Overview of Research Types

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Research Types:
CONFLICTS OF INTEREST

- None
Research Types: INTRODUCTION

- Who cares?
### Research Types: INTRODUCTION

- **Who cares?**

- **Wrong plan** – a lot of effort extended with nothing to show for it. A waste of time at best, bad data at worst.

- **Don’t pick the type of research – pick the question to answer, type derives from that!**
Research Types:
INTRODUCTION

- Clinical research
- Basic science research
- Industry sponsored trials
- Analysis and calculation, others
Research Types: INTRODUCTION

• All differ according to:
  – Amount of preplanning
  – IRB and subject protection, animal welfare
  – External oversight
  – Funding, cost
  – Coordinator
  – Statistician
  – Contribution to our knowledge
### Research Types: Clinical

- Case studies
- Small series
- Retrospective review
- Prospective database
- Prospective randomized trial
Research Types: CLINICAL

- Case studies
- Small series
  - Fairly easy to do
  - Often trivial
  - Of value if they TEACH US SOMETHING or change our management somehow.
Superior mesenteric artery dissection: Case report

Yann Gouëffic, MD, a Alain Costargent, MD, a Benoît Dupas, MD, b Marie-Françoise Heymann, MD, c Philippe Chaillou, MD, a and Philippe Patra, MD, a Nantes, France

Spontaneous dissections of the superior mesenteric artery are exceptional events because only 26 reports have been published. We present a new case, revealed with an acute abdominal syndrome. Computed tomographic angiography and arteriography allowed a rapid diagnosis and urgent surgical intervention. Progress in imagery makes diagnosis and follow-up examination easier. Surgery is indicated for acute symptomatic forms with suspicion of mesenteric ischemia. In the other cases, a simple follow-up examination may be appropriate. (J Vasc Surg 2002;35:1003-5.)

CASE REPORT

In January 2000, a 56-year-old man, with no clinical history, was rushed to the hospital with sudden epigastric and paraumbilical pain, which had started 2 hours previously. Cardiovascular risk factors known at the time were smoking (15 packs/year) and overweight (body mass index, 29.38). Postoperative findings revealed hypertriglyceridemia at 2.26 mmol/L (healthy level, 0.45 to 1.80 mmol/L), with a glycemia level within the normal limits. The lack of physical signs during clinical examination and the normal aspect of the abdominal plain films contrasting with the intensity of pain led us to perform an abdominal computed tomographic (CT) angiography. This exploration revealed small bowel ischemia with a parietal thickening and, at the early arterial phase, a 90% reduction of the superior mesenteric artery (SMA) lumen 2 cm from its origin (Fig 1), combined with a dishomogeneous soft tissue density. Postoperative results were normal, with resumption of gastrointestinal function on the fourth day. Histopathologic examination results revealed a dissection in the media, located at the junction of the internal two-thirds with the external third, without thrombus in the false lumen, which was aneurysmal. No histologic anomaly, such as medial necrosis and fibromuscular dysplasia, was observed. Ten days after the operation, CT angiographic results with reconstruction (Fig 3) showed a patent bypass. The patient left the hospital with a platelet-inhibiting treatment and was reexamined 3 months later and found to be asymptomatic.

DISCUSSION

Spontaneous SMA dissections are exceptional events. During a period of 50 years, only 27 cases (including this one) have been reported. 1 Nevertheless, they represent the
Research Types: CLINICAL

- Retrospective review
  - Most common
  - Fairly easy
  - Now need IRB approval
  - How do you ensure you are capturing all the cases?
  - Databases
  - Chart review
Is the rationale for carotid angioplasty and stenting in patients excluded from NASCET/ACAS or eligible for ARChER justified?

Karl A. Illig, MD, Renyu Zhang, William Tanski, MD, Curt Benesch, MD, Yaron Sternbach, MD, and Richard M. Green, MD, Rochester, NY

Purpose: To compare outcome after carotid endarterectomy (CEA) in patients who would have been excluded from the North American Symptomatic Carotid Endarterectomy Trial (NASCET) or the Asymptomatic Carotid Atherosclerosis Study (ACAS) or would have been eligible for Acculink for Revascularization of Carotids in High Risk Patients (ARChER), a current high-risk stent registry, with outcome in a similar cohort at low risk.

Methods: Records of all CEAs performed at our institution from July 1993 to December 2000 were reviewed. Patients were assigned to groups either eligible or ineligible for NASCET and ACAS or ARChER, and criteria were stratified according to whether risk was defined by anatomic or medical problems or whether patients were ineligible according to nonmedical protocol exclusion criteria only.

Results: Preoperative and postoperative data were sufficient to determine risk status according to various study criteria in 857 patients. Stroke or death within 30 days, the primary end point, occurred in 2.1% of patients. Rates were similar in patients excluded from (2.7%) or included in (1.6%) NASCET and ACAS and in patients eligible (3.1%) or ineligible (2.1%) for ARChER. Rates did not differ according to whether exclusion or inclusion was based on anatomic risk, medical risk, or protocol exclusion, although trends favored worse outcome in the ARChER medical risk subgroup. A higher rate of minor complications was found in the elderly; however, stroke and death rates were similar according to age, gender, repeat procedure, or the presence of contralateral occlusion.

Conclusions: No statistically or clinically significant differences were found in combined 30-day stroke or death rates after CEA in any group defined by previous surgical trials or current ongoing high-risk stent registry. While high-risk groups may exist, the premise that operative risk is higher in patients excluded from NASCET and ACAS or eligible for ARChER is not supported. (J Vasc Surg 2003;37:575-81.)
Research Types: CLINICAL

- Prospective database
  - Albany!
  - VQI
  - NSQIP
  - NIS

- Can answer questions about rare things or make large summary statements, but details unknown
Research Types: CLINICAL

- Prospective randomized trial
  - Can be extraordinarily expensive and difficult (but not always)
  - Usually need “professional help”
  - IRB, DSMC
Protected carotid stenting in high-surgical-risk patients: The ARCHeR results

William A. Gray, MD, a L. Nelson Hopkins, MD, b Sanjay Yadav, MD, c Thomas Davis, MD, d Mark Wholey, MD, e Richard Atkinson, MD, f Alberto Cremonesi, MD, g Ronald Fairman, MD, h Gary Walker, PhD, i Patrick Verta, MD, j Jeff Popma, MD, k Renu Virmani, MD, l and David J. Cohen, MD, MSc, l for the ARCHeR Trial Collaborators,* New York and Buffalo, NY; Cleveland, Ohio; Detroit, Mich; Pittsburgh and Philadelphia, Penn; Sacramento, Calif; Ravenna, Italy; Boston, Mass; and Bethesda, Md

Background: Carotid endarterectomy is the standard of care for most patients with severe extracranial carotid bifurcation disease. However, its safety and efficacy in patients with significant surgical risk are unclear. The ARCHeR (ACCLink for Revascularization of Carotids in High-Risk patients) trial was performed to determine whether carotid artery stenting with embolic protection is a safe and effective alternative to endarterectomy in high-surgical-risk patients.

Methods: The ARCHeR trial is a series of three sequential, multicenter, nonrandomized, prospective studies. Forty-eight sites enrolled 581 high-surgical-risk patients between May 2000 and September 2003. Patients with severe carotid artery stenosis (angiographically defined, symptomatic ≥50%, or asymptomatic ≥80%) had an ACCLink nitinol stent implanted. The ACCUNET filter embolic protection system was added to the procedure in the final 2 studies (422 patients). The primary efficacy end point was a composite of periprocedural (≤30 days) death, stroke, and myocardial infarction, plus ipsilateral stroke between days 31 and 365.

Results: The 30-day rate of death/stroke/myocardial infarction was 8.3% (95% confidence interval [CI], 6.2%-10.8%), and that of stroke/death was 6.9% (95% CI, 5.0%-9.3%). Most (23/32) strokes were minor, of which more than half (12/23) returned to baseline National Institutes of Health Stroke Scale scores within 30 days. The 30-day major/fatal stroke rate was 1.5% (95% CI, 0.7%-2.9%). No hemorrhagic strokes were observed in the study. Ipsilateral cerebrovascular accident occurred in 1.3% between 30 days and 1 year, thus giving a primary composite end point of 30-day death/stroke/myocardial infarction plus ipsilateral stroke at 1 year of 9.6% (95% CI, 7.2%-12.0%), which is below the 14.4% historical control comparator. Target lesion revascularization at 12 months and 2 years was 2.2% and 2.9%, respectively.

Conclusions: The ARCHeR results demonstrate that extracranial carotid artery stenting with embolic filter protection is...
Protected carotid stenting in high-surgical-risk patients: The ARCHeR results

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Carotid Endarterectomy and Prevention of Cerebral Ischemia in Symptomatic Carotid Stenosis

Marc R. Mayberg, MD; S. Eric Wilson, MD; Frank Yatsu, MD; David G. Weiss, PhD; Louis Messina, MD;
Linda A. Hershey, MD; Cindy Colling, RPh; Joseph Eskridge, MD; Daniel Deykin, MD; H. Richard Winn, MD;
for the Veterans Affairs Cooperative Studies Program 309 Trialist Group

Objective.—To determine whether carotid endarterectomy provides protection against subsequent cerebral ischemia in men with ischemic symptoms in the distribution of significant (>50%) ipsilateral internal carotid artery stenosis.

Design.—Prospective, randomized, multicenter trial.

Setting.—Sixteen university-affiliated Veterans Affairs medical centers.

Patients.—Men who presented within 120 days of onset of symptoms that were consistent with transient ischemic attacks, transient monocular blindness, or recent small completed strokes between July 1988 and February 1991. Among 5000 patients screened, 189 individuals were randomized with angiographic internal carotid artery stenosis greater than 50% ipsilateral to the presenting symptoms. Forty-eight eligible patients who refused entry were followed up outside of the trial.

Outcome Measures.—Cerebral infarction or crescendo transient ischemic attacks in the vascular distribution of the original symptoms or death within 30 days of randomization.

Intervention.—Carotid endarterectomy plus the best medical care (n = 91) vs the best medical care alone (n = 98).

Results.—At a mean follow-up of 11.9 months, there was a significant

THE PRESUMED relationship between atheromatous disease of the cervical carotid artery and cerebral infarction has led to widespread use of carotid endarterectomy to prevent stroke; an estimated 100,000 endarterectomies of cervical extracranial vessels were performed annually in the United States in the early 1980s. In recent years, the therapeutic efficacy of this procedure has been questioned, noting the considerable variability in outcome among surgeons compared with the indeterminate risk of stroke from extracranial occlusive disease, geographical variations in the application of carotid endarterectomy, and widespread differences in surgical indications.
Research Types: BASIC SCIENCE

- Basic science
- Translational research – animals, engineering
Research Types: INDUSTRY SPONSORED TRIALS

- Industry sponsored trials
INVESTIGATIONAL PLAN

STUDY DEVICE: Harvest SmartPReP®2 Bone Marrow Aspirate Concentrate System

PROTOCOL: Pivotal Study of the Safety and Effectiveness of Autologous Bone Marrow Aspirate Concentrate (BMAC) for the treatment of Critical Limb Ischemia due to Peripheral Arterial Occlusive Disease

SPONSOR: Harvest Technologies Corp

PROTOCOL NUMBER CLI-2011-1

REVISION 04-27-12
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**Attachment I** Clinical Protocol
**Attachment II** Anticipated Adverse Events
**Attachment III** Case Report Forms
**Attachment IV** Blank-no documents
**Attachment V** Sample Informed Consent
**Attachment VI** Draft Product Labeling
**Attachment VII** Photography Release Form
**Attachment VIII** Bibliography
**Attachment IX** Draft DSMB Charter
**Attachment X** S.O.P.’s
Research Types: INDUSTRY SPONSORED TRIALS

- Industry sponsored trials
  - Typically are paid, but extensive bureaucratic responsibilities. Full-time study coordinator.
  - Early access to great things
  - Much less opportunity for authorship
Research Types: OTHERS?

- Meta analysis
- Decision analysis/QALYs
- Cost:Benefit analysis
- Review articles
- Consensus statements
- Education and training
Sensitivity Analysis on prob develop TAAA with med management

Expected Value

prob develop TAAA with med management
Research Types: WHAT TYPE IS BEST?

Observation, clinical trick to share
We’ve made a change – how have we done?
There is a common problem with two possible options
We have an extensive experience with something
There is a new product on the market – does it work?
Research Types: WHAT TYPE IS BEST?

- There are lots of published trials, but they don’t all say the same thing
- We are doing something in the short term but neglecting the long-term outcomes
Research Types:
WHAT TYPE IS BEST?

- I’d like to generate a hypothesis
- I have a hypothesis that I want to prove true
- I have a hypothesis and I want to figure out how and why it works
Research Types: SUMMARY

- FIRST, figure out what question you are trying to answer.
- This will guide the type of study you will be doing.
- Get help!
  - Mentor
  - Experienced colleagues/peers
  - Your group
Research Types: SUMMARY

• Basically, figure out how to best answer your question (given the resources you have at your disposal)
  – Money
  – Time
  – Experience
  – Background