What This Talk is About

Definitions

Is Perioperative Stroke a problem?
Who is at risk?
How can we reduce risk?

Only Human data

No Conflicts of Interest

Stroke

A focal or global neurological deficit of rapid onset and vascular origin with symptoms lasting 24 hours or longer or leading to death

Ng J, Chan M, Gelb AW. Anesthesiology 2011; 115:879

Transient Ischemic Attack

A focal or global neurological deficit of rapid onset and vascular origin with symptoms lasting less than 24 hours

Ng J, Chan M, Gelb AW. Anesthesiology 2011; 115:879

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Stroke

A focal or global neurological deficit of rapid onset and vascular origin with symptoms lasting 24 hours or longer or leading to death

Ng J, Chan M, Gelb AW. Anesthesiology 2011; 115:879
What is the Perioperative Period?

No standard definition
Usually defined as intraoperative and within 3 - 30 days after surgery

Is There a Problem

Perioperative Stroke Incidence

“The incidence of perioperative stroke in the cohort was 0.1%”

Table 1. Common Procedures in the Definition Cohort and the Associated Stroke Incidence

<table>
<thead>
<tr>
<th>Procedure</th>
<th>Stroke Age 0-5 y</th>
<th>Stroke Age &gt;65 y</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hip arthroplasty N = 1,908</td>
<td>0.4 (5)</td>
<td>0.5 (9)</td>
</tr>
<tr>
<td>Lung resection N = 1,496</td>
<td>0.3 (5)</td>
<td>0.7 (9)</td>
</tr>
<tr>
<td>Cholecystectomy N = 30,219</td>
<td>0.4 (5)</td>
<td>0.7 (9)</td>
</tr>
<tr>
<td>Most common procedures</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hepatobiliary / biliary tree N = 32,209</td>
<td>0.1 (5)</td>
<td>0.2 (2)</td>
</tr>
<tr>
<td>Intestinal resection N = 35,789</td>
<td>0.0 (1)</td>
<td>0.1 (2)</td>
</tr>
<tr>
<td>Hernia inguinal hernia/femoral N = 32,038</td>
<td>0.1 (5)</td>
<td>0.2 (1)</td>
</tr>
<tr>
<td>Hernia inguinal/femoral incisional N = 30,440</td>
<td>0.1 (1)</td>
<td>0.1 (1)</td>
</tr>
<tr>
<td>Colorectal appendectomy N = 20,546</td>
<td>0.3 (5)</td>
<td>0.5 (9)</td>
</tr>
<tr>
<td>Esophagegastroduodenal ulcer N = 28,769</td>
<td>0.0 (0)</td>
<td>0.0 (0)</td>
</tr>
<tr>
<td>Head and neck tumor N = 20,092</td>
<td>0.0 (0)</td>
<td>0.1 (9)</td>
</tr>
<tr>
<td>Minor cardiac: other/valvulotomy N = 8,833</td>
<td>0.0 (0)</td>
<td>0.0 (0)</td>
</tr>
<tr>
<td>Small intestine: resection/loosening N = 5,840</td>
<td>0.5 (17)</td>
<td>0.7 (12)</td>
</tr>
<tr>
<td>Small intestine: resection of adhesions, other N = 6,613</td>
<td>0.0 (0)</td>
<td>0.0 (0)</td>
</tr>
<tr>
<td>Thoracodorsal resection N = 3,870</td>
<td>0.3 (5)</td>
<td>0.5 (9)</td>
</tr>
<tr>
<td>Hepatobiliary: pancreas N = 4,835</td>
<td>0.5 (10)</td>
<td>0.7 (10)</td>
</tr>
<tr>
<td>Miscellaneous: (abdominal) N = 4,469</td>
<td>0.3 (5)</td>
<td>0.7 (10)</td>
</tr>
<tr>
<td>Esophagogastroduodenal resection N = 4,749</td>
<td>0.3 (5)</td>
<td>0.7 (10)</td>
</tr>
<tr>
<td>Hepatobiliary N = 4,042</td>
<td>0.0 (0)</td>
<td>0.3 (5)</td>
</tr>
</tbody>
</table>

Bateman BT Anesthesiology 2009; 110:232
Nationwide Inpatient Sample; 2000-4

Mashour, G. Anesthesiology 2011; 114:1289. DOI: 10.1097/ALN.0b013e318216e7f4
Time of Stroke Recognition
2003 - 2009

- 8% on emergence from anesthesia
- 62% within 48 hours
- 27% 3 to 30 days

Unpublished data: Moore, Mashour, Gelb

Why is perioperative stroke important?

Perioperative Stroke

Mortality

<table>
<thead>
<tr>
<th></th>
<th>1984</th>
<th>1993</th>
<th>1990</th>
</tr>
</thead>
<tbody>
<tr>
<td>Stephen</td>
<td></td>
<td></td>
<td>33%</td>
</tr>
<tr>
<td>Parikh</td>
<td>1993</td>
<td></td>
<td>26%</td>
</tr>
<tr>
<td>Landercasper</td>
<td>1990</td>
<td></td>
<td>60%</td>
</tr>
</tbody>
</table>

* All patients with previous CVA

Kim J. Gelb AW. J Neurosurg Anesth 1995; 7:211

Incidence of Major Complications & Mortality after Complications According to Hospital Quintile of Mortality

<table>
<thead>
<tr>
<th>Variable</th>
<th>Very Low Mortality</th>
<th>Low Mortality</th>
<th>Medium Mortality</th>
<th>High Mortality</th>
<th>Very High Mortality</th>
</tr>
</thead>
<tbody>
<tr>
<td>Myocardial Infarction</td>
<td>0.5</td>
<td>0.4</td>
<td>0.5</td>
<td>0.4</td>
<td>0.5</td>
</tr>
<tr>
<td>Stroke</td>
<td>0.2</td>
<td>0.3</td>
<td>0.2</td>
<td>0.3</td>
<td>0.2</td>
</tr>
</tbody>
</table>

Mortality after Complication

<table>
<thead>
<tr>
<th>Variable</th>
<th>Very Low Mortality</th>
<th>Low Mortality</th>
<th>Medium Mortality</th>
<th>High Mortality</th>
<th>Very High Mortality</th>
</tr>
</thead>
<tbody>
<tr>
<td>Myocardial infarction</td>
<td>29</td>
<td>28</td>
<td>27</td>
<td>36</td>
<td>40</td>
</tr>
<tr>
<td>Stroke</td>
<td>23</td>
<td>30</td>
<td>35</td>
<td>41</td>
<td>46</td>
</tr>
</tbody>
</table>

National Surgical Quality Improvement Program; 109 hospitals; 64,730 patients

Added cost of a Periop Stroke: $24,000

Ghaferi AA: NEJM 2009; 361:1368
**Why is the mortality so high??**

- Delayed diagnosis
- Delayed treatment

Perioperative stroke is initially a nursing diagnosis

But

Routine post op care does not include neuro screening

**IL-6 Stroke & Outcome**

Twelve-month Kaplan-Meier survival curve for patients with peak plasma IL-6 concentration less than, or greater than, the sample median (30.5 pg/ml, n = 34).

Smith RF. BMC Neurology 4:6, 2004

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**IL-6 after hip surgery**

Sedlär M. Archives of Gerontology and Geriatrics 51:3, 2010

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**Surgery**

- **Inflammatory Response**
  - L.6-4
  - TNFα
  - C-Reactive Protein

- **Pro-Atherogenic**
  - Plaque maturation
  - Plaque instability/rupture

- **Pro-thrombotic**
  - Stimulation coagulation cascade
  - Decrease fibrinolysis
  - Leukocytes
  - Platelet activation
  - Endothelial dysfunction

**Brain**

- Microglial activation
- BBB disruption

**Synergistic Amplification**

Stroke + Surgery

**Stroke Mortality >25%**

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**Stroke**

- **Inflammatory Response**
  - L.6-4
  - TNFα
  - C-Reactive Protein

**Stroke Mortality ± 10%**

Ng J, Chan M, Gelb AW. Anesthesiology 2011; 115:879
Who is at risk & When

Risk Factors for Stroke

<table>
<thead>
<tr>
<th>Risk Factor</th>
<th>OR</th>
</tr>
</thead>
<tbody>
<tr>
<td>Previous Stroke</td>
<td>2  – 14</td>
</tr>
<tr>
<td>Peripheral Vasc Dis</td>
<td>8</td>
</tr>
<tr>
<td>Renal Failure</td>
<td>3</td>
</tr>
<tr>
<td>Hyperuricemia</td>
<td>3.5</td>
</tr>
<tr>
<td>Cancer</td>
<td>1.6</td>
</tr>
<tr>
<td>Atrial Fibrillation</td>
<td>2</td>
</tr>
<tr>
<td>Hip Fracture</td>
<td>3.8</td>
</tr>
<tr>
<td>Valvular Heart Disease</td>
<td>1.5</td>
</tr>
</tbody>
</table>

Ng J, Chan M, Gelb AW. Anesthesiology 2011; 115:879

What can we do about it

Postoperative Stroke

Etiology

- Hypotensive
- Embolic
- Thrombotic

Hemorrhagic stroke is rare in the periop period
What is Hypotension?

Surprisingly, *none of the expected factors* intuitively associated with postoperative stroke could be demonstrated:

- BP drop *during* the procedure
- high hematocrit

Case control study: n=61 cases & 122 controls
Risk Factors: Prev stroke; COPD; PVD

Limburg M. Neurology 1998;50:895

Secondary Outcomes

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Metoprolol (N=4174)</th>
<th>Placebo (N=4177)</th>
<th>HR (95% CI)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Stroke</td>
<td>41 (1.0%)</td>
<td>19 (0.5%)</td>
<td>2.17 (1.26-3.73)</td>
<td>0.005</td>
</tr>
</tbody>
</table>

Lancet 2008; 371:1839
Predictors of Stroke
60 strokes - 49 ischemic, 3 hemorrhagic, 8 uncertain

<table>
<thead>
<tr>
<th>Risk Factor</th>
<th>Adjusted odds ratio (95% CI)</th>
<th>Frequency of risk factor n (%)</th>
<th>PAR* (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>History of stroke or transient ischaemic attack</td>
<td>2.80 (1.66-4.73)</td>
<td>1759 (21.1%)</td>
<td>30.5% (17-1-48.2)</td>
</tr>
<tr>
<td>Use of clopidogrel or ticlopidine in 24 h before surgery</td>
<td>3.12 (1.43-6.77)</td>
<td>330 (4.9%)</td>
<td>9.1% (3-23-3)</td>
</tr>
<tr>
<td>Clinically significant hypotension</td>
<td>2.14 (1.15-3.66)</td>
<td>1029 (12.3%)</td>
<td>14.7% (5-2-35-4)</td>
</tr>
<tr>
<td>Significant bleeding</td>
<td>2.18 (1.06-4.48)</td>
<td>553 (6.6%)</td>
<td>10.1% (3-0-28-0)</td>
</tr>
<tr>
<td>New clinically significant atrial fibrillation</td>
<td>3.51 (1.45-8.52)</td>
<td>200 (2.4%)</td>
<td>6.9% (2-1-20-4)</td>
</tr>
<tr>
<td>Total explained</td>
<td>-</td>
<td>-</td>
<td>5.1% (3-1-66-2)</td>
</tr>
</tbody>
</table>

PAR = population attributable risk. *Proportion of all outcomes attributable to the relevant risk factor if causality were proven. We calculated PAR from a multivariate logistic regression analysis and PAR estimates were calculated with ESPRIT (US National Cancer Institute, 2002). 1

Table 5: Independent predictors of death and stroke and their associated population attributable risks

Lancet 2008; 371:1839

30% decr in MAP associated with stroke

There is no evidence based guide to BP thresholds

<table>
<thead>
<tr>
<th>Basis for Decisions</th>
<th>Marker</th>
<th>Measuring Device</th>
</tr>
</thead>
<tbody>
<tr>
<td>Eminence</td>
<td>Radiance of white hair</td>
<td>Luminometer</td>
</tr>
<tr>
<td>Vehemence</td>
<td>Level of stridency</td>
<td>Audiometer</td>
</tr>
<tr>
<td>Eloquence</td>
<td>Smoothness of tongue</td>
<td>Teflometer</td>
</tr>
</tbody>
</table>

Bijker, JB. Anesthesiology. 2012;116:658

Healthy vessels
No co-morbidities

20-30% decr from PreOp baseline

Vascular Disease
Intracranial Disease
Decr O₂ delivery

Maintain BP at ~baseline

Perioperative Stroke

- Intraoperative hypotension is not the most frequent cause of stroke
- Postoperative hypotension is probably a much bigger risk factor
- Hypotension will worsen an embolic stroke

**Postoperative Stroke**

**Etiology:**
- Embolic
- Thrombotic

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**Hypercoagulable after Surgery**

- NOXIOUS STIMULI
- INHIBITION OF FIBRINOLYSIS
- INCREASE IN VIIIC AND VIIIRag:vWF
- INCREASE IN FIBRINOGEN
- THROMBOCYTOSIS
- DECREASE IN NATURAL ANTI COAGULANTS
- PLATELET ACTIVATION
- NEUROENDOCRINE RESPONSE
- ACUTE PHASE RESPONSE

Gibbs NM. Australasian Anaesthesia 1994

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Leonardi-Bee, J et al. Stroke 2002;33:1315-1320

Died by 14 days (solid lines); Dead or Dependent 6 months (dashed lines)
Perioperative Stroke by Surgery

Perioperative Stroke Management

- Early Nursing diagnosis
- Early Neurology consult (code stroke)
- Early CT scan
- Move to ICU or Stroke Unit
- Tx arrhythmias
- Give aspirin
- Consider (intra-arterial) thrombolysis

Perioperative Stroke Conclusions

Needs

- Acceptance that it is a problem
- Tell patients the risks esp if had a previous stroke
- Standardized definitions
- Better prospective data collection
- Better understanding of the process
- Earlier diagnosis & treatment

Thanks
All published studies are retrospective analyses of hospital discharge notes