Faculty Disclosure

Faculty: Rick Swartz MD, PhD, FRCPC
Scientist, Assistant professor, Sunnybrook Health Sciences Centre

Relationships with commercial interests:
  • None - Not Applicable

Potential for conflict(s) of interest:
  • None - Not Applicable
Mitigating Potential Bias

• All scientific research referred to, reported, or used is in the support or justification of patient care.

• Recommendations conform to the generally accepted standards.

• We may be discussing off-label uses of drugs as they apply to pregnancy.

• Use of at least one unauthorized “Simpson’s” image.
Overview

- Incidence and overview of stroke in pregnancy
- Framework and Consensus process
- Consensus Statements
Stroke in pregnancy

- Major cause of morbidity & mortality during pregnancy and post-partum
  - ICH from aneurysm or AVM causes 5-12% all maternal deaths
- Overall mortality higher for hemorrhagic than Ischemic
- Low absolute risks – most pregnancies are OK – but high relative risk (pregnancy is riskier than not being pregnant).
- Incidence estimate vary widely.
Stroke in pregnancy

• Can include ischemic stroke, venous sinus thrombosis, hemorrhagic stroke (note: overlaps)

• Risk is much higher immediately peri-partum and 6 weeks post-partum (days -2 to +1 have 34x RR) Epidemiology 2001, 12(4):456-460

R.H. Swartz, University of Toronto
The incidence of pregnancy-related stroke: A systematic review and meta-analysis

- **Inclusion**
  - English language papers
  - Includes any type of stroke
  - Reports stroke rate from a defined number of pregnancies

- **Exclusion**
  - Abstracts, conference proceedings, care reports
  - Single stroke type
  - Published before 1990
    - because of limitations in imaging and diagnosis
- 30/100,000 (95% CI 18.8-47.9)
- 3 times the overall 18-44 incidence (10/100,000)
- No trend over time
- Variation among types, methods, countries/health systems

Swartz, IJS 2017
Risk Factors and Etiologies

- **Common etiologies**
  - Aneurysm
  - AVM
  - Gestational hypertension, HELLP, Pre-eclampsia, eclampsia

- **Common risk factors**
  - Congenital heart disease and other cardiac conditions
  - Hypertension
  - Diabetes
  - Thrombocytopenia
  - Sickle cell anemia
  - Migraine
  - Systemic lupus erythematosus
  - Skidmore: 29% of women with ischemic stroke in pregnancy had a history of stroke prior to pregnancy

- **Pregnancy specific issues**
  - Prothrombic changes
  - Dehydration
  - Hypertensive disorders
  - RCVS
  - Sheehan’s syndrome
  - CVST

*Swartz, IJS 2017*
- Hemorrhagic stroke
  12.2 / 100,000
  (95% CI 6.4 - 23.2)

- Ischemic stroke
  12.2 / 100,000
  (95% CI 6.7 – 22.2)

- CVST
  9.1 / 100,000
  (95% CI 4.3-18.9)
Common but uncommon

• High-volume stroke and OB centres encounter stroke in pregnancy

• Most clinicians only see a handful.

• Each case differs:
  • stages of pregnancy, timing of stroke preceding or within pregnancy, stroke severity, stroke/medical comorbidities, stroke etiology, pregnancy history, family situation etc.

• Evidence & guidelines for stroke management

• Evidence and guidelines for routine OB management. But none of this applies to women with BOTH.

• How to approach seemingly one-off patients? Is there order in chaos?
Stroke in Pregnancy - Overriding principles in management

- Maternal health is vital for fetal wellbeing
- How would you treat the stroke if the patient wasn’t pregnant?
- How would you manage the pregnancy if she hadn’t had a stroke?
- Many issues to consider:
  a) How will the pregnancy affect the disease?
  b) How will the disease affect the pregnancy / fetus?
  c) How will the treatment affect the pregnancy / fetus?
  d) Special considerations for labour/delivery & anaesthesia?
  e) Special considerations for breast feeding?

- A team approach is essential
- Planning is important
- Management of these cases should be individualized but based on best available evidence.
Approach to any neurological issue in pregnancy

1. Neurology’s 5 questions
2. Is the issue neurology with pregnancy or pregnancy with neurology?
3. What would I do if the patient wasn’t pregnant?
4. Issues to consider:
   a) How will the pregnancy affect the disease?
   b) How will the disease affect the pregnancy / fetus?
   c) How will the treatment affect the pregnancy / fetus?
   d) Special considerations for labour/delivery & anaesthesia?
   e) Special considerations for breast feeding?

Adapted with permission from S. Gandhi. R.H. Swartz, University of Toronto
SiP Consensus Statement

How do we distinguish consensus statements from recommendations?

**Guideline Recommendations**: recommendations intended to optimize patient care that are informed by a systematic review of evidence and an assessment of the benefits and harms of alternative care options (IOM)

**Consensus Statements**: comprehensive analysis of a scientific or medical issue by a panel of experts … need for a consensus statement arises when clinicians or scientists desire guidance on a subject for which there is a relative deficiency of comprehensive evidence that might otherwise allow for a more definitive statement to be made.

<table>
<thead>
<tr>
<th>A</th>
<th>B</th>
<th>C</th>
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<td>Should be done;</td>
<td>Should be considered/</td>
<td>May be considered/</td>
<td>Based on expert opinion,</td>
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<td>recommended</td>
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<td>- may be considered</td>
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## Expert Group

**Collaboration between Neurology, Obstetrics, Maternal Fetal Medicine, Obstetrical Anaesthesiology**

<table>
<thead>
<tr>
<th>Rick Swartz</th>
<th>Noor Ladhani</th>
<th>Eric Smith</th>
<th>Patrice Lindsay</th>
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<tr>
<td>Co-Chair</td>
<td>Co-Chair</td>
<td>SBP Advisory Cmte Chair</td>
<td>CSBPR Senior Editor</td>
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<td>Simerpreet Bal</td>
<td>Gordon Gubitz</td>
<td>Pascale Lavoie</td>
<td>Natalie Rashkovan</td>
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<tr>
<td>Jon Barrett</td>
<td>Michael Hill</td>
<td>Lisa Rae Leffert</td>
<td>Joel Ray</td>
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<tr>
<td>Cheryl Bushnell</td>
<td>Andra (Andi) James</td>
<td>Jennifer Mandzia</td>
<td>Evelyne Rey</td>
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<tr>
<td>Megan Cayley</td>
<td>Thomas Jeerakithil</td>
<td>Bijoy Menon</td>
<td>Gustavo Saposnik</td>
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<tr>
<td>Wee-Shian Chan</td>
<td>Albert Jin</td>
<td>Kara Nerenberg</td>
<td>Mike Sharma</td>
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<tr>
<td>Radha Chari</td>
<td>Michael Kelly</td>
<td>Jeyaraj Pandian</td>
<td>Elisabeth Smitko</td>
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<tr>
<td>Dariush Dowlatshahi</td>
<td>Adam Kirton</td>
<td>Aleksandra Pikula</td>
<td>Padma Vasantha</td>
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<tr>
<td>Meryem El Amrani</td>
<td>Sylvain Lanthier</td>
<td>Alexandre Poppe</td>
<td>Norine Foley</td>
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<tr>
<td>Shital Gandhi</td>
<td>Andrea Lausman</td>
<td>Jayson Potts</td>
<td>Sanjit Bhogal</td>
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Stroke in Pregnancy Consensus Process

**Research**
- Systematic search of evidence – published and grey literature
- Build/update evidence tables

**Writing and Refinement**
- Working group meetings and discussions
- Draft consensus statements
- Internal reviews process

**Release and Dissemination**
- External Reviews
- Publication and broad dissemination
- KT Implementation Tools, website updates

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<tr>
<th>Recommendations</th>
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<tr>
<td>Rationale</td>
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<td>System Implications</td>
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<td>Performance Measures</td>
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<td>Implementation Resources</td>
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<td>Summary of the Evidence</td>
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<td>Evidence Tables</td>
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**Stroke in Pregnancy Framework**

**Group A: Women with Past History of Stroke Becoming Pregnant**

Group A: Women who have a previous history of stroke ...

- who are planning to become pregnant (A1)
- who are pregnant (A2)

- Planning or Already Pregnant?
- Type of Stroke and Etiology
- Group A: Previous History of Stroke
- Recovery & Residual Deficits
- Age of Stroke Onset
- Pre-Pregnancy Prevention Therapies
- Stage of Pregnancy
Stroke in Pregnancy Framework

**GROUP B: WOMEN WHO EXPERIENCE A STROKE DURING PREGNANCY**

**Group B:**
- Women who are pregnant...
- who experience a stroke during pregnancy (B1)
- who experience a stroke in early post-partum (B2)

**Stage of Pregnancy when Stroke Occurred**

**Type of Stroke and Etiology (AIS, ICH)**

**Presentation and Deficits**

**Medical Co-Morbidities (e.g., eclampsia, diabetes)**

**Stroke Severity**

**Stage of Stroke Care (emergent, acute, post acute, prevention)**

**Group A:**
- Previous History of Stroke

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The Big Picture

- Stroke Prevention
- Acute Stroke Management
- Neurological Considerations
- Obstetrical Considerations
Key Topic Areas
- Initial emergency management
- Diagnostic imaging
- Medical management
- Anaesthetic considerations
- Acute and post-stroke obstetric management

Full first draft in development
- Undergoing internal review
- Winter ‘17-’18: Finalize manuscript & submission
Key Topic Areas

- General management considerations
  - Pre-conception, antenatal, and postpartum
- Secondary stroke prevention
  - Antithrombotics
  - Blood Pressure management
  - Statins
  - Diabetes management
- Management consideration for specific stroke etiologies
Canadian stroke best practice consensus statement: Secondary stroke prevention during pregnancy

Richard H Swartz, Noor Niyar N Ladhani, Norine Foley, Kara Nerenberg, Simerpreet Bal, Jon Barrett, Cheryl Bushnell, Wee-Shian Chan, Radha Chari, Dariush Dowlatshahi, Meryem El Amrani, Shital Gandhi, Gord Gubitz, Michael D Hill, Andra James, Thomas Jeerakathil, Albert Jin, Adam Kirton, Sylvain Lanthier, Andrea Lausman, Lisa Rae Leffert, Jennifer Mandzia, Bijoy Menon, Aleksandra Pikula, Alexandre Poppe, Jayson Potts, Joel Ray, Gustavo Saposnik, Mukul Sharma, Eric E Smith, Sanjit Bhogal, Elisabeth Smitko and M Patrice Lindsay; on behalf of the Heart and Stroke Foundation Canadian Stroke Best Practice Advisory Committees

Published November 24th, 2017
International Journal of Stroke
Stroke Prevention in Pregnancy

- Management through pregnancy
  - Pre-conception counselling
  - Antenatal & Intrapartum Screening,
  - Post-partum management.

- Secondary prevention
  - General Considerations
  - Antithrombotics – antiplatelets and anticoagulation
  - Blood pressure management
  - Statins
  - Diabetes
  - Specific etiologies – cardioembolic stroke; CVST, cervical artery dissection, antiphospholipid antibody syndrome.
Some key consensus statements

• Changing to low-dose Aspirin (81 mg daily) is preferred.
  • Multiple RCTs showing ASA safety after 11 weeks
  • Fewer RCT’s showing safety preconception to 11 weeks
  • ASA not excreted into breast milk.
• Warfarin is potentially teratogenic and should be avoided, especially between 6 to 12 weeks
• There is insufficient data on the safety of direct oral anticoagulants (DOACs)
• When anti-coagulation is indicated, low molecular weight heparin (LMWH) is preferred throughout pregnancy
Some key consensus statements

- Management of hypertension in pregnancy is reviewed in detail elsewhere: SOGC, NICE, Canadian Hypertension Guidelines.
- ACE-I’s and ARB’s increase the risk of congenital abnormalities (switch and, if needed, refer for fetal screening).
- The three most commonly used antihypertensive agents in pregnancy are labetalol, long-acting nifedipine, and methyldopa.
- Measurement of lipid levels are unreliable in pregnancy and should not be followed.
- Insufficient evidence for safety of statins in pregnancy.
- PFO closure not recommended during pregnancy – no evidence for safety or efficacy.
CT in pregnancy (not consensus statement)

• NOTE: acute management statement not released

• CT = ionizing radiation…
  … of the HEAD. Shield the abdomen/pelvis.

• Fetal radiation exposure from a plain CT head is <0.05 cGy
  (the max dose for total safe fetal exposure <5 cGy, so this is <1%).

• Avoid iodinated contrast – allergy, fetal kidneys, fetal dehydration, screen baby for thyroid dysfunction.

• CT Perfusion uses more radiation and contrast – time-of-flight MR preferred
**MRI in pregnancy**
*(not consensus statement)*

• Recent studies have begun to offset theoretical fears of acoustic damage (noise) or heating.

• Animal models have shown theoretical concerns (teratogenicity), especially in 1st trimester. ?higher risk with high-field strengths.

• Bottom line: Plain MRI OK even in 1st trimester; avoid Gadolinium.
**MRI in pregnancy**
*(not consensus statement)*

  - Birth Cohort – Ontario 2003-2015. n = 1,424,105

- Exposures: a) 1st trimester MRI (n=1,737), b) Gad exposure at any time in pregnancy (n= 397).
  - A) No increase in stillbirth or death, congenital anomalies, neoplasm or vision or hearing loss
  - B) Gadolinium associated with increased risk stillbirth/death (HR 3.7; 95% CI 1.55-8.85) and “any rheumatological, inflammatory or infiltrative skin conditions” (HR 1.36; 95% CI 1.09-1.69).

- Breastfeeding - <1% gadolinium crosses into breastmilk and <1% of that absorbed by baby’s GI tract.

R.H. Swartz, University of Toronto
Healthy Mother Healthy Baby

- Addressing emotional dilemmas and mitigating risk
  - Patient-centred team approach
  - Consistent and clear information
  - Weigh multiple considerations
  - Risk assessment
  - Support systems

- Consider effects of disease & treatment:
  - on mother
  - on fetus
  - on labour & delivery plans
  - on breastfeeding plans
Overriding principles in management

- Maternal health is vital for fetal wellbeing
- How would you treat the stroke if the patient wasn’t pregnant?
- How would you manage the pregnancy if she hadn’t had a stroke?
- A team approach is essential
- Planning is important
- Management of these cases should be individualized
QUESTIONS?
Questions?