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

• No disclosures
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

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 asymptomatic ICA stenosis):
    • Veterans Affairs Cooperative Study Group (VA Trial)\textsuperscript{1}
    • Asymptomatic Carotid Atherosclerosis Study (ACAS)\textsuperscript{2}
    • Asymptomatic Carotid Surgery Trial (ASCT)\textsuperscript{3}

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
Crea

• 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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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

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 MI¹,² (a CREST substudy)

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 heterogeneity 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

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

CAS Trials

• Trial utilizing direct CCA access:
  – Roadster Study (11/2012 to 7/2014, 208 patients)\textsuperscript{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

\textsuperscript{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
  – Original NASCET accepted complication rate <6%, now closer to <3%...will this continue to improve?

• And what of OMT?

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

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Why CEA?

- Society guidelines for asymptomatic ICA stenosis treatment (cont.):
  
  Society for Vascular Surgery\textsuperscript{1,2}:
  
  - Recommends \textit{CEA as first line treatment} for most patients with asymptomatic carotid stenosis of 60-99%.
  - \textbf{CAS is not recommended} for patients with asymptomatic carotid stenosis.
  - Note these recommendations from the SVS are from 2010.

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)

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