WELCOME!!

McMaster University
Evidence-Based Clinical Practice Workshops

June 4-8, 2018
And Now…

A day in Sheri’s GIM Clinic
Disclosures

• Paid Editorial Role JAMA’s The Rational Clinical Examination

• No other disclosures or conflicts of interest, but…
Sorry about our president.
Perdón por nuestro presidente.
为总统感到抱歉
Désolé pour notre président.
Tut mir leid wegen unseres Präsidenten.
Elnézést az elnökünk miatt.
Oprostite nam za nasega predsednika.
מְצַוֵּרים על המישה שולן
Undskyldninger for vores præsident.
ما را ببخش كه ترامب را انتخاب كردیم
Mijn excuses voor onze president.
Przepraszam za naszego prezydenta.
우리 대통령 때문에 미안해
Thunderclap
Objectives

• By attending the session, participants will be able to:
  • Apply the 5 elements of the evidence cycle
  • Differentiate between foreground and background questions and match information resources for each
  • Identify search terms to find evidence for a prognosis question
  • Apply communication techniques for engaging patients in discussion about prognosis
Ask
Acquire
Appraise

Evidence-based medicine cycle

Apply

Hierarchy of Evidence

Assess

Patient dilemma

Values & Preferences
Written informed consent was obtained to share this story...
Go to Audio…

• Listen to the audiotape.
• Please decide what is the most important question being posed in this case…
Interactive using your cell phone!

• Back to slido.com

• What is the most important question being posed in this case? (answer in words or short phrases, may answer multiple times)
Slido: What is AA’s Prognosis?

- “...on a scale of these things that I’ve seen you seem to be on the good end of things”

- From the patient’s perspective, what level of confidence do you have in this estimate?
Slido: Audience Participation

- Everyone in the audience has just had a Thunderclap headache. Your fate is linked to the index card that you have been given.

- Please Raise Cards as I name your file card color
  - WHITE
  - BLUE
Slido: Audience Participation

- Everyone in the audience has just had a Thunderclap headache. Your prognosis is linked to the sticker in the upper right hand corner of the file card you have been given.

- Please Raise Cards as I name your sticker color
  - Pink
  - Yellow
  - Orange
  - Green

- We will return to this.
AA’s Prognosis: Go to Audio...
Audience Participation

• Everyone please stand

• I’m sorry. People with the following cards have a cerebral aneurysm.
  • WHITE CARDS Please Sit Down

• Dodged a bullet. NOT a Cerebral Aneurysm
  • BLUE CARDS

• Go to Slido
“… 19 out of 20 times when there is bleeding in your brain, it’s an aneurysm. We think you might be the 1 out of 20 times where a vein bled.”

From the patient’s perspective, what level of confidence do you have in this estimate? (single answer)

Describe what you think the patient is feeling (words or short phrases); you may provide multiple answers.
RCVS: Go to Audio…
Just a simple request

• AA: I want to see another Neurologist for another opinion…
• SK: Why?
• AA: So many questions…What is RCVS? What will happen? I don’t understand what this means or what I am supposed to do.
• SK: (inside voice: Ugh… )
Now what?

• AA’s questions…
  • What is RCVS?
  • What will happen?
  • I don’t understand what this means or what I am supposed to do.

• Background vs. Foreground question?

• Go to Slido
What is RCVS: Background

• Go to UpToDate
## Summary of critical elements for the diagnosis of reversible cerebral vasoconstriction syndromes

1. Recurrent acute, severe headaches, with or without additional neurologic signs and symptoms.

2. Transfemoral angiography or indirect (CT or MR) angiography documenting segmental cerebral artery vasoconstriction.

3. No evidence for aneurysmal subarachnoid hemorrhage.

4. Normal or near-normal cerebrospinal fluid analysis results (total protein content < 80 mg/dL, white blood cell count < 10/mm³, normal glucose content).

5. The diagnosis cannot be confirmed until reversibility of the angiographic abnormalities is documented within 12 weeks after onset or, if death occurs before the follow-up studies are completed, autopsy rules out conditions such as vasculitis, intracranial atherosclerosis, and aneurysmal subarachnoid hemorrhage, which can also manifest as headache and stroke.

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RCVS: reversible cerebral vasoconstriction syndromes; CT: computed tomography; MR: magnetic resonance.

From Annals of Internal Medicine, Calabrese LH, Dodick DW, Schwedt TJ, et al. Narrative review: Reversible cerebral vasoconstriction syndromes, Volume 146, Issue 1, Pages 34-44. Copyright © 2007 American College of Physicians. All Rights Reserved. Reprinted with the permission of American College of Physicians, Inc.
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Evidence-based medicine cycle

Hierarchy of Evidence

Patient dilemma

Values & Preferences
Your Clinical Questions

• P: Patient, population, problem
• I: Intervention, exposure, prognostic factor
• C: Comparison
• O: Outcome
• T: Type of question
• T: Type of study design
My Clinical Question

• **P:** Headache and intracranical vasospasm
• **I:** Followed over time
• **C:** --
• **O:** Rebleed, headaches, mortality
• **T:** Prognosis
• **T:** Cohort or Follow up Study (Prospective)
<table>
<thead>
<tr>
<th></th>
<th>Search Term</th>
<th>Results</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Headache</td>
<td>71,156</td>
</tr>
<tr>
<td>2</td>
<td>Intracranial vasospasm</td>
<td>4,385</td>
</tr>
<tr>
<td>3</td>
<td>#1 AND #2</td>
<td>250</td>
</tr>
<tr>
<td>4</td>
<td>Cohort Study</td>
<td>1,604,949</td>
</tr>
<tr>
<td>5</td>
<td>#3 AND #4</td>
<td>27</td>
</tr>
</tbody>
</table>
Another Search

#1  “reversible cerebral vasoconstriction syndrome” 379
#2  Cohort Study 1,604,949
#3  #1 AND #2 30
#4  Prospective Study 496,275
#5  #3 AND #4 7

Chen et al. Neurology 2015; 84(15):1552-8
My Paper’s MeSH Terms

• Follow up- studies
• Headache
• Recurrence
• Vasospasm

- MeSH Terms
  - Adult
  - Female
  - Follow-Up Studies
  - Headache/diagnosis
  - Headache/epidemiology*
  - Headache/etiology
  - Humans
  - Male
  - Middle Aged
  - Recurrence
  - Sexual Behavior
  - Syndrome
  - Taiwan/epidemiology
  - Time Factors
  - Vasospasm, Intracranial/complications
  - Vasospasm, Intracranial/diagnosis
  - Vasospasm, Intracranial/epidemiology*
Searching for Cohort Studies

- Cohort Study
  - Follow-up Studies
  - Longitudinal Studies
  - Prospective Studies
  - Retrospective Studies
Patient dilemma

Ask

Acquire

Appraise

Evidence-based medicine cycle

Hierarchy of Evidence

Apply

Values & Preferences
Critical Appraisal Framework

I. How serious is the risk of bias? (*used to be called are the results valid?)

II. What are the results?
   • Magnitude of effect
   • Confidence / precision of estimate

III. How can I apply to patient care
Risk of Bias: Chen 2015

• Representative?
  • Prospective cohort of 210 RCVS patients from Tai Pei Veteran’s Clinic: initial thunderclap between 2000-12
  • Tertiary care referral filter

• Prognostically homogeneous? Yes. All with first thunderclap (early and uniform)

• Objective and unbiased outcomes?
<table>
<thead>
<tr>
<th>Table 2</th>
<th>Diagnostic evaluations for patients with suspected RCVS in our headache center</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Investigations for patients with suspected RCVS</strong></td>
<td></td>
</tr>
<tr>
<td>Comprehensive history-taking and headache intake form</td>
<td>H &amp; P, neurological exam, surgical, headache, medication, and personal history</td>
</tr>
<tr>
<td>Neurologic examination</td>
<td>Edema and meningeal signs</td>
</tr>
<tr>
<td>Blood testing</td>
<td>Complete blood counts, biochemical panels, thyroid function, autoimmune profiles</td>
</tr>
<tr>
<td>MRIs</td>
<td>MRI sequences include T1, T2, FLAIR, CUBE FLAIR, T1 with contrast, T1-FLAIR with contrast, T2 gradient echo and/or SWI, DWI, ADC, MRA, and magnetic resonance venography</td>
</tr>
<tr>
<td>Extracranial and transcranial duplex sonography</td>
<td>V\textsubscript{MCA}, V\textsubscript{ICA}, and Lindegaard</td>
</tr>
<tr>
<td>CSF studies</td>
<td>Xanthochromia, cell counts, glucose, protein, cultures</td>
</tr>
</tbody>
</table>

Abbreviations: ADC = apparent diffusion coefficient; DWI = diffusion weighted image; FLAIR = fluid-attenuated inversion recovery; MRA = magnetic resonance angiography; RCVS = reversible cerebral vasoconstriction syndrome; SWI = susceptibility weighted image.

\( a \) The severity of vasoconstrictions on MRA was graded on a 5-point scale: 0 (0% to <10%), 1 (10% to <25%), 2 (25% to <50%), 3 (50% to <75%), and 4 (\geq75%), and designated the “vasoconstriction score” of each arterial segments for computations. The vasoconstriction scores of both sides were averaged to derive a mean score. The mean scores of different arterial segments were averaged to derive a combined score.

\( b \) \( V\textsubscript{MCA} \) = mean flow velocity of the middle cerebral artery; \( V\textsubscript{ICA} \) = mean flow velocity of the distal extracranial internal carotid artery; Lindegaard index = \( V\textsubscript{MCA}/V\textsubscript{ICA} \).
What are the Results: Chen 2015

• How likely are outcomes?
  • 12 year study
  • Mean follow up 37.5 +/- 24.4 months
  • Thunderclap headaches:
    • New thunderclap: 18/168 (~10%)
    • Probable RCVS: 9/168 (~5%)
  • Re-bleed: 0
  • Dead from Neurologic Complication: 0
What are the Results: Chen 2015

- How precise are the estimates?
  - No 95% CI anywhere in the paper
    - New thunderclap: 18/168 (~10%)
    - Probable RCVS: 9/168 (~5%)
  - Re-bleed / death: 0; might be as high as 1.8%*
  - What about lost to follow up? 40 patients-contributes uncertainty 40/210 = ~20%

*rule of 3’s for extreme results- Table 20-1
And One More…

• Second Prospective trial (Ducros Brain 2007; 130:3091)
• Paris Headache Center 67 consecutive patients
• 24/67 (35%) mild persistent headache, 2 (3%) depressive symptoms (compared to?)
• No death, no relapse, no re-bleeds in 16 +/- 12.4 months of follow up
Application: Back to AA

• Curbside a neurology colleague
• Sheri says:
  • RCVS prognosis looks good!
  • Does she have RCVS?
  • Have a look?
• Neurologist verdict: Vein bleed…
• Sheri (inside voice: Ugh….)
Vein Bleed Prognosis

- Vein Bleed: Perimesencephalic SAH
- Multiple cohorts (differing quality) but all show good prognosis
- Look at Greebe et al
Life expectancy after perimesencephalic subarachnoid hemorrhage

Greebe et al. Stroke 2007; 38:1222-4
• Retrospective analysis of prospectively collected data (Netherlands)

• 160 patients with vein bleed followed for 1213 patient years (1983 to 2005)

• Mean follow up 7.5 years (1 to 23 years)
Greebe et al

- 11 patients died
  - MI, cardiac failure, cerebral infarction, cancers, infection in old age
- Standardized mortality ratio that was age and sex adjusted 0.61 (95% CI, 0.34 to 1.1)
- Worst case scenario (2 patients abroad counted as dead) 0.72 (95% CI, 0.42-1.24)
- No new SAH - 0% with 95% CI (0 -0.3%)
What about functional Status?
Raise your card when I call out the STICKER colors

• **White Cards**
  - Aneurysm: Pink sticker = Dead 57
  - Aneurysm: Yellow sticker = Stroke 56
  - Aneurysm: Green sticker = Alive and Well 29

• **Blue Cards**
  - RCVS or VEIN bleed: Orange sticker = Headache 1
  - RCVS or VEIN bleed: Green sticker = Alive & Well 7

• What about AA concerns? Exercise? 35 lbs?
What did I tell her?

- Go to document camera
Putting it all together

• Demonstrated tools and strategies
  • Evidence cycle, PICO, critical appraisal questions

• Modeled interactive teaching methods
  • Patient audiotape, live polling, luck of the draw cards

• Reinforce principles
  • Not all evidence is created equal (hierarchy of evidence)
  • Evidence alone is never enough (values and preferences)
Putting it all together

• Why could I help her?
  • Not afraid of what I don’t know and know how to find out
  • Numbers
  • See past the labels to the person

• Approach this week
  • Unafraid
  • Step out of your comfort zone
  • Never lose sight of the humanity