The Evolution of Carotid Disease Research - CREST2

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Overview

• Many trials completed to evaluate efficacy of carotid endarterectomy, stenting, and medical therapy for carotid artery disease

• Satisfactory conclusion still not reached about best treatment
NASCET

- North American Symptomatic Endarterectomy Trial
- To evaluate the safety and efficacy of CEA in symptomatic patients as opposed to optimal medical therapy
- Measured the rates of perioperative stroke and death
- 1453 patients randomized to CEA arm
- 1415 patients planned for CEA, moderate in 1087, severe in 328
Patient Selection:

Inclusion Criteria
• Hemispheric TIA
• Transient monocular blindness
• Nondisabling stroke
• With angiographically documented ipsilateral carotid artery disease 30-99%

Exclusion Criteria
• Unable to consent
• No angiographic studies
• Intracranial carotid lesion > cervical
• Expected survival < 5 years
• Had a disabling stroke (mRs > 3)
• Prior ipsilateral CEA
NASCET

Events for patients in CEA Arm:

- Disabling Ipsilateral Stroke: 4.3%
- Ipsilateral Stroke: 14.6%
- Any Stroke: 24.3%
- Any Stroke or Death: 33.8%

Proportion without Events vs Years after Surgery
NASCET

• There is clear benefit from CEA in the settings of symptomatic severe (>70%) carotid stenosis
• Benefit increases with increasing stenosis severity (95%)
• The benefit is modest in patients with 50-69% stenosis but increases with highest risk patient selection
CREST — Carotid Revascularization Endarterectomy vs Stenting Trial

- One of the largest stroke prevention trials ever completed (2502 patients). Efficacy and safety of the two procedures largely the same with equal benefits.
  - Prospective, multicenter randomized controlled trial with blinded endpoint adjudication
  - CAS vs CEA in both symptomatic and asymptomatic patients
  - 108 US and 9 Canadian sites
- The rate of stroke and death in the surgical group was the lowest ever reported in a large stroke prevention trial.
- It was also the lowest in any RCT with CAS.
CREST Eligibility

• Conventional (not low surgical risk) patients with carotid stenosis
  – Both symptomatic and asymptomatic

• Exclusion criteria
  – Evolving stroke or prior major stroke
  – Chronic atrial fibrillation
  – Recent (<30 days) MI
  – Unstable angina
CREST

![Graph showing the number of patients in different age groups for CEA and CAS procedures.](chart.png)
CREST-1 – The Bottom Line

CAS is non-inferior to CEA for peri-procedure death, stroke or MI
CREST-2

2 parallel multi-center randomized, observer-blinded endpoint clinical trials.

– One trial will assess differences between intensive medical management (IMM) alone vs. CEA plus IMM.

– Second trial will assess differences between IMM alone compared to CAS plus IMM.

– IMM will involve control of blood pressure, LDL cholesterol, cigarette smoking, and other vascular risk factors.
CREST-2 Enrollment

- Total Enrollment = 2480 subjects
- 120 Sites Nationally
- Strict Eligibility Criteria
  - Medical
  - Angiographic
- Accompanying Crest-2 Registry (C2R) allows CAS of patients who fall out of the trial
Strict Angiographic Exclusions for CAS:

- Type III, aortic arch anatomy.
- Angulation or tortuosity (≥ 90 degree) of the CCA
- Severe angulation or tortuosity of the ICA, defined as 2 or more ≥ 90 degree angles within 4 cm of the target stenosis.
- Proximal/ostial CCA, innominate stenosis or distal/intracranial stenosis greater than index lesion.
- Excessive circumferential calcification of the stenotic lesion
- Target ICA vessel reference diameter <4.0 mm or >9.0 mm
- Inability to deploy or utilize an EPD
- Non-contiguous lesions and long lesions (>3 cm)
CREST-2 Angiographic Criteria

Meets Enrollment Criteria:
Case 1
CREST-2 Angiographic Criteria

Meets Enrollment Criteria:
Case 2
CREST-2 Angiographic Criteria

Meets Enrollment Criteria:
Case 2
Post Procedure
CREST-2 Angiographic Criteria

Does NOT meet Enrollment Criteria:
Case 3
CREST-2 Endpoints

• Primary:
  – Any stroke/death within 44 days post-procedure
  – Ipsilateral stroke within 4 years post-procedure

• Secondary:
  – Difference between IMM vs. CEA or CAS for cognitive function for 4 years of follow-up
  – Find if CEA or CAS vs IMM difference is affected by patient age, sex, severity of carotid stenosis, restenosis, risk factor level, and duration of asymptomatic period
The Past, Present and Future of Carotid Artery Disease

- **NASCET**
  - CEA better than optimal medical management

- **CREST-1**
  - CAS non-inferior to CEA

- **CREST-2**
  - Either CAS or CEA vs IMM
    - Will Medicare cover CAS for asymptomatic, high-risk patients?
THANK YOU!

Questions?