**MHIF FEATURED STUDY: HighLife**

**DESCRIPTION:**
Purpose: to evaluate the safety and efficacy of the HighLife trans-septal access 28mm Transcatheter Mitral valve and its delivery system (transfemoral venous access and interatrial puncture) in patients with moderate-severe or severe mitral regurgitation who are at a high risk for surgical treatment.

Primary Feasibility endpoint: technical success
Safety: all cause mortality at 30 days
Performance: total MR reduction to 1+ or less as assessed by core lab

**CRITERIA LIST/ QUALIFICATIONS:**
Inclusion: moderate-severe or severe mitral regurgitation; NYHA class II, III; or ambulatory class IV
Exclusion: mitral stenosis; Flail Leaflet or prolapse; severe calcification; prior mitral intervention; mitral annulus <30 mm & >45 mm; Aortic prosthesis; LVEF<30%; PAS >70mmHg; TR requiring intervention

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**MHIF FEATURED STUDY: KPL-301-C203**

**DESCRIPTION:**
Phase 2/3, randomized, double-blind, placebo-controlled study to evaluate the efficacy and safety of single IV dose of mavrilimumab in adult subjects hospitalized with severe COVID-19 pneumonia and hyper-inflammation to reduce progression to respiratory failure or death. Mavrilimumab targets the GM-CSF receptor, neutralizing overexpression of GM-CSF associated with inflammation. This may address severe cytokine storm syndrome seen in subjects with COVID-19 and the immediate need to reduce rising mortality.

**CRITERIA LIST/ QUALIFICATIONS:**
Inclusion:
- >18 years old
- Positive SARS-CoV-2 within 14 days
- Bilateral pneumonia on chest x-ray or CT
- Elevated ferritin, CRP, D-dimer, LDH, or history of fever <7 days
- Requiring non-invasive ventilation or oxygen supplementation to maintain SpO2 >92% (i.e. nasal cannula, face mask, BIPAP, CPAP) or invasive ventilation <48 hours

Exclusion:
- Onset of COVID-19 symptoms >14 days
- Hospitalized for SARS-CoV-2 >7 days
- Prior severe or concomitant illness (i.e. pulmonary alveolar proteinosis, severe and uncontrolled pulmonary disease other than COVID-19 pneumonia, pre-existing LVEF <35%, MI/stroke/ hemodynamic instability/cardiogenic or septic shock <30 days, concomitant uncontrolled systemic or bacterial infection)
- Recent cell-depleting biological therapies or immunosuppressants (except corticosteroids)
- Received hydroxychloroquine within last 3 months
Disclosures

- Silk Road Medical (TCAR)
  - Site PI: ROADSTER and ROADSTER-2
  - Physician Education/Training/Certification
- Medtronic
  - Physician/Trainee Education
- Endospan
  - Chair, Clinical Events Committee (TRIOMPHE)

- No discussion of “off label” devices/techniques
- Opinions are my own and do not represent official societal/committee endorsements
Learning Objective

- Understand the epidemiology and pathophysiology of carotid artery disease
- Describe the advantages and risks with endarterectomy and stent placement
  - Discussion on TF-CAS vs TCAR
- Explain the rationale for carotid revascularization in select patients
  - Focus on asymptomatic carotid stenosis

Epidemiology of Stroke

  - Heart, cancer, unintentional injuries, respiratory disease
  - 2007 to 2017, age-adjusted stroke death decreased 13.6% and actual number declined 7.7%
  - 146,383 people (1 of 19 deaths)
- Leading cause of serious long term disability (~$45.5B in 2014-15)
  - Health care services, medications, missed days of work
- 795,000 new strokes per year
  - 610K first attacks, 185K recurrent attacks
- US: Stroke (every 40 seconds); Death (every 3 min 35 sec)

- Mortality in the United States, 2018: NCHS Data Brief, No 355, January 2020
Epidemiology of Stroke

NHANES indicates National Health and Nutrition Examination Survey.
Source: Unpublished National Heart, Lung, and Blood Institute tabulation using NHANES, 2013 to 2016.206

Epidemiology of Stroke

Chart 14-7. Probability of death within 1 year after first stroke, United States, 1995 to 2011.*
Chart 14-8. Probability of death within 5 years after first stroke, United States, 1995 to 2011.*
Pathophysiology of Stroke

- 87% of stroke are ischemic (10% ICH; 3% SAH)
- 15-30% secondary to extracranial internal carotid artery disease

Symptomatic Carotid Artery Disease

- TIA (transient ischemic attack) – “crescendo”
- Amaurosis fugax (ophthalmic artery)
- Stroke – “stroke in evolution”

- Must correlate with symptom/cerebral territory with carotid disease

- Syncope (on if severe, bilateral disease)
- Other clinical conditions likely not associated with carotid artery disease
  - Unconsciousness, seizures, vertigo
  - Incontinence, amnesia, memory loss, forgetfulness, dementia
Asymptomatic Carotid Stenosis

- Overall prevalence in general population is low, but increases with age
- Associated w/cardiovascular risk factors (HTN, DM, HC, tobacco)
- Estimated risk of stroke 0.5-1%/year
  - Preceded by TIA?
  - No linear correlation between degree of stenosis and stroke risk

Screening for Asymptomatic Carotid Stenosis

1. Duplex ultrasonography to detect hemodynamically significant carotid stenosis may be considered in asymptomatic patients with extracranial carotid and vertebral artery disease.

2. Duplex ultrasonography might be considered to detect carotid stenosis in asymptomatic patients without clinical evidence of atherosclerosis who have 2 or more of the following risk factors: hypertension, hyperlipidemia, tobacco smoking, a family history of premature or first-degree relative of atherothrombosis manifested before age 60 years, or a family history of ischemic stroke. However, it is unclear whether establishing a diagnosis of ECVD would justify actions that affect clinical outcomes. (Level of Evidence: C)
Screening for Asymptomatic Carotid Stenosis

- July 8, 2014 USPSTF Recommendation
  - 2020-21: Update in Progress

U.S. Preventive Services Task Force

Screening for Asymptomatic Carotid Artery Stenosis
Clinical Summary of U.S. Preventive Services Task Force Recommendation

| Population | Adults without a history of transient ischemic attack, stroke, or other neurologic signs or symptoms |
| Recommendation | Do not screen for asymptomatic carotid artery stenosis in the general adult population. |
| Grade: | D |

Diagnosis of Carotid Artery Disease

- Duplex ultrasound
  - Low cost, noninvasive
  - Velocity criteria (cm/s)

<table>
<thead>
<tr>
<th>Stenosis</th>
<th>PSV</th>
<th>EDV</th>
<th>IC/CC</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;50%</td>
<td>&lt;125</td>
<td>&lt;40</td>
<td>&lt;2.0</td>
</tr>
<tr>
<td>50-69%</td>
<td>125-230</td>
<td>40-100</td>
<td>2.0-4.0</td>
</tr>
<tr>
<td>≥70%</td>
<td>&gt;230</td>
<td>&gt;100</td>
<td>&gt;4.0</td>
</tr>
</tbody>
</table>

- Technician dependent
- Limited anatomic information
- Use for initial diagnosis, longitudinal follow-up
Diagnosis of Carotid Artery Disease

- Cross Sectional Imaging (CT/MR)
  - Higher cost, contrast utilization
  - Additional anatomic information
    - Arch anatomy
    - Circle of Willis
  - Accuracy affected by calcification/artifact

- Contrast Angiography
  - “Gold standard”
  - Invasive procedure, access complications
  - Periprocedural risk of stroke (“1%”)

Treatment of Carotid Artery Disease

- Medical Management: “best practice” for all patients
  - Antiplatelet therapy
  - Aggressive statin therapy
  - Management of comorbid conditions
    - Hypertension
    - Diabetes
  - Lifestyle modification
    - Smoking cessation
Carotid Endarterectomy (CEA)

- Postoperative stroke/death/MI
  - AHA guidelines: 30 day stroke/death (<3% ASX; 6% SX)
- Exploration for bleeding (1-4%); wound infection (<1%)
- Cranial nerve injury (palsy vs permanent)
  - Vagus, hypoglossal, facial nerves
  - Significantly decreased from 8% to <2%
  - Fewer than 1/7 are permanent
- Hyperperfusion syndrome (BP control)
- Recurrent stenosis (6% in 2 years)

Complication After CEA

Evidence for CEA (Symptomatic)

- **NASCET trial (＞50% stenosis for symptomatic patients)**

  BENEFICIAL EFFECT OF CAROTID ENDARTERECTOMY IN SYMPTOMATIC PATIENTS WITH HIGH-GRADE CAROTID STENOSIS
  NORTH AMERICAN SYMPTOMATIC CAROTID ENDARTERECTOMY TRIAL COLLABORATORS*  
  
  • **70-99%** (26% vs 9%, 2 years)  
  
  BENEFIT OF CAROTID ENDARTERECTOMY IN PATIENTS WITH SYMPTOMATIC MODERATE OR SEVERE STENOSIS  
  
  • **50-69%** (15.7% vs 22.2%, 5 years)

Evidence for CEA (Asymptomatic)

- **ACAS/ACST trial (＞60% stenosis for asymptomatic patients)**

  Prevention of disabling and fatal strokes by successful carotid endarterectomy in patients without recent neurological symptoms: randomised controlled trial
“High Risk” For CEA

- Patients at potential for higher risk for complications during CEA

**ANATOMIC HIGH RISK**
- Prior head/neck surgery or irradiation
- Spinal immobility
- Restenosis post CEA
- Surgically inaccessible lesion
- Laryngeal palsy; Laryngectomy
- Permanent contralateral cranial nerve injury
- Contralateral occlusion
- Severe tandem lesions
- Bilateral stenosis requiring treatment

**PHYSIOLOGIC HIGH RISK**
- Age ≥75
- Congestive Heart Failure
- Left Ventricular Ejection Fraction ≤35%
- ≥2 diseased coronaries with ≥70% stenosis
- Unstable angina
- Myocardial infarction within 6 weeks
- Abnormal stress test
- Need for open heart surgery
- Need for major surgery (including vascular)
- Uncontrolled diabetes
- Severe pulmonary disease

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Carotid Angioplasty and Stenting (*TF-CAS*)

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20
Evidence for TF-CAS (High Risk Patients)

Protected Carotid-Artery Stenting versus Endarterectomy in High-Risk Patients


March 2005 (CMS NCD)
- High risk, symptomatic, >70% stenosis
- Additional allowances for clinical trials

ICSS (TF-CAS)

Carotid artery stenting compared with endarterectomy in patients with symptomatic carotid stenosis (International Carotid Stenting Study): an interim analysis of a randomised controlled trial

- Suitable for both CEA/CAS
- Experience: 50 total (10/yr)
CREST (TF-CAS)

Stenting versus Endarterectomy for Treatment of Carotid-Artery Stenosis

• Suitable for both CEA/CAS
• “Lead-in” phase for physicians

### Table 2: Primary End Point, Components of the Primary End Point, and Other Events, According to Treatment Group

<table>
<thead>
<tr>
<th>End Point</th>
<th>CAS (N=1262)</th>
<th>CEA (N=1348)</th>
<th>Absolute Treatment Effect of CAS vs. CEA (95% CI)</th>
<th>Hazard Ratio for CAS vs. CEA (95% CI)</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Death</td>
<td></td>
<td></td>
<td>0.4 (0.1 to 0.8)</td>
<td>2.25 (0.98 to 5.01)</td>
<td>0.11</td>
</tr>
<tr>
<td>Any stroke</td>
<td>54 (41.2%)</td>
<td>73 (54.3%)</td>
<td>0.7 (0.4 to 1.2)</td>
<td>1.79 (1.22 to 2.62)</td>
<td>0.001</td>
</tr>
<tr>
<td>Major ischemal</td>
<td>11 (0.9%)</td>
<td>12 (0.9%)</td>
<td>-0.1 (0.2 to 1.1)</td>
<td>2.67 (0.95 to 7.84)</td>
<td>0.09</td>
</tr>
<tr>
<td>Major non-ischemal</td>
<td>6 (0.5%)</td>
<td>26 (1.9%)</td>
<td>0.5 (0.2 to 0.9)</td>
<td>4.62 (2.21 to 9.64)</td>
<td>0.001</td>
</tr>
<tr>
<td>Minor ischemal</td>
<td>37 (3.0%)</td>
<td>27 (2.0%)</td>
<td>0.1 (0.3 to 0.4)</td>
<td>1.02 (0.50 to 2.07)</td>
<td>0.98</td>
</tr>
<tr>
<td>Minor non-ischemal</td>
<td>4 (0.5%)</td>
<td>10 (0.8%)</td>
<td>0.3 (0.1 to 0.6)</td>
<td>0.63 (0.19 to 1.94)</td>
<td>0.53</td>
</tr>
<tr>
<td>Myocardial infarction</td>
<td>14 (1.1%)</td>
<td>25 (1.9%)</td>
<td>-1.1 (0.2 to 0.1)</td>
<td>0.50 (0.20 to 1.08)</td>
<td>0.03</td>
</tr>
<tr>
<td>Any peri-procedural stroke or post-procedural</td>
<td>52 (4.1%)</td>
<td>29 (2.2%)</td>
<td>1.8 (0.4 to 3.2)</td>
<td>1.78 (1.22 to 2.62)</td>
<td>0.002</td>
</tr>
<tr>
<td>Major stroke</td>
<td>11 (0.9%)</td>
<td>8 (0.6%)</td>
<td>-0.2 (0.5 to 0.9)</td>
<td>1.15 (0.54 to 2.46)</td>
<td>0.52</td>
</tr>
<tr>
<td>Minor stroke</td>
<td>51 (4.1%)</td>
<td>21 (1.6%)</td>
<td>1.6 (0.3 to 3.5)</td>
<td>3.01 (1.33 to 6.73)</td>
<td>0.001</td>
</tr>
<tr>
<td>Any peri-procedural stroke or death or post-</td>
<td>51 (4.1%)</td>
<td>29 (2.2%)</td>
<td>2.0 (0.6 to 3.4)</td>
<td>1.96 (1.22 to 3.38)</td>
<td>0.005</td>
</tr>
<tr>
<td>peri-procedural stroke</td>
<td>51 (4.1%)</td>
<td>29 (2.2%)</td>
<td>2.0 (0.6 to 3.4)</td>
<td>1.96 (1.22 to 3.38)</td>
<td>0.005</td>
</tr>
<tr>
<td>Primary end point (any peri-procedural stroke, myocardial infarction, or death or post-procedural stroke)</td>
<td>51 (4.1%)</td>
<td>29 (2.2%)</td>
<td>2.0 (0.6 to 3.4)</td>
<td>1.96 (1.22 to 3.38)</td>
<td>0.005</td>
</tr>
</tbody>
</table>
CREST (TF-CAS)

- "efficacy of CAS and CEA approximately ~ at age 70"
- Stroke: equal risk at ~64 years
- Periprocedural risk higher in women (CAS)
- No difference by symptomatic status; Restenosis similar after 2 years (6%)

ACT-1 (TF-CAS)

Randomized Trial of Stent versus Surgery for Asymptomatic Carotid Stenosis

- age <80, >70% stenosis, asymptomatic, not high risk
- 1453 patients: 3:1 CAS:CEA
- "lead in phase"
- 1st endpoint: 3.8% CAS vs 3.4% CEA
- 30d S/D: 2.9% CAS vs 1.7% CEA
- 5y FF S: 93.1 CAS vs 94.7% CAS
- CAS "noninferior" to CEA
**Carotid Revascularization in the US**

- **March 2005 (CMS NCD)**
  - Not changed since then

**Are Carotid Stent Durable?**

- **CREST (10 year data)**
  - No difference w/10 year “postprocedural” ipsilateral stroke rate
  - Difference attributable to “peri-procedural” risk (4.1% CAS vs 2.3% CEA)
Are Carotid Stent Durable?

**Long-term outcomes of stenting and endarterectomy for symptomatic carotid stenosis: a preplanned pooled analysis of individual patient data**

Lancet Neurol 2013; 12: 348-56

Pooled Analysis (10 year data)
- 4 largest RCT on CAS/CEA
- “improvement in periprocedural safety of CAS could provide similar outcomes”

Causes of Stroke During TF-CAS

**Three Procedural Phases**

1. Catheterization
   - Passage of aortic arch
   - Catheterize target vessel
   - Introduction of sheath

2. “Unprotected” crossing of lesion
   - Placement of embolic protection device (EPD)

3. Intervention
   - Balloon angioplasty
   - Stent deployment
   - Recovery of EPD
Causes of Stroke During TF-CAS

Three Procedural Phases

1. Catheterization
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3. Intervention
   - Balloon angioplasty
   - Stent deployment
   - Recovery of EPD

TransCarotid Artery Revascularization (TCAR)

- Continuous high rate of flow reversal to remove micro and macro debris throughout intervention
- Direct Carotid Access
- CCA Proximal Control
TransCarotid Artery Revascularization (TCAR)

Results of the ROADSTER multicenter trial of transcarotid stenting with dynamic flow reversal

(J Vasc Surg. 2015;62:1227-35.)

- 141 “pivotal” patients in 18 sites
- 2012 to 2013
- 30 day all-stroke per protocol 0.7%

- “The overall stroke rate of 1.4% is the lowest reported to date for any prospective, multi-center trial of carotid stenting.” (FDA approval in 2015)

High Surgical Risk

Standard Surgical Risk

4.1% TF-CAS (CREST)

2.3% CEA (CREST)

1.4% ROADSTER

TransCarotid Artery Revascularization (TCAR)

Early Outcomes in the ROADSTER 2 Study of Transcarotid Artery Revascularization in Patients With Significant Carotid Artery Disease


- FDA mandated post-approval TCAR registry
- 81.2% TCAR-naïve operators
- 692 “high risk” patients over 43 sites
- Analysis of 632 “per-protocol”
  - 4 strokes (0.6%); 1 death (0.2%), 6 MI (0.9%)
  - 30 day composite stroke/death/MI of 1.7%

ROADSTER2

0.6% High Surgical Risk
Current Practice Guidelines

Guidelines for the Primary Prevention of Stroke
A Statement for Healthcare Professionals From the American Heart Association/American Stroke Association
(Stroke. 2014;45:3754-3832.)

- Prescribed daily aspirin and statin
- **Reasonable to consider CEA in asymptomatic patients with >70% stenosis if risk of perioperative stroke/MI/death is low (<3%), however, its effectiveness compared to BMT is not well established**
- **Prophylactic CAS might be considered in highly selected patients, but its effectiveness compared to BMT is not well established**
- **In patients at high risk of complication by either CEA/CAS, effectiveness of revascularization versus medical therapy alone is not well established**

How Many Strokes Can We Prevent???

- Decreasing incidence of stroke (AHA, Circulation, 2020)
- Medical intervention is improving

---

[Image of graph showing decreasing trend in stroke incidence over time]
“Effectiveness” for CEA

- “real world data”: efficacy vs effectiveness

Variation in Carotid Endarterectomy Mortality in the Medicare Population
Trial Hospitals, Volume, and Patient Characteristics

Conclusion—Medicare patients’ perioperative mortality following CEA is substantially higher than that reported in the trials, even in those institutions that participated in the randomized studies. Caution is advised in translating the efficacy of carefully controlled studies of CEA to effectiveness in everyday practice.

“Effectiveness” for CEA/CAS

Stroke/Death Rates Following Carotid Artery Stenting and Carotid Endarterectomy in Contemporary Administrative Dataset Registries: A Systematic Review

- Higher than 3% stroke/death for asymptomatic
  - 9 of 21 CAS studies
  - 1 of 21 CEA studies
“Effectiveness” for TCAR

- National Coverage Decision for Carotid Stenting
  - Since 2005, symptomatic, high risk, \( \geq 70\% \)

- September 2016: SVS-PSO-VQI-TSP
  - “Real-world” outcome of TCAR vs CEA
  - Asymptomatic, high risk, \( \geq 80\% \) stenosis
  - Symptomatic, high risk, \( \geq 50\% \) stenosis
  - All data is collected

TCAR vs TF-CAS

- 9/16 to 4/19; 1035 physicians from 319 centers; 95.4% of all TCAR procedures
- 3282 propensity matched “pairs”
- TCAR: Vascular surgeons (85%), general surgeons (9%), neurosurgeon (2%), cardiologist (1%)
- TF-CAS: VS (28%), rad (21%), card (20%), NS (13%), neuro (11%), GS (3%)
TCAR vs TF-CAS

- Lower risk of in-hospital stroke or death, stroke, and death
- No difference in MI

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Transcatheter Artery Revascularization (n = 5285)</th>
<th>Transfemoral Carotid Artery Stenting (n = 3286)</th>
<th>Absolute Difference (95% CI)</th>
<th>Relative Risk (95% CI)</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Stroke or death</td>
<td>5.2 (1.6)</td>
<td>102 (1.1)</td>
<td>-1.52 (-2.29 to -0.75)</td>
<td>0.51 (0.37 to 0.72)</td>
<td>&lt; .001</td>
</tr>
<tr>
<td>Stroke or death, 30 d</td>
<td>64 (1.9)</td>
<td>121 (2.7)</td>
<td>-1.73 (-2.57 to -0.90)</td>
<td>0.53 (0.39 to 0.72)</td>
<td>&lt; .001</td>
</tr>
<tr>
<td>Stroke</td>
<td>4.3 (1.3)</td>
<td>75 (2.4)</td>
<td>-1.10 (-1.79 to -0.41)</td>
<td>0.54 (0.38 to 0.75)</td>
<td>.001</td>
</tr>
<tr>
<td>Stroke, 30 d</td>
<td>4.4 (1.3)</td>
<td>83 (2.5)</td>
<td>-1.19 (-1.89 to -0.49)</td>
<td>0.53 (0.37 to 0.76)</td>
<td>&lt; .001</td>
</tr>
<tr>
<td>Transient ischemic attack</td>
<td>22 (0.8)</td>
<td>32 (1.0)</td>
<td>-0.10 (-0.77 to 0.56)</td>
<td>0.69 (0.40 to 1.18)</td>
<td>.17</td>
</tr>
<tr>
<td>Death</td>
<td>14 (0.4)</td>
<td>32 (1.0)</td>
<td>-0.55 (-0.98 to -0.11)</td>
<td>0.44 (0.23 to 0.82)</td>
<td>.006</td>
</tr>
<tr>
<td>Death, 30 d</td>
<td>25 (0.8)</td>
<td>45 (2.5)</td>
<td>-0.70 (-1.24 to -0.16)</td>
<td>0.52 (0.32 to 0.84)</td>
<td>.007</td>
</tr>
<tr>
<td>Myocardial infarction</td>
<td>20 (0.2)</td>
<td>10 (0.2)</td>
<td>-0.09 (-0.27 to 0.09)</td>
<td>0.70 (0.27 to 1.94)</td>
<td>.47</td>
</tr>
</tbody>
</table>

TCAR vs CEA

- 9/16 to 5/19: 5719 TCAR (236 centers) and 44442 CEA (354 centers)
- TCAR: older, more symptomatic, more comorbidities, more likely redo-carotid intervention/CEA
TCAR vs CEA

**Propensity Score and Coarsened-Exact Matching**

<table>
<thead>
<tr>
<th>In-Hospital Outcomes</th>
<th>Propensity Score Matching (n=8,160 in each)</th>
<th>1:1 CEM (n=4,885 in each)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>OR (95% CI)</td>
<td>p-value</td>
</tr>
<tr>
<td>Death</td>
<td>0.88 (0.46-1.61)</td>
<td>0.63</td>
</tr>
<tr>
<td>Ipsilateral Stroke</td>
<td>0.92 (0.64-1.32)</td>
<td>0.64</td>
</tr>
<tr>
<td>Stroke</td>
<td>0.80 (0.56-1.11)</td>
<td>0.18</td>
</tr>
<tr>
<td>MI</td>
<td>0.44 (0.26-0.66)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Stroke/Death</td>
<td>0.77 (0.57-1.04)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Stroke/Death/MI</td>
<td>0.65 (0.50-0.84)</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Cranial Nerve Injury</td>
<td>0.13 (0.07-0.22)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Post-procedural Hypotension</td>
<td>1.66 (1.47-1.87)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Post-procedural Hypertension</td>
<td>0.64 (0.57-0.71)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Bleeding with intervention</td>
<td>1.17 (0.83-1.66)</td>
<td>0.38</td>
</tr>
<tr>
<td>Non-Home discharge</td>
<td>0.75 (0.64-0.87)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Hospital Stay for more than 1 day</td>
<td>0.74 (0.68-0.80)</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

Matched on symptomatic status, age, CAD, CHF, COPD, OXID, prior ipsilateral CEA, prior ipsilateral CAS, contralateral occlusion, ASA Class and statin use.

TCAR Learning Curve

**Learning Curve for Surgeons Adopting Transcarotid Artery Revascularization**

Based on the Vascular Quality Initiative-Transcarotid Artery Revascularization Surveillance Project


- No differences in stroke/mortality
- Increasing experience associated w/improved efficiency, more complex patients, less use of general anesthesia
- Expert level had no failures
Optimize TCAR Effectiveness

Early Outcomes in the ROADSTER 2 Study of Transcarotid Artery Revascularization in Patients With Significant Carotid Artery Disease

- 692 “high risk” patients over 43 sites
- Analysis of 60 “protocol violations”
  - 11 inclusion/exclusion criteria; remainder had medication noncompliance
  - 9 more strokes; 11 stroke/death; no change in MI

Who Will I Treat in 2021???

- **Symptomatic** patients (≥70% and select ≥50%)
- **Asymptomatic** patients
  - Good surgical candidate (active/functioning, comorbidities well controlled)
  - **3-5 year** life expectancy
  - Carotid stenosis ≥80% (EDV >140, CTA)
  - Perioperative mortality/morbidity <1%

- “TCAR first” in high risk patients...but only with appropriate anatomy
- Otherwise CEA, rare situation require TF-CAS
Anything Else We Should Know?

**The Carotid Revascularization and Medical Management for Asymptomatic Carotid Stenosis Study**

- Health and Hope for Patients at Risk for Stroke

- Started in 2014
- Two parallel multi-center RCT
  - Aggressive medical management vs CEA
  - Aggressive medical management vs CAS (TCAR)
  - >70% asymptomatic patients (2480 participants; 40% women; 12% minorities)

Anything Else We Should Know?

- Identification of “high risk” patients with carotid stenosis
  - Sub-stratify lesions, overall cranial perfusion, cognitive effects
  - Ultrasound: plaque evaluation (thrombus)
  - CT/MRI: plaque characteristics/silent embolic infarcts
  - PET: inflammatory markers/plaque stability
  - Transcranial Doppler (TCD)
    - Microembolic signal
    - Velocity/flow measurement
Anything Else We Should Know?

• Improvement in Stent Design

<table>
<thead>
<tr>
<th>Stent Name</th>
<th>Stent Image</th>
<th>Stent Design</th>
<th>Free Cell Area</th>
<th>Specifics of Design</th>
<th>Stent Diameter (unconstrained)</th>
<th>Stent Length (unconstrained)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gore</td>
<td><img src="gore.png" alt="Stent Image" /></td>
<td>Mesh Covered</td>
<td>0.5mm²</td>
<td>PTFE mesh (heparin coated) on nitinol stent</td>
<td>unable to obtain specifics</td>
<td></td>
</tr>
<tr>
<td>Roadsafer</td>
<td><img src="roadsafer.png" alt="Stent Image" /></td>
<td>Mesh Covered</td>
<td>0.4mm²</td>
<td>Nitinol double layer micromesh</td>
<td>5 - 10mm (15 - 30Fr)</td>
<td>25 - 43mm</td>
</tr>
<tr>
<td>InspireMD Cguard</td>
<td><img src="inspiremd.png" alt="Stent Image" /></td>
<td>Mesh Covered</td>
<td>0.18mm² <em>2</em></td>
<td>PET MicroNet on nitinol stent</td>
<td>6 - 10mm (18 - 30Fr)</td>
<td>20 - 60mm</td>
</tr>
</tbody>
</table>


Anything Else We Should Know?

A First-in-Human Evaluation of a Novel Mesh-Covered Stent for Treatment of Carotid Stenosis in Patients at High Risk for Endarterectomy

Clinical trial of carotid artery stenting using dual-layer CASPER stent for carotid endarterectomy in patients at high and normal risk in the Japanese population

JACC: Cardiovascular Interventions Vol. 11, No. 23, 2018

Use of Dual-Layered Stents in Endovascular Treatment of Extracranial Stenosis of the Internal Carotid Artery

Results of a Patient-Based Meta-Analysis of 4 Clinical Studies

JACC: Cardiovascular Interventions Vol. 11, No. 23, 2018

Reduction of cerebral DWI lesion burden after carotid artery stenting using the CASPER stent system

J Neurointerv Surg 2019;
Summary/Conclusion

- Stroke and carotid artery stenosis remain significant disease processes
- Optimal medical management is mandatory for all patients with carotid stenosis
- There appears to be potential benefit in appropriate screening in otherwise asymptomatic patients
- Carotid revascularization remains an important treatment option for select patients
  - Optimal approach (TCAR vs CEA) dependent on patient anatomy
- Future research will further identify “high risk” asymptomatic patients and continue to reduce risks associated with carotid revascularization
Jeffrey Jim, MD, MPHS, FACS
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