CEA arm (n=328)
  - Reduction in major or fatal ipsilateral stroke, from 13.1% to 2.5%
  - For those with >70% stenosis, number needed to treat (NNT) to prevent one stroke over five years for this group was 6.3, with an absolute RR of 16%
  - For those with 50-69%, NNT was 22, with an ARR of 4.6%.
  - The study was compelling enough that was halted at mean of 18 months follow up due to the diverging outcomes of medical vs. surgical therapy

CEA

- With success with symptomatic patients, what about reduction of risk for asymptomatic patients, to avoid irreversible CVA events?
  - 3 high quality RCT (for aysmptomatic ICA stenosis):
    - Veterans Affairs Cooperative Study Group (VA Trial)[1]
    - Asymptomatic Carotid Atherosclerosis Study (ACAS)[2]
    - Asymptomatic Carotid Surgery Trial (ASCT)[3]

1) Hobson, RW, et al. Efficacy of carotid endarterectomy for asymptomatic carotid stenosis. The Veterans Affairs Cooperative Study Group. NEJM 1993, 328:221.
2) Endarterectomy for asymptomatic carotid artery stenosis. Executive Committee for the Asymptomatic Carotid Atherosclerosis Study. JAMA 1995; 273:1421.
3) Halliday A, et al. Prevention of disabling and fatal strokes by successful carotid endarterectomy in patients without recent neurological symptoms: randomised controlled trial. Lancet 2004; 363:1491

CEA for asymptomatic patients

- VA trial:
  - N=444, 50-99% stenosis, asymptomatic (asa vs. asa and CEA)
  - At four years:
    - lower incidence of stroke or tia (8% versus 20.6%)
    - Nonsignificantly lower incidence of ipsilateral stroke (4.75 vs. 9.4%)
    - No difference in combined stroke and death rate at 30 days or 4 yrs
    - Absolute risk reduction (ARR) for stroke of 1% over four years
- ACAS:
  - N=1662 (40-79 y.o.), 60-99% asymptomatic (asa vs. asa and CEA)
  - Median follow up 2.7 years:
    - Lower incidence of ipsilateral stroke and any perioperative stroke or death rate was significantly lower in the surgical group vs. ASA alone (5% vs. 11%)
    - Incidence of major ipsilateral stroke, major perioperative stroke, and death was lower in the surgical group compared with ASA alone, but not statistically significant (3.4% vs. 6%)
    - ARR was 3.0% over 2.7 years

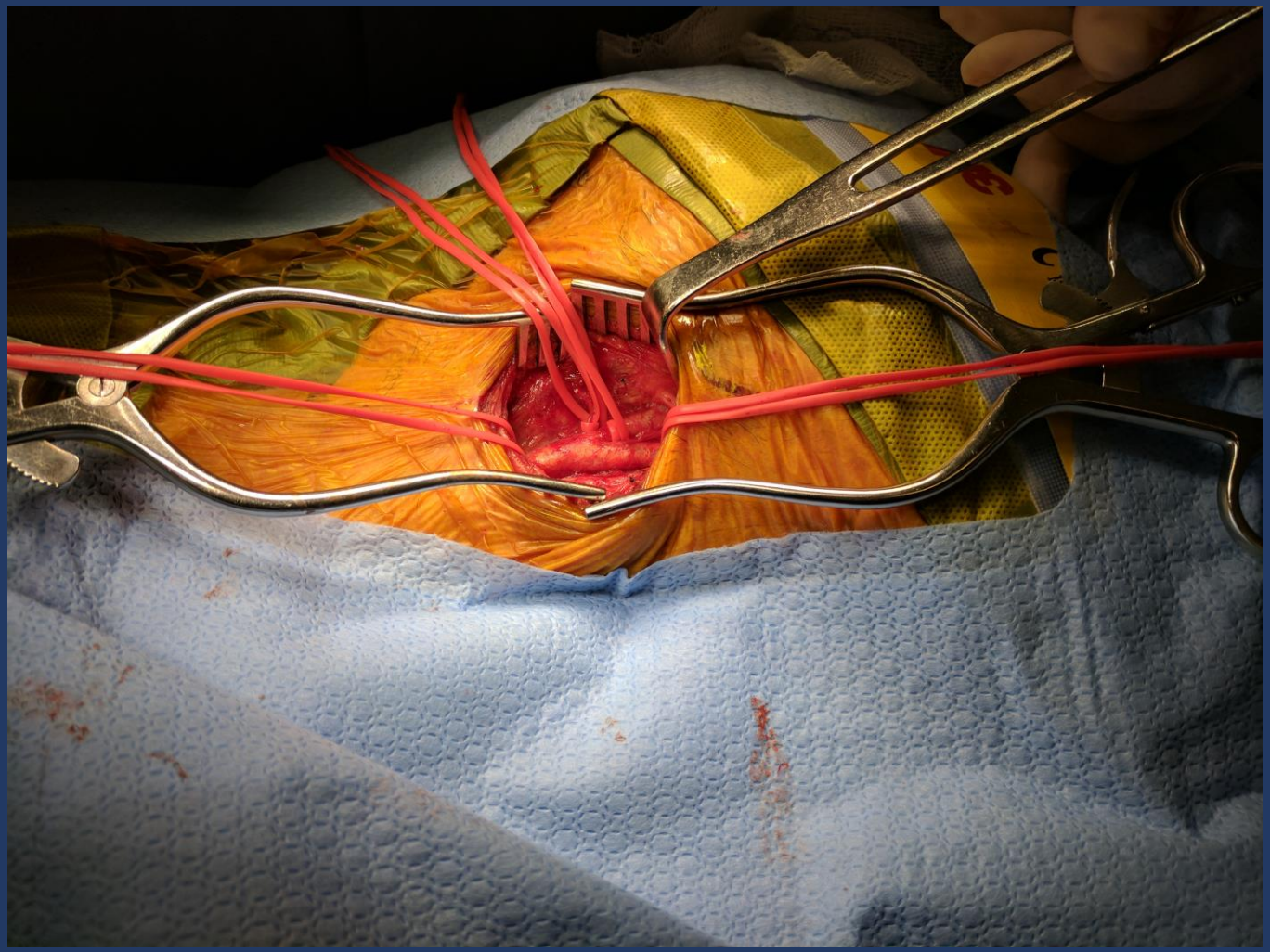
CEA (for asymptomatic patients)

- ACST trial:
  - N=3120, enrolled over 1993-2003, ages 40-91, >60% asymptomatic stenosis to either (A) immediate CEA (goal of one month, 88% were done within one year) vs. (B) CEA for symptoms if they occurred (of this latter group,~4%/yr subsequently received CEA)
  - At mean of 3.4 years:
    - CEA had perioperative risk of stroke or death of 3.1% within 30 days
    - Net 5 yr risk for all strokes or perioperative death was reduced by half (6.4% vs. 11.8%)
    - Similar benefit for fatal or disabling stroke (3.5% vs. 6.1%)
    - Benefit of CEA was statistically significant for patients <75 y.o.
    - Benefit of CEA was statistically significant as well for contralateral strokes (not just ipsilateral)
    - Net benefit manifested >2 years after surgery (surgical risk up front, benefit later, with natural history of asymptomatic ICA stenosis conversion to symptomatic 1-2%/yr)
    - ARR (preventing nonperioperative stroke) over 5 years was 8.2% for men, 4.08% for women

CEA

- Important points from these asymptomatic trials:
  - ACAS and ACST showed that in those with >60% stenosis, risk of stroke or death was lower with endarterectomy than the contemporary optimal medical therapy
  - Caveat: the rationale for procedural intervention in the asymptomatic patient is predicated on low perioperative complication rate (cva, mi, death) : <3%
  - Note also, this benefit is realized over time (as stroke risk rises over time without intervention, when on OMT only)

CEA



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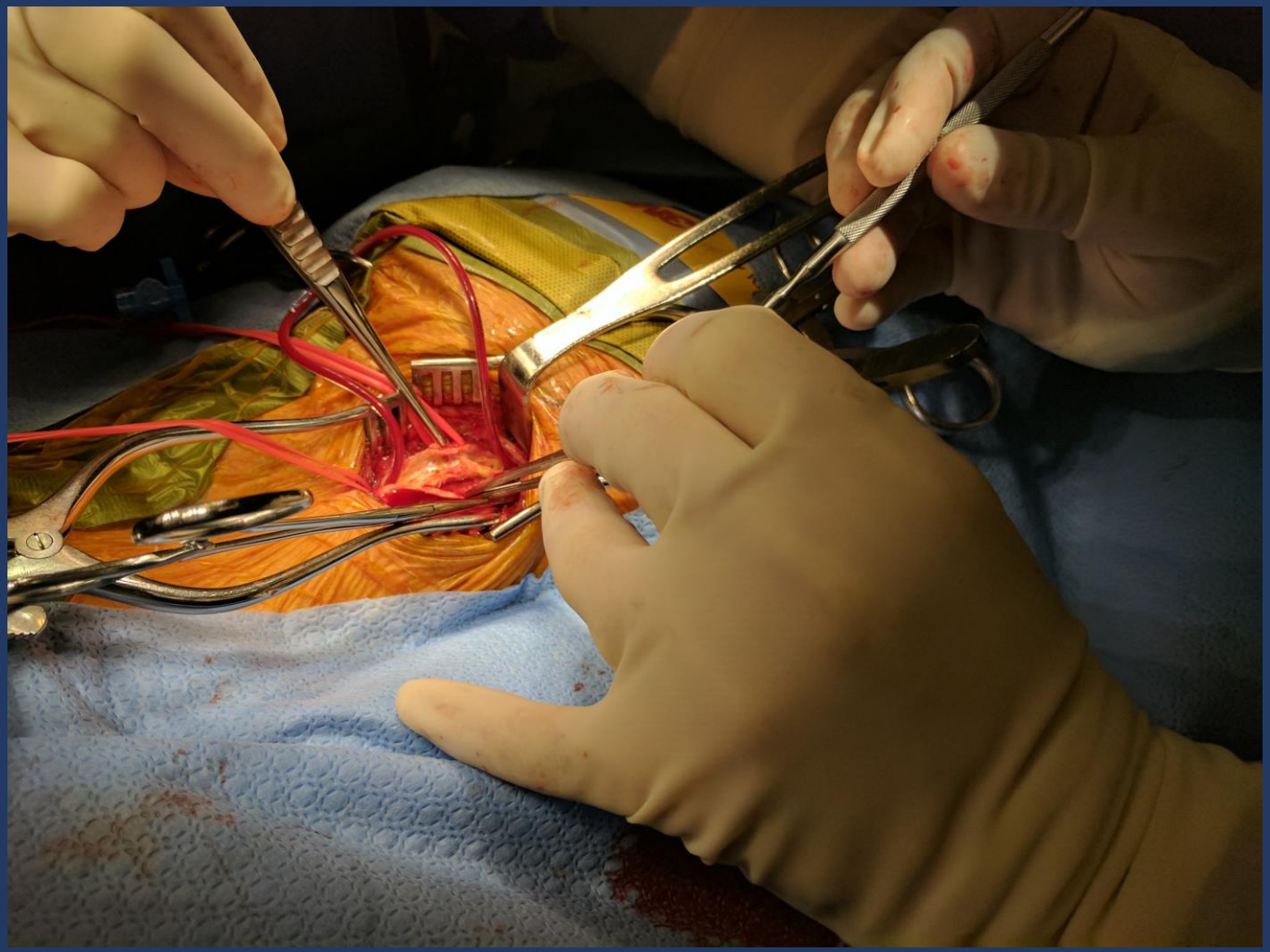

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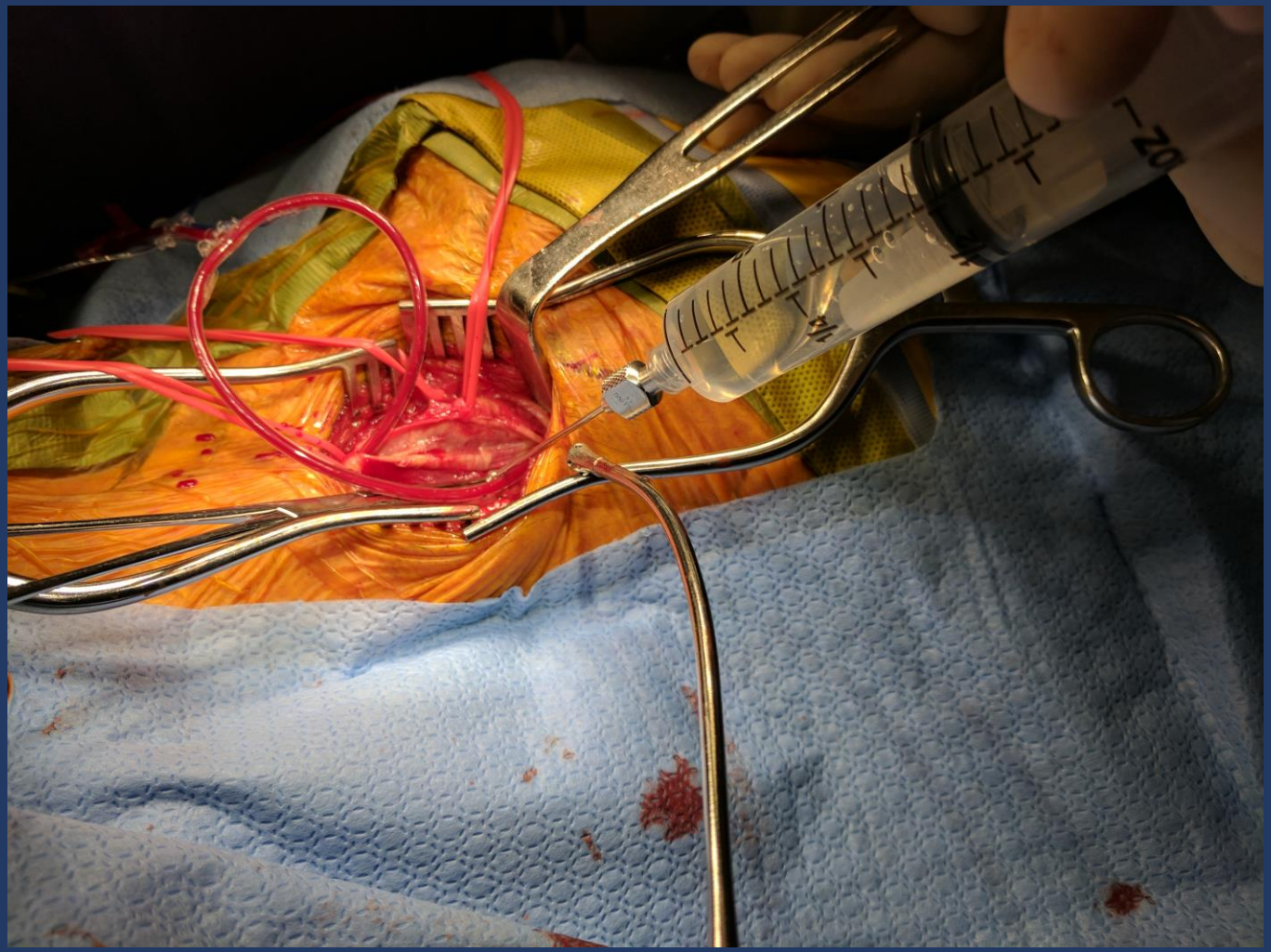

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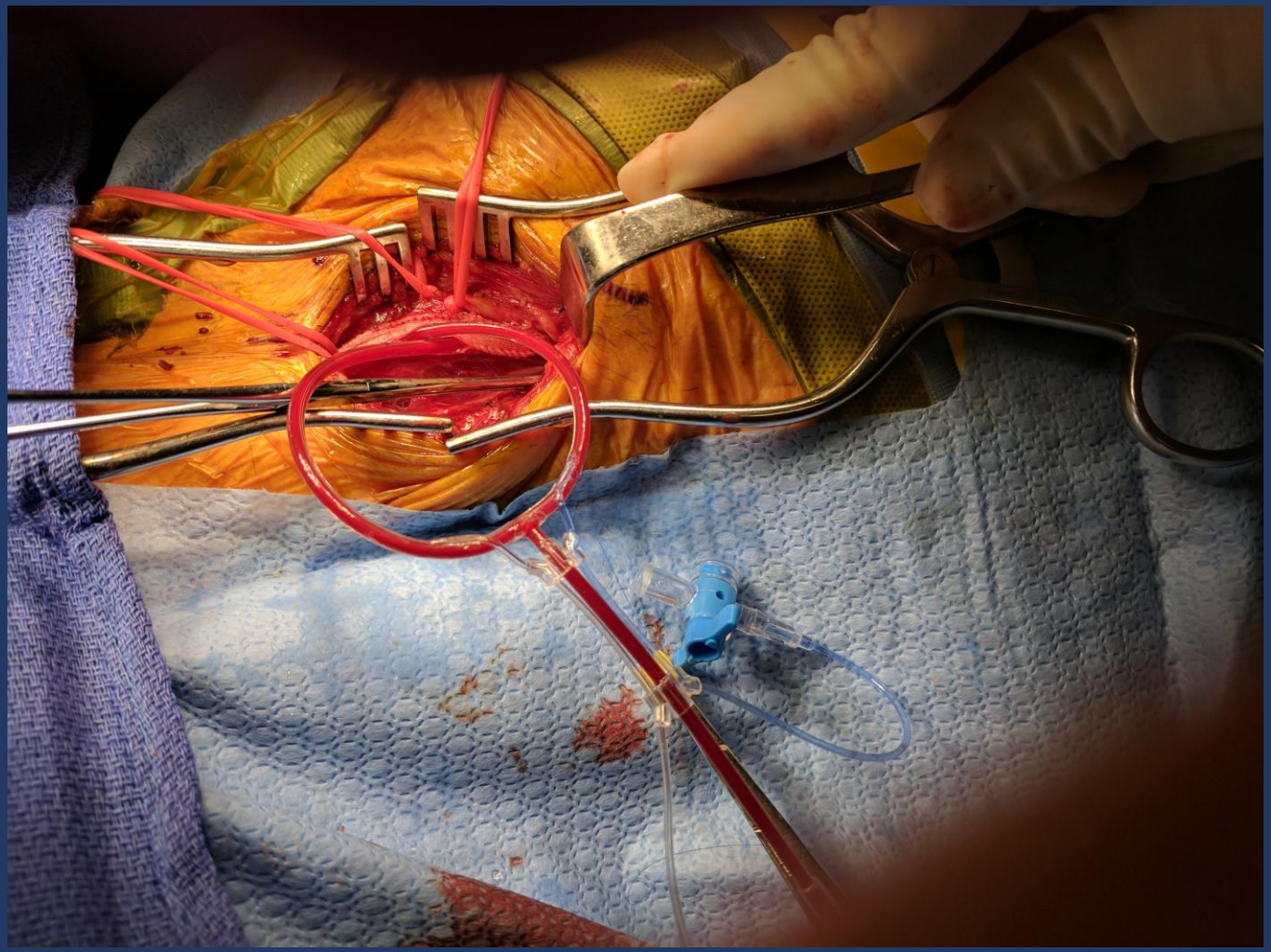
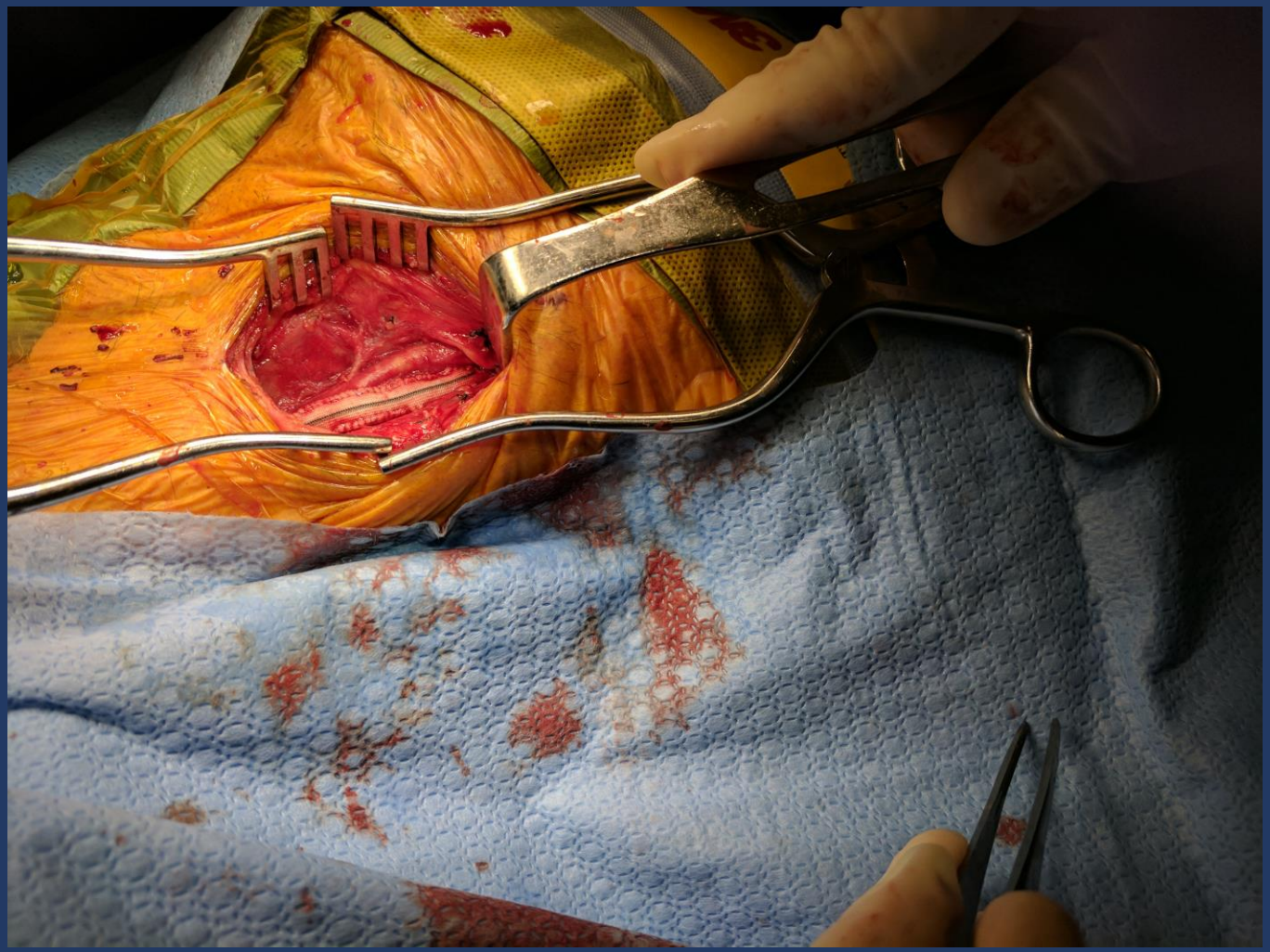


CEA



CEA

CEA vs. CAS

- Back to our scenario:
  - Based on the asymptomatic trials, appears that statistically, he would be a good candidate for CEA (and of course OMT concurrently)
  - What about CAS, beginning in earnest in the late nineties?

CAS

- CAS: a component of the endovascular revolution
  - Minimize procedural morbidity, mortality, diminish LOS without compromise of outcomes (patency rates, durability of intervention)

- Pertinent questions (specifically with regard to CAS vs. CEA):
  - Is it equal to or better than CEA?
  - Which has fewer complications, and of what type?
  - Are there patient selection issues (subgroups more appropriate for one or the other procedure)?
  - CAS approaches have changed over time

CAS Trials

- A Few Chosen Trials (many done):
  - CREST[1]:
    - 2502 patients randomized (symptomatic and, later, asymptomatic) to either CAS versus CEA
    - Composite endpoints: death, stroke, MI, any cause over 4 year (median 2.5 year) follow up
      - Periprocedural difference: death (0.7% CAS, 0.3% CEA), stroke (4.1% CAS, 2.3% CEA), MI (1.1%CAS, 2.3% CEA)
      - Longer term incidence of ipsilateral stroke: equal

1) Brott, TG, et al. Stenting versus Endarterectomy for Treatment of Carotid Artery Stenosis. NEJM 2010; 363:11-23

CAS Trials

- CREST (continued):
  - Some important points that emerged:
    - For patients >70 years old, rate of primary endpoint and adverse events increasingly favored surgery over CAS
    - The proportion of patients with stroke or death within 30 days of the procedure was significantly higher in the CAS group, vs. CEA (4.4% vs. 2.3%)
    - The frequency of MI within 30 days of the procedure was significantly lower in the CAS group versus CEA(1.1% vs. 2.3%)

    **At one year after the procedure, quality of life was significantly diminished for patients who developed stroke (even a minor stroke) compared to those who developed MI[1,2] (a CREST substudy)

1) Brott TG, et al. Stenting versus endarterectomy for treatment of carotid artery stenosis. NEJM 2010; 363:11.
2) Cohen DJ, et al. Health-related quality of life after carotid stenting versus carotid endarterectomy: results from CREST. J Am Coll Cardiol 2011; 58:1557.

CAS

- Meta-analysis[1]:
  - 10 RCT with 3178 patients published by March 2007 that compared CEA with CAS in both symptomatic and asymptomatic populations
    - The primary outcome measure of any stroke or death at 30 days favored CEA
    - During long term follow up, the overall analysis found no significant difference between CEA and CAS in the risk of stroke or death
  - There was significant heterogenity of trial design, wide confidence intervals in this meta analysis study but, at that time (2009) the conclusion was that there was insufficient evidence to support a move away from recommending CEA as the treatment of choice for suitable carotid stenosis

1) Ederle, J, et al. Randomized controlled trials comparing endarterectomy and endovascular treatment for carotid artery stenosis: a Cochrane systematic review. Stroke 2009; 40:1373

CAS Trials

ACT 1[1]:

- CAS with EPD (embolic protection device) versus CEA, asymptomatic patients <80 y.o., not high surgical risk
- Halted early due to slow enrollment (n=1453), 5 yr follow up
- Endpoints: death, stroke, MI within 30 days or ipsilateral stroke within one year
- Result: noninferior to CEA

1) Rosenfield K, et al. Randomized Trial of Stent versus Surgery for Asymptomatic Carotid Stenosis. NEJM, 2016; 374:1011-1020

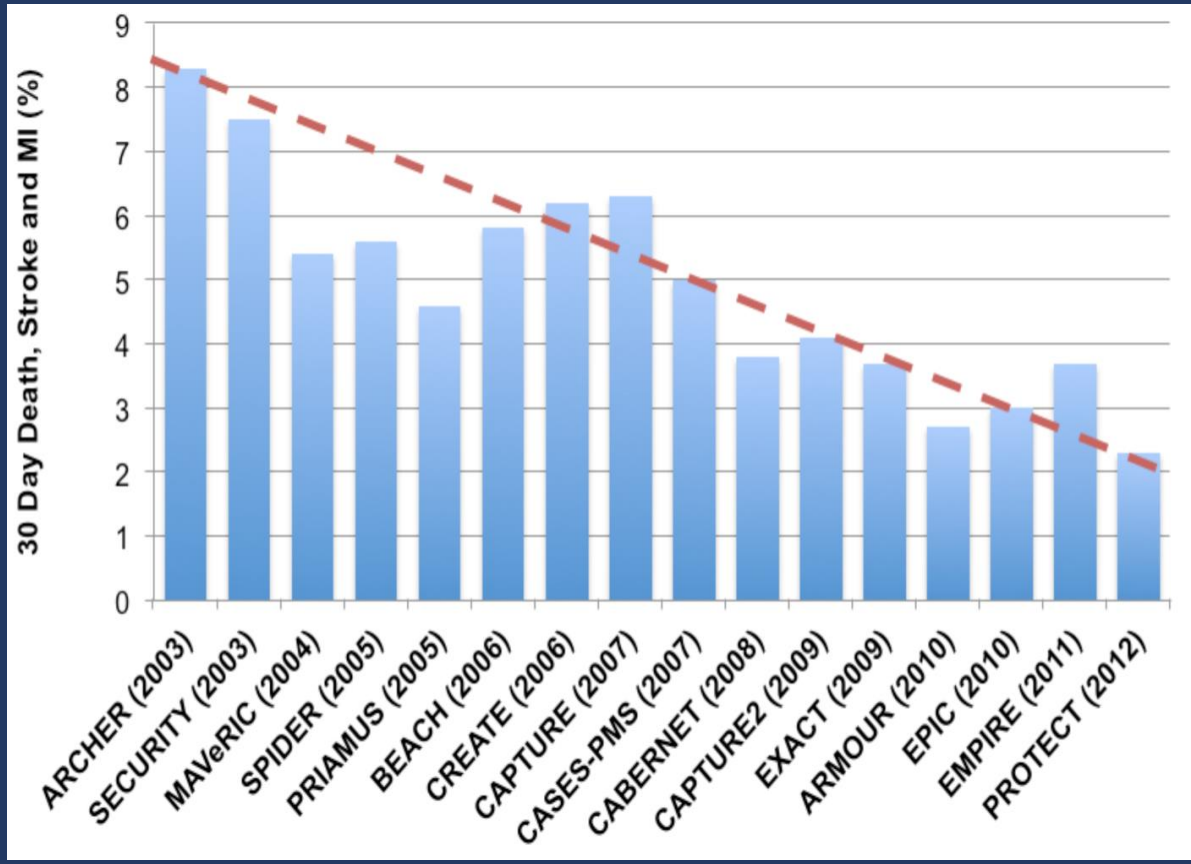
CAS Trials

- Trial utilizing direct CCA access:
  - Roadster Study (11/2012 to 7/2014, 208 patients)[1]:
    - ENROUTE Transcarotid Neuroprotection System (NPS) in high surgical risk patients.
    - Novel approach, avoiding the arch (embolic source) using direct CCA access, and utilizing reversal of flow instead of EPD
    - 30 day all stroke rate for TCAR 1.4%, versus 2.3% CEA

1) Kwolek CJ, Shah, RM, et al. Results of the ROADSTER multicenter trial of transcarotid stenting with dynamic flow reversal. JVS 2015 Nov; 62(5):1227-34

CEA vs. CAS

- Lessons learned:
  - Stent design evolution
  - Arch anatomy, and the perils thereof
  - Anatomic approach: Transfemoral approach Direct CCA approach
  - Pharmacology
  - Embolic protection strategies:
    - EPD
    - Reversal of flow



CEA vs. CAS

- Note the goal of all these stent trials initially:
  - Clinical equivalence or noninferiority to CEA; implicit in this statement is the acknowledgment of what is the true procedural "Gold Standard"
- Technological improvements have, and continue to, result in improved clinical outcomes with regard to periprocedural stroke, MI, death and longer term equipoise of outcomes with CAS
- But what about improved outcomes with older methods..CEA?
  - Cranial nerve injury incidence down from 8% (predominantly vagus and hypoglossal) to 1-2% over last 35 years[1]
  - Original NASCET accepted complication rate <6%, now closer to <3%...will this continue to improve?
- And what of OMT?

1) Kakisis, JD, et al. Cranial Nerve Injury After Carotid Endarterectomy: Incidence, Risk Factors, and Time Trends. European Journal of Vascular and Endovascular Surgery, March 2017; vol 53, issue 3, pg.320-335.

Why CEA?

- Society Guidelines for Asymptomatic Carotid Stenosis:
  - American Heart Association/American Stroke Association[1]
    - All patients should receive maximal medical therapy, including Aspirin and statin daily
    - "reasonable to consider performing" CEA in patients having >70% stenosis of the ICA if the risk of perioperative stroke, myocardial infarction and death is low (<3%).
    - Prophylactic CAS might be considered in highly selected patients with asymptomatic (>70% ica stenosis by duplex) , but effectiveness vs OMT in this situation is not well established
    - If to undergo CEA, aspirin throughout
  - Multispecialty guidelines[2]:
    - Concordant with above

1) Meschia JF, et al. Guidelines for the primary prevention of stroke: a statement for healthcare professionals from the AHA/ASA. Stroke 2014; 45:3754.
2) Brott TG, et al. ASA/ACCF/AHA/AANN/AANS/ACR/ASNR/CNS/SAIP/SCAI/SIR/SNIS/SVM/SVS guideline on the management of patients with extracranial carotid and vertebral artery disease. Stroke 2011; 42:e464.

Why CEA?

- Society guidelines for asymptomatic ICA stenosis treatment (cont.):

  Society for Vascular Surgery[1]:[2]

  - Recommends CEA as first line treatment for most patients with asymptomatic carotid stenosis of 60-99%
  - CAS is not recommended for patients with asymptomatic carotid stenosis
  - Note these recommendations from the SVS are from 2010

1) Ricotta JJ, et al. Updated Society for Vascular Surgery guidelines for management of extracranial carotid disease: Executive summary. JVS 2011; 54;832.
2) Fairman, RM, et al. Management of asymptomatic carotid atherosclerotic disease. UpToDate, literature review current through Jan 2017, last updated June 2016.

So, why CEA?

- Back to our 65y.o. patient:
  - life expectancy of 84.3 yrs, on average in the US (per SSA)
  - Implementations of OMT imperative: RX BP, chol, DM, tobacco, weight, diet, exercise, ASA, statin
  - CEA affords:
    - long term durable result of patency and stroke risk reduction, with minimal perioperative morbidity and mortality
    - Results replicated widely by many practitioners utilizing various anesthetics, differing philosophies on shunting, proponents of traditional endarterectomy with patch or eversion endarterectomy
    - Minimal improvement to be had employing CAS in lowering LOS, M/M (vs other vascular beds; i.e. aortoiliac, ascending aorta, arch, descending thoracic aorta, venous, complicated infrainguinal issues with severely ill patient cohorts)
    - From visceral standpoint, allows the physical removal of offending pathology, rather than shouldering aside
  - CAS affords:
    - Approaching equipoise with CEA for periprocedural morbidity and mortality, long term not yet known, as iterations of approach and materials have changed
    - Valuable tool in those with compelling comorbidities: tracheostomy, prior irradiation, high carotid bifurcation (surgically challenging/inaccessible)

CEA vs CAS

- Important closing points:
    - These modalities are already complementary; CAS continues to evolve, closing in on overall efficacy of CEA, but there will always be a prominent role for CEA
    - Patient selection will be imperative for best approach (anatomy, comorbidities, etc)
    - Needs to be intellectual openmindedness regarding the data as it continues to unfold
    - Need to avoid inflexible thinking regarding newer technologies; “If all you have is a hammer, everything looks like a nail”

CEA vs CAS
(Newer not necessarily better)

J Sebastian Bach

Sebastian Bach