The Perioperative Stress Response: Harmful

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Outline

• Define the perioperative stress response
• Causes
• Affects on patients
• Affects on outcomes
• Conclusions
What is “Stress”?
What is “Stress”?

“Our bodies are built such that when we are attacked by a saber-tooth tiger, we either die in three days or get better.”

P. Wischmeyer M.D.
The Perioperative Stress Response

Definition:

“The human response to physical trauma such as surgery is a complex integration of events designed to heal injured tissue, prevent infection, and restore homeostasis.”

Rassias, A.J., MD Consult, Disease-a-Month, 2003;49:9
The Perioperative Stress Response

- Fever
- Tachycardia
- Leukocytosis
- Tachypnea
- Pain
- Erythema
- Swelling
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Causes

• Surgical Insult Induces …

• Acute Phase Reactants
  – Hepatocytes, monocytes, endothelial cells, fibroblasts, adipocytes
  – CRP, serum amyloid, complement, fibrinogen, α1-antitrypsin
Causes

• Surgical Insult
  Induces …

• Hormonal Response
  – HPA axis
  – Cortisol
  – Aldosterone
  – Glucagon
HPA axis response to surgery

Overall effect:

Increase secretion of catabolic hormones

- gluconeogenesis
- glycogenolysis
- fluid retention
- mobilization of fat stores
- breakdown of lean muscle
- hyperglycemia

Desborough, Brit Jour Anes, 2000;85:109-117
Causes

• Surgical Insult Induces …

• Inflammatory Response
  – Pro-inflammatory (IL-1, IL-6, TNF-α, IFN-γ)
    • SIRS
  – Anti-inflammatory (IL-1ra, IL-4, IL-10, TGF-β)
    • CARS
Inflammatory Response

Injury

Pro-inflammatory

IL-1, TNF-α, IL-6

Early MOF

Anti-inflammatory

CARS

IL-4, IL-10, TGF-β, IL-1ra

Infection

Sepsis

MOF

Adapted from EE Moore, et al, Shock, 2005;24:71-74
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Cytokine Levels after Operation

- Cytokine response (IL-6, IL-1β, and INF-γ) after AAA (n=20) and inguinal hernia repair (n=5).
- Divided AAA pts into those with major and minor complications.
- Pts with complications has increase in IL-6 levels from 8-72 hours post-op (p<0.05).
Cytokine Levels after Operation

• Prospective study, 66 patients
• Elective aortic surgery (n = 18)
• 20 pts with ruptured AAA
• 28 pts with blunt trauma (ISS>25)
• Measured IL-1β, TNF-α, and IL-6 after above insult.
• ARDS/MOF vs. no ARDS/MOF
Figure 3. Plasma cytokine concentration during the first 2 weeks of ICU admission in 10 patients with ARDS/MOF (○) and 41 patients without ARDS/MOF (●). The data are expressed as the mean ± standard error of the mean. (*), 0.05 ≤ p ≤ 0.10; *, 0.01 ≤ p < 0.05; **, p < 0.01.
Prospective study, 30 pts undergoing major cancer operation.

3 groups
- uncomplicated (n=11)
- sepsis or severe sepsis (n=14)
- septic shock (n=5)

Septic shock had ↑ IL-6 and IL-1ra, trend towards ↑ IL-10

IL-6

![Graph showing IL-6 levels over time for different patient groups.](image)

*Fig. 1* Interleukin (IL)-6 levels for the three patient groups. Values are mean ± s.e.m. *P < 0.01, †P < 0.001 versus uncomplicated group (Mann-Whitney U test).

IL-1ra

**Fig. 2** Interleukin 1 receptor antagonist (IL-1ra) levels for the three patient groups. Values are mean (s.e.m.). *P < 0.04, †P < 0.004 versus uncomplicated group (Mann-Whitney U test).

**IL-10**

Fig. 3: Interleukin (IL) 10 levels for the three patient groups. Values are mean±s.e.m. *P < 0.05 vs uncomplicated group (Mann-Whitney U test)

- 31 pts admitted with chest pain with subsequent diagnosis of MI

- ↑ IL-6 in pts with signs HF at 6 and 12 weeks

- Pts with LV fxn below median had ↑ IL-6 at 6 and 12 weeks
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- 2300 SICU admits
- Combination of non-op, emergent, and elective
- SIRS score (1 pt per parameter) and LOS, MOD score, mortality

- National Surgical Quality Improvement Program (NSQIP)
- Beneficiary Identification and Records Locator Subsystem (BIRLS)
- All VA med centers that perform major operations
- Total n = 105,951

• 8 operations;
  – AAA (5000)
  – infra-inguinal vascular reconstruction (19,117)
  – CEA (16,880)
  – Colectomy (19,895)
  – Open cholecystectomy (9345)
  – Laparoscopic cholecystectomy (14,295)
  – Lobectomy/Pneumonectomy (8935)
  – THA (12,184)
<table>
<thead>
<tr>
<th>Procedure</th>
<th>Ratio Infective comp</th>
<th>5 yr Mortality with Comp</th>
<th>5 yr Mortality without Comp</th>
</tr>
</thead>
<tbody>
<tr>
<td>AAA</td>
<td>3/5</td>
<td>52.4</td>
<td>34.2</td>
</tr>
<tr>
<td>Inf-ing re-vasc</td>
<td>4/5</td>
<td>53.2</td>
<td>43.6</td>
</tr>
<tr>
<td>CEA</td>
<td>2/5</td>
<td>54.1</td>
<td>41.2</td>
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<tr>
<td>Colectomy</td>
<td>4/5</td>
<td>65.2</td>
<td>47.7</td>
</tr>
<tr>
<td>Open Chole</td>
<td>4/5</td>
<td>51.2</td>
<td>31.7</td>
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<tr>
<td>Lap Chole</td>
<td>4/5</td>
<td>47.2</td>
<td>31.0</td>
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<td>Lobe/Pneu</td>
<td>3/5</td>
<td>74.4</td>
<td>55.3</td>
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<tr>
<td>THA</td>
<td>4/5</td>
<td>41.3</td>
<td>29.8</td>
</tr>
</tbody>
</table>

Conclusions

The peri-operative stress response is harmful!!!!