CAROTID SURGERY VS. CAROTID STENTING – HAS ANYTHING BEEN SETTLED?

L F KNOEPP, MD
ANMED VASCULAR MEDICINE
FINANCIAL DISCLOSURES

INVESTIGATOR FOR EV-3

GORE MEDICAL
FOCUS OF THIS TALK

BRIEF REVIEW OF THE EPIDEMIOLOGY / PATHOPHYSIOLOGY OF STROKE AS IT RELATES TO CAROTID STENOSIS.

REVIEW THE SURGICAL TREATMENT OF CAROTID STENOSIS – CAROTID ENDARTERECTOMY (CEA).

SCIENTIFIC RATIONALE FOR USING CEA TO TREAT CAROTID STENOSIS.

DEFEND CEA VS. THE NEWCOMER: CAROTID ARTERY STENTING (CAS).
Epidemiology of Stroke: What's at Stake

- 800,000 strokes/year in the US
- 144,000 deaths in US secondary to Stroke
- 2nd leading cause of death worldwide accounting for over 5 million deaths per year
- 20% of Strokes are attributed to Carotid stenosis

AHA/ASA
PATHOPHYSIOLOGY OF CAROTID STENOSIS RELATED STROKE

While it is likely that some strokes associated with carotid artery disease result from hypoperfusion, the majority of such strokes appear to result from embolization from an atherosclerotic plaque or acute occlusion of the carotid artery and propagation of thrombus distally.

Golledge, et al, stroke 2000
PATHOPHYSIOLOGY – IMPORTANT DISTINCTION:

PRESENCE OR ABSENCE OF PRIOR CAROTID SYMPTOMS HELPS DEFINE THE RISK OF STROKE

A) ASYMPTOMATIC – BRUIT ON EXAM OR CAROTID SCREENING

B) SYMPTOMATIC – CURRENT/RECENT/ACUTE STROKE OR RECENT NEUROLOGIC EVENT – MINI-STROKE/TIA OR RIND

*DEGREE OF STENOSIS IMPORTANT ALSO.
Current treatment arms

- Medical therapy
- Catheter based therapy/Carotid artery stenting (CAS)
- Surgical therapy/Carotid endarterectomy (CEA)

- CEA originally described in 1950’s
- 15,000 performed in 1970 and increased to 107,000 in 1985 (Pokras, et al).
- Came under fierce attack, as many as 2/3rds may be inappropriately performed
IS CEA APPROPRIATE IN THE TREATMENT OF CAROTID STENOSIS – WHERE IS THE SCIENCE?

NORTH AMERICAN SYMPTOMATIC CAROTID ENDARTERECTOMY TRIAL (NASCET), 1991
- CEA VS. MEDICAL TREATMENT IN PATIENTS WITH SYMPTOMATIC, 70-99% STENOSIS.
- OVER 1700 PTS ENDPOINTS - DEATH OR STROKE
- 9% RISK IN SURGERY GROUP VS. 26% RISK IN MEDICAL CONTROLS AT TWO YEARS.
- FDA ISSUED A WARNING AND TRIAL STOPPED

EUROPEAN CAROTID SURGERY TRIAL (ECST), LARGELY CORROBORATED THESE RESULTS
NASCET AND ECST TRIALS – SEVERAL CAVEATS

- MAXIMUM BENEFIT IS TIME DEPENDENT (FIRST 7-14 DAYS). PATIENTS ARE AT HIGH RISK FOR RECURRENT SYMPTOMS

- NASCET II (1998) REVIEWED TWO OTHER GROUPS:
  - PATIENTS WITH SYMPTOMATIC, <50% STENOSIS GAINED NO BENEFIT FROM SURGERY
  - PATIENTS WITH SYMPTOMATIC, 50-69% STENOSIS HAD BENEFIT – BUT BENEFIT WAS MARGINAL. MALE PATIENTS, PROMPT SURGERY, AND PATIENTS WITH HEMISPHERIC SYMPTOMS HAD BETTER OUTCOMES. BENEFITS OF SURGERY WERE EVEN MORE TIME DEPENDANT WITH MODERATE STENOSIS.
IS THERE A ROLE FOR CEA IN THE TREATMENT OF ASYMPTOMATIC CAROTID STENOSIS?

-ASYMPTOMATIC CAROTID ARTERY STUDY (ACAS), US – 1662 PTS WITH 60-99% STENOSIS
5YR RISK OF STROKE/DEATH WAS 5.1% IN SURGERY GROUP VS. 11% IN MEDICAL GROUP. (P < .05)*

-ASYMPTOMATIC CAROTID SURGERY TRIAL (ACST-1), EUROPE – 3120 PTS
5YEAR RISK (STROKE/DEATH) WAS 3.8% VS. 11%. (P < .05)

*CAVEAT
- BENEFIT IN ASSX PATIENTS ARE LESS CLEAR AND ARE CLEARLY DEPENDENT ON EXCELLENT OUTCOMES (ASSX STENOSIS IS NOT THE DANGER THAT SX STENOSIS IS).
- ENDPOINTS (STROKE AND DEATH) WERE CLINICAL.
- ALTHOUGH ACST-1 ENDED IN 2003 AND HAD STATIN THERAPY – SOME OF PATIENTS IN THESE STUDIES MAY HAVE HAD MEDICAL THERAPY THAT WOULD BE CONSIDERED INADEQUATE TODAY
IS THERE A CONTINUED ROLE FOR CEA WITH RECENT ADDITION OF CAS TO AS A TREATMENT OPTION?

TWO GROUPS OF CAROTID STUDIES:

1) INDUSTRY DRIVEN/FINANCED STUDIES

2) CONTROLLED, RANDOMIZED TRIALS COMPARING EFFICACY OF CAS VS. CEA
INDUSTRY DRIVEN CAROTID TRIALS

- SAPPHIRE (CORDIS)*
- SECURITY (ABBOTT)
- ARCHER I (ABBOTT)
- ARCHER II
- CREATE I (EV3)
- CREATE II
- MAVERIC (MEDTRONIC)
- CABERNET (BOSTON-SCIENTIFIC)
- EPIC (LUMEN BIOMEDICAL)
COMPARISON OF CAS TO CEA IN PATIENTS CONSIDERED HIGH RISK FOR SURGERY:

**SAPPHIRE*** (STENTING AND ANGIOPLASTY WITH PROTECTION IN PATIENTS AT HIGH RISK FOR ENDARTERECTOMY)

-TWO GROUPS OF PATIENTS: THOSE WITH ADVANCED MEDICAL ISSUES AND ADVANCED ANATOMIC ISSUES (MAJORITY OF PATIENTS WERE ASSX).

-PRIMARY ENDPOINT (STROKE/DEATH/MI*):  
  -30DAY CAS VS CEA: 4.8 VS. 9.8% (P VALUE >.05)  
  -ONE YEAR CAS VS. CEA: 12.2 VS. 20.1% (P VALUE = .05)  
  -THREE YEAR CAS VS. CEA: 24.6 VS. 26.9% (P VALUE > .05)
HEAVY INDUSTRY INFLUENCE.

OVER 700 ENROLLED – 400 EXCLUDED AND 334 WERE RANDOMIZED/TERRIBLE SELECTION BIAS.

70% OF PATIENTS WERE ASSX – HIGH RISK ASSX PATIENTS NEED MEDICAL THERAPY.

30 DAY DEATHS: CAS = 2/167 CEA = 4/167
ONE YEAR DEATHS: CAS = 12/167 CEA = 21/167

25% OF PATIENTS IN BOTH ARMS HAD A MAJOR EVENT (STROKE/DEATH/MI) BY THREE YEARS.
the overall rates
for stroke (1.65%; P .69), death (1.65%; P .09), and MI (0.83%; P .71) were not significantly different from those
in the study population.
Conclusions: CEA can be performed in patients at high risk, with stroke and death rates well within accepted standards. These data question the use of CAS as an alternative to CEA, even in patients at high risk. (J Vasc Surg 2004;39:958-66.)
PROSPECTIVE RANDOMIZED CAS VS. CEA TRIALS

1) SPENT PROTECTED ANGIOPLASTY VS CAROTID ENDARTERECTOMY (SPACE) 2001-2006, 1214 PTS W/ SYMPTOMS
ENDPOINT (STROKE/DEATH): 10.7% (CAS) VS 11.1% (SURGERY) – p VALUE >.05

2) INTERNATIONAL CAROTID STENT STUDY (ICSS), 1713 PTS W/ SYMPTOMS
ENDPOINT (STROKE/DEATH/MI): 8.5% (CAS) VS 5.2% (SURGERY) – P VALUE <.05

3) ENDARTERECTOMY VS ANGIOPLASY - SEVERE SYMPTOMATIC STENOSIS (EVA-3S), 527 PTS
ENDPOINT (STROKE/DEATH): 11.1 (CAS) VS 6.2 (CEA) – P VALUE <.05

*META-ANALYSIS SHOWED CAS TO HAVE WORSE OUTCOMES AND RISK ESPECIALLY HIGH IN PATIENTS WHEN CAS PERFORMED CLOSER TO THE ONSET OF SYMPTOMS – WHEN PATIENT SHOULD GET GREATEST BENEFIT. (RANTNER, ET AL)
ICSS-MRI SUBSET ANALYSIS

50% of patients undergoing CAS had new MRI findings after CAS as compared to 17% with CEA (Bonati, et al)

Anywhere from one to greater than five new lesions. (Gensicke, et al)

Finding was not improved with the use of cerebral protection devices
CAROTID REVASCULARIZATION
ENDARTERECTOMY VERSUS STENTING TRIAL (CREST) - US

- 2502 PATIENTS RANDOMIZED - TWO GROUPS (CAS OR CEA)
- PRIMARY ENDPOINTS WERE CVA, DEATH, AND MI
- CAS (7.2%) VS. CEA (6.8%) P>.05
- 30 DAY RISK OF STROKE AND DEATH WORSE WITH CAS (4.1% VS. 2.3%), P<.05
- RISK OF MI WAS WORSE WITH CEA (2.3% VS. 1.1%), P<.05
CAROTID REVASCULARIZATION
ENDARTERECTOMY VERSUS STENTING TRIAL (CREST) – NOTES:

- CEA VS CAS ENDPOINTS WERE COMPARABLE IN PATIENTS LESS THAN 70 YEARS OLD

- HIGHER COMPLICATION RATE IN CAS GROUP AS COMPARED TO CEA IN PATIENTS AGED 70 OR GREATER

- MAJOR STROKES WERE COMPARABLE IN BOTH GROUPS (CEA VS. CAS)

- MINOR/MODERATE STROKES HIGHER IN THE CAS GROUP

- QUALITY OF LIVE MEASURES/MORBIDITY MEASURES WERE WORSE IN THE STROKE GROUP AS COMPARED TO THE MI GROUP.
To Cath Lab
WHAT DO WE DO NOW? (WHAT SHOULD WE RECOMMEND FOR OUR PATIENTS)

- FOR ACUTE, SYMPTOMATIC PATIENTS WITH SEVERE STENOSIS – CEA IS LIKELY BEST (SX CAS TRIALS/MRI).

- SYMPTOMATIC PATIENTS WITH MODERATE (50-69%) STENOSIS WOULD BENEFIT FROM CEA IF SURGICAL COMPLICATION RATE IS LOW (SX. CAS TRIALS AND MRI).

- SYMPTOMATIC PATIENTS WHO NEED THEIR INTERVENTION DEFERRED PROBABLY BENEFIT FROM SAFE/LOW-RISK CEA OR CAS.

- HIGH-RISK FOR SURGERY, SYMPTOMATIC PATIENTS???
WHAT DO WE DO NOW? (WHAT SHOULD WE RECOMMEND FOR OUR PATIENTS)

- ASSYMPTOMATIC, GOOD-RISK PATIENTS WITH HIGH GRADE STENOSIS CAN BE OFFERED LOW-RISK CEA OR CAS OR MEDICAL THERAPY.

- ASSYMPTOMATIC, HEALTHY PATIENTS WITH “TRUE” ANATOMIC CHALLENGES NEED CAS

- ASSYMPTOMATIC, HIGH RISK MEDICAL PATIENTS NEED MEDICAL THERAPY (IN SPITE OF SAPPHIRE).

- COLLABORATION BETWEEN CAS AND CEA PRACTITIONERS AND A TRUE ASSESSMENT OF THE PATIENTS STROKE RISK.
CONTROVERSIES:

*A TRIAL IS NEEDED WITH A MEDICAL ARM – ESPECIALLY IN PATIENTS WITH CAROTID STENOSIS THAT ARE AT INTERMEDIATE OF RISK FOR STROKE.

*WE NEED TO ESTABLISH THE IMPORTANCE OF ENZYME POSITIVE MI:

ARE WE USING MORE SENSITIVE MEASURES TO ESTABLISH MI TO STRENGTHEN THE CASE FOR CAS? OUR METHODS FOR DETECTION OF MI ARE PROBABLY MORE SENSITIVE THAN OUR METHODS FOR DETECTION OF STROKE (AREN’T WE HERE TO PREVENT STROKE?).

IF ENZYME POSITIVE MI IS IMPORTANT THEN THE MEDICAL ARM MAY WIN OUT IN PATIENTS WITH INTERMEDIATE RISK FOR STROKE OVER CEA AND CAS.