Enhanced Recovery After Surgery (ERAS) in paediatrics

Koen Huysentruyt
Overview

- Introduction
- Preoperative nutritional assessment
- Preoperative fasting guidelines
- Metabolic response to surgical stress in children
- Postoperative early oral nutrition
- Current experience for ERAS in children
- Conclusion
ERAS elements

- **Preoperative**
  - Preadmission counseling
  - Fluid & CHO loading
  - No prolonged fasting
  - No/selective bowel preparation
  - Antibiotic prophylaxis
  - Thromboprophylaxis
  - No premedication

- **Intraoperative**
  - Short-acting anesthetic agents
  - Epidural anesthesia/analgesia
  - No drains
  - Avoidance of salt & water overload
  - Maintenance of normothermia
  - Surgical techniques

- **Postoperative**
  - Epidural anesthesia/analgesia
  - No nasogastric tubes
  - Prevention of nausea/vomiting
  - Avoidance of salt & water overload
  - Audit of compliance outcomes

- **Conclusion**
  - Early removal of catheter
  - Early oral nutrition
  - Early mobilisation
  - Non-opioid oral analgesia/NSAIDs
  - Stimulation of gut motility
ERAS: aggregation of marginal gains to provide large benefits

Introduction
Nutritional assessment
Pre-op fasting
Metabolic response
Postop feeding
Current evidence for ERAS
Conclusion

Adapted from “The Slight Edge”, by Jeff Olsen
ERAS in paediatrics?

Children are **not small adults**

Need for **age-dependent** protocols

Majority of paediatric surgery is **outpatient**
Prevalence of under-nutrition: general vs surgical population

**Europe (2014)**

- **Surgical population**
  - Surgical: 20%
  - Paediatric: 80% (7.1% under-nutrition)

- **Nutritional status**
  - Under-nutrition: 7%
  - No undernutrition: 93%

**Belgium (2013)**

- **General population**
  - Surgical: 10%
  - Infectious: 62% (11.2% under-nutrition)
  - Other: 28% (5.6% under-nutrition)

- **Nutritional status**
  - Under-nutrition: 13%
  - No undernutrition: 87%

Surgical vs paediatric under-nutrition:
- **Europe (2014)**: p=0.897
- **Belgium (2013)**: p=0.230

**Introduction**

- Nutritional assessment
- Pre-op fasting
- Metabolic response
- Postop feeding
- Current evidence for ERAS

**Conclusion**

- Hecht et al. Clinical nutrition 2014
Inclusion of 6 articles in review:
- 3 prospective cohort studies
- 3 retrospective chart studies
## Study specifics

### Major (non-cardiac) thoracic or abdominal surgery

<table>
<thead>
<tr>
<th>Setting</th>
<th>Design</th>
<th>N</th>
<th>Nutrition assessment</th>
<th>Outcome</th>
</tr>
</thead>
<tbody>
<tr>
<td>Canada, 2007</td>
<td>Prospective</td>
<td>175</td>
<td>SGNA, albumin, transferrin, WFA, HFA, BMI, MUAC, TSF, hand grip strength</td>
<td>30d mortality, surg/inf complic., LoS, inf</td>
</tr>
</tbody>
</table>

### Cardiac surgery

<table>
<thead>
<tr>
<th>Setting</th>
<th>Design</th>
<th>N</th>
<th>Nutrition assessment</th>
<th>Outcome</th>
</tr>
</thead>
<tbody>
<tr>
<td>Japan, 2011</td>
<td>Retrospective</td>
<td>36</td>
<td>SGNA, albumin, HFA, WFA</td>
<td>Mortality, PICU LoS, mech vent, LoS</td>
</tr>
<tr>
<td>Brazil, 2005</td>
<td>Prospective</td>
<td>30</td>
<td>Albumin, WFA, HFA, WFH</td>
<td>30d mortality, LoS, inf</td>
</tr>
<tr>
<td>Mexico</td>
<td>Retrospective</td>
<td>289</td>
<td>WFA at birth, BMI</td>
<td>LoS&gt;6d, mortality</td>
</tr>
<tr>
<td>USA/Guatemala, 2014</td>
<td>Prospective (2 centres)</td>
<td>41/30</td>
<td>TSF, albumin, pre-albumin</td>
<td>30d mortality, PICU LoS, mech vent., inotropics</td>
</tr>
<tr>
<td>USA, 2014</td>
<td>Retrospective</td>
<td>121</td>
<td>WFH, HFA</td>
<td>LoS, PICU LoS, mech vent.</td>
</tr>
</tbody>
</table>
## Anthropometric assessment

<table>
<thead>
<tr>
<th></th>
<th>HFA</th>
<th>BMI/WFH</th>
<th>TSF</th>
<th>MUAC</th>
</tr>
</thead>
<tbody>
<tr>
<td>Secker, Canada</td>
<td>✓ LoS</td>
<td>✗ LoS</td>
<td>✗ LoS</td>
<td>✗ LoS</td>
</tr>
<tr>
<td></td>
<td>✗ complic.</td>
<td>✗ complic.</td>
<td>✗ complic.</td>
<td>✗ complic.</td>
</tr>
<tr>
<td></td>
<td>✗ mortality</td>
<td>✗ mortality</td>
<td>✗ mortality</td>
<td>✗ mortality</td>
</tr>
<tr>
<td>Wakita, Japan</td>
<td>✗ LoS</td>
<td>✗ LoS</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>✗ mechanical ventilation</td>
<td>✗ mechanical ventilation</td>
<td></td>
</tr>
<tr>
<td>Vivanco-Munoz, Mexico</td>
<td></td>
<td></td>
<td>✓ mortality</td>
<td></td>
</tr>
<tr>
<td>Radman, USA/Guatemala</td>
<td></td>
<td></td>
<td></td>
<td>✓ LoS (USA) \ ✗ LoS (Guat.)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>✓ mechanical ventilation (USA) \ ✗ mechanical ventilation (Guat.)</td>
</tr>
<tr>
<td>Toole, USA</td>
<td>✓ LoS</td>
<td>✗ LoS</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>✗ inverse ?</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>✗ mechanical ventilation</td>
<td>✗ mechanical ventilation</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Biochemical assessment

- **Albumin**
  - Leite (Brazil):
    - ↑ post-op infections
    - ↑ mortality
  - Secker (Canada):
    - ↑ post-op infections
    - ↑ minor complications
    - ↑ LoS
    - Albumine in normal range for all children!
  - Radman (USA/Guat):
    - ↑ mech ventilation (USA)

- **Pre-albumin**
  - Radman (USA/Guat):
    - ↑ mech ventilation (USA)

### TABLE 4
Relation between malnutrition and outcomes

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Well-nourished (n = 85)</th>
<th>Malnourished (n = 90)</th>
<th>P²</th>
</tr>
</thead>
<tbody>
<tr>
<td>n (%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Infectious complications</td>
<td>24 (28)</td>
<td>39 (43)</td>
<td>0.042</td>
</tr>
<tr>
<td>Noninfectious complications</td>
<td>7 (8)</td>
<td>10 (11)</td>
<td>0.614</td>
</tr>
<tr>
<td>Major complications</td>
<td>16 (19)</td>
<td>27 (30)</td>
<td>0.114</td>
</tr>
<tr>
<td>Minor complications</td>
<td>14 (17)</td>
<td>28 (31)</td>
<td>0.033</td>
</tr>
<tr>
<td>Nonprophylactic antibiotic use</td>
<td>27 (32)</td>
<td>34 (38)</td>
<td>0.404</td>
</tr>
<tr>
<td>Unplanned reoperation</td>
<td>5 (6)</td>
<td>6 (7)</td>
<td>0.831</td>
</tr>
<tr>
<td>Unplanned readmission</td>
<td>5 (6)</td>
<td>12 (13)</td>
<td>0.096</td>
</tr>
<tr>
<td>Postoperative length of stay (d)</td>
<td>5.3 ± 5.4</td>
<td>8.2 ± 10</td>
<td>0.001</td>
</tr>
</tbody>
</table>

*Data presented as the number of children with that outcome; % within nutritional classification in parentheses.*

*P* values were determined with the use of Pearson chi-square test for all outcomes except postoperative length of stay, which was tested with the Mann-Whitney nonparametric test for independent means.

*x ± SD; 1 child with severe malnutrition and a postoperative stay of 306 d was removed from this analysis as an extreme outlier.*
Preoperative fasting guidelines

- “Children **encouraged** to drink **clear fluids** up to **2h before** elective surgery”
  - Applies for neonates, infants and children
  - Comfort ↑, thirst ↓, risk of dehydration ↓
  - Permitted volume does not impact intragastric volume of pH

- “**Breast milk** safe up to **4h before** elective surgery”

- “**Other milk** safe up to **6h before** elective surgery”
Operative trauma = “controlled injury”

Triggers range of inflammatory pathways

Can be the setting for deleterious effects
- Systemic inflammatory response syndrome
- Prolonged catabolism of body stores

Different in children from adults

## Cytokine response

<table>
<thead>
<tr>
<th>Cytokine</th>
<th>Targets</th>
<th>Actions</th>
</tr>
</thead>
<tbody>
<tr>
<td>IL-1α</td>
<td>thymocytes, neutrophils, T and B cells, skeletal muscle, hepatocytes, osteoblasts</td>
<td>immunoregulation, inflammation, fever, anorexia, acute phase protein, muscle proteolysis</td>
</tr>
<tr>
<td>IL-1β</td>
<td>fibroblasts, endothelium, skeletal muscle, hepatocytes, osteoblasts</td>
<td>immunoregulation, inflammation, fever, anorexia, acute phase protein, muscle proteolysis</td>
</tr>
<tr>
<td>TNF-α</td>
<td>thymocytes, T and B cells, hepatocytes</td>
<td>immune cell differentiation, acute phase protein</td>
</tr>
<tr>
<td>IL-6</td>
<td>monocytes, SMC’s, ....</td>
<td>suppresses the production of pro-inflammatory cytokines</td>
</tr>
</tbody>
</table>
Factors affecting response

- Age
- Nutrition and fasting
- Anaesthesia
- Operative stress & surgical approach
- Temperature

**Metabolic responses to surgery**

### Introduction

#### Nutritional assessment

#### Pre-op fasting

#### Metabolic response

#### Postop feeding

#### Current evidence for ERAS

#### Conclusion

### Metabolic Response to Operative Stress in the Adult and Neonate

<table>
<thead>
<tr>
<th>Metabolite</th>
<th>Adult</th>
<th>Neonate</th>
</tr>
</thead>
<tbody>
<tr>
<td>Metabolic rate and oxygen consumption</td>
<td>Briefly, then ↑</td>
<td>Compared with adults (minimal change compared to age-matched controls)</td>
</tr>
<tr>
<td>Carbohydrate</td>
<td>Hyperglycemic response ↑</td>
<td>Glucose, 2 times immediately postoperatively (less persistent than in adults), probably secondary to glycogenolysis rather than ↑ gluconeogenesis—neonates may be unable to carry out hepatic gluconeogenesis secondary to lack of key enzyme</td>
</tr>
<tr>
<td>Protein</td>
<td>Glucose use ↓, ↑ Hyperglycemic response</td>
<td>Negative nitrogen balance 72–96 h postoperatively.</td>
</tr>
<tr>
<td></td>
<td>Amino acid utilization for gluconeogenesis, acute phase reactant synthesis and synthesis of components of healing process.</td>
<td>↑ Nitrogen loss in neonates compared with older infants.</td>
</tr>
<tr>
<td></td>
<td>Protein synthesis in extrahepatic tissues.</td>
<td>↑ Muscle protein breakdown, impaired nitrogen use, transient ↑ nitrogen excretion.</td>
</tr>
<tr>
<td></td>
<td>Amino acid utilization for gluconeogenesis, acute phase reactant synthesis and synthesis of components of healing process.</td>
<td>↓ (versus adult) in gluconeogenic amino acids in postoperative plasma.</td>
</tr>
<tr>
<td></td>
<td>Nitrogen excretion—sustained ≤5 d.</td>
<td>Lipolysis + ketogenesis (possible catecholamine stimulated) → ↑ total ketone bodies.</td>
</tr>
<tr>
<td></td>
<td>Adipose tissue lipolysis → mobilization of nonesterified fatty acids and ↑ ketone body formation</td>
<td>↑ glycerol, ↑ nonesterified fatty acids. Postoperative fat utilization exceeds rate of mobilization of free fatty acids.</td>
</tr>
<tr>
<td></td>
<td>75–90% of postoperative requirements supplied by fat metabolism (10–25% by protein)</td>
<td></td>
</tr>
</tbody>
</table>
In contrast to adults, the energy metabolism of newborns undergoing major operations seems to be only minimally modified by the operative trauma per se.
Postoperative feeding

- Oral intake when possible, avoid unnecessary NG tube placement
- Avoid opioids if possible
- Pyloromyotomy:
  - Oral feeding possible as early as 2h postoperatively
  - Full enteral intake within 24-48h after operation
  - Gradual increase vs liberal intake?
  - Post-op vomiting related to degree of pre-op electrolyte disturbances and dehydration
Limited experience of “fast-track surgery” in paediatrics

- Mixed procedures (pyeloplasty, appendectomy, bowel anastomosis, fundoplication, hypospadia repair, nephrectomy)
- Ambulatory surgery
- Colonic surgery
- Cardiac surgery
### Mixed procedures: The Hannover criteria

<table>
<thead>
<tr>
<th>Element</th>
<th>Definition of successful application</th>
</tr>
</thead>
<tbody>
<tr>
<td>Analgesia</td>
<td>Pain intensity &lt;1/3 of the maximum scale points at the evening of the day of operation</td>
</tr>
<tr>
<td>Postoperative nutrition</td>
<td>Full oral nutrition by the evening of the 2(^{nd}) postoperative day (without nausea/vomiting)</td>
</tr>
<tr>
<td>Postoperative mobilisation</td>
<td>2-score points at the evening of the 2(^{nd}) postoperative day</td>
</tr>
<tr>
<td>Applicability of minimally invasive surgery</td>
<td>No conversion and no postoperative complication with any adverse effect in procedures suitable for MIT</td>
</tr>
</tbody>
</table>
| Hospital stay                                | Significantly shorter compared to national data for similar patients in hospitals with a similar case mix index and similar structure |}

Hannover 2007 (university hospital)

- Pyeloplasty, appendectomy, bowel anastomosis, fundoplication, hypospadia repair, nephrectomy
- Excluded: additional diseases, reoperation, perforated appendicitis

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Fig. 1 Feasibility of fast-track (FT) surgery. Number of patients treated according to the fast-track protocols compared with the number of patients excluded from fast-track surgery.

Hannover 2009 (university hospital)

- Elective abdominal, thoracic or urological surgery
- Excluded: age ≤ 4 weeks, prematurity, reoperation, pectus excavatum repair, consulted decision based on general condition and co-morbidities

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Hannover 2012 (university hospital)

- Elective abdominal, thoracic or urological surgery
- Excluded: age ≤ 4 weeks, prematurity, need for post-op PICU admission

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Hannover 2014 (non-university hospital)

- Pyeloplasty, appendectomy, pyloromyotomy, fundoplication, hypospadia repair, nephrectomy
- Excluded: age ≤ 4 weeks and >16 years

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Mixed procedures: Hannover 2007 study

**Fig. 3** Mean hospital stay. Fast-track data compared with data derived from the German reimbursement system with G-DRGs for patients with a similar case mix index and hospitals with a similar structure.
Mixed procedures: Hannover 2009 study

- Pain control:

![Graph showing pain intensity over days for fast-track and G-DRG groups]
Successful implementation of fast-track elements

<table>
<thead>
<tr>
<th>Procedure</th>
<th>Sufficient analgesia</th>
<th>Early nutrition</th>
<th>Early mobilization</th>
<th>No nausea or vomiting</th>
<th>No complication</th>
<th>Use of minimally invasive techniques</th>
<th>Early discharge compared with G-DRG data</th>
</tr>
</thead>
<tbody>
<tr>
<td>Thoracic surgery</td>
<td>83%</td>
<td>100%</td>
<td>98%</td>
<td>88%</td>
<td>100%</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hypospadia repair</td>
<td>88%</td>
<td>100%</td>
<td></td>
<td>94%</td>
<td>94%</td>
<td>p = 0.01</td>
<td></td>
</tr>
<tr>
<td>Appendectomy</td>
<td>84%</td>
<td>100%</td>
<td>100%</td>
<td>97%</td>
<td>97%</td>
<td>94%</td>
<td></td>
</tr>
<tr>
<td>Bowel anastomosis</td>
<td>80%</td>
<td>95%</td>
<td>95%</td>
<td>90%</td>
<td>95%</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Other laparoscopic procedures</td>
<td>94%</td>
<td>100%</td>
<td>94%</td>
<td>95%</td>
<td>100%</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pyeloplasty</td>
<td>80%</td>
<td>100%</td>
<td>93%</td>
<td>80%</td>
<td>100%</td>
<td>78%</td>
<td></td>
</tr>
<tr>
<td>Surgery of benign and malignant tumors</td>
<td>100%</td>
<td>83%</td>
<td>100%</td>
<td>100%</td>
<td>100%</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pull-through procedure</td>
<td>89%</td>
<td>100%</td>
<td>100%</td>
<td>89%</td>
<td>89%</td>
<td>100%</td>
<td>p &lt; 0.01</td>
</tr>
<tr>
<td>Fundoplication</td>
<td>78%</td>
<td>100%</td>
<td>100%</td>
<td>100%</td>
<td>100%</td>
<td>100%</td>
<td>p &lt; 0.01</td>
</tr>
<tr>
<td>Kasai procedure</td>
<td>88%</td>
<td>100%</td>
<td></td>
<td>75%</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ureteral reimplantation</td>
<td>100%</td>
<td>100%</td>
<td></td>
<td>86%</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Mixed procedures: Hannover 2014 study

- **Pain control**
  - Mean pain scores <1/3 on the evening of operation

- **Difference in inclusion?**
  - Perforated appendicitis
  - Comorbidities

- **Mobilisation**
  - 79% fully mobilised at 2nd post-op day

- **Financial reimbursement?**

- **Oral nutrition**
  - Completed after mean of 1.8 ±1.4 days

- **Length of stay**
  - No difference compared to national data

---

*Mean hospital stay*
Children >7 years post-op randomly sent to PACU (standard, no parents present) or second-stage recovery unit (parents present):

Table 2. Recovery Care

<table>
<thead>
<tr>
<th>Variable</th>
<th>Control group</th>
<th>Fast-Track group</th>
</tr>
</thead>
<tbody>
<tr>
<td>OR recovery time (min)(^a)</td>
<td>3.5 ± 1.7</td>
<td>3.4 ± 2.0</td>
</tr>
<tr>
<td>Vomiting(^b) (%)</td>
<td>4.2</td>
<td>4.8</td>
</tr>
<tr>
<td>Pain medication administered(^b) (%)(^*)</td>
<td>62.0</td>
<td>40.5</td>
</tr>
<tr>
<td>Total fluids (mL/kg)(^**)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total recovery time (min)(^*)</td>
<td>99.4 ± 48.6</td>
<td>79.1 ± 48.3</td>
</tr>
<tr>
<td>PACU time (min)</td>
<td>20.9 ± 15.3</td>
<td>0.00 ± 0.0</td>
</tr>
<tr>
<td>SSRU time (min)</td>
<td>78.6 ± 45.3</td>
<td>79.1 ± 48.3</td>
</tr>
</tbody>
</table>

Ramesh et al. Anesth Analg 2001
Prospective Italian study (2009)

- 46 children (38 Hirschprung, 8 IBD)
- 100% oral feeding on post-op day 1
- 100% discharge before post-op day 5
- 2 re-admissions

**Fast-track protocol**

- **Pre-op:** standardized bowel preparation, Ab, standardized fasting, full pre-op evaluation
- **Intra-op:** muscle-sparing approach
- **Post-op:** avoiding drain, early removal of NG tube, pain control, minimize opioids
Colonic surgery

- Retrospective US study (2014)
  - 71 children (all Crohn's disease)
  - 45 fast-track vs 26 conventional

- **Pre-op:** "counseled"
- **Intra-op:** laparoscopic approach
- **Post-op:** oral intake within 24h, no routine NG tube, rectal suppository if no stool on day 2, minimize opioids, avoid drainage

### Table 1
Complications experienced following laparoscopic ileocectomy for Crohn's disease.

<table>
<thead>
<tr>
<th>Complication</th>
<th>Fast-track (n = 45)</th>
<th>Conventional (n = 26)</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bleeding</td>
<td>2</td>
<td>0</td>
<td>0.40</td>
</tr>
<tr>
<td>SSI</td>
<td>5</td>
<td>2</td>
<td>0.49</td>
</tr>
<tr>
<td>Abscess</td>
<td>1</td>
<td>1</td>
<td>0.60</td>
</tr>
<tr>
<td>Stricture</td>
<td>2</td>
<td>1</td>
<td>0.70</td>
</tr>
<tr>
<td>Fistula</td>
<td>0</td>
<td>1</td>
<td>0.37</td>
</tr>
<tr>
<td>SBO</td>
<td>4</td>
<td>0</td>
<td>0.15</td>
</tr>
<tr>
<td>Other readmission</td>
<td>2</td>
<td>2</td>
<td>0.47</td>
</tr>
</tbody>
</table>
• Mind the nutritional status also in children
• No overnight fasting
• Metabolic response is different, especially in small children
• Paucity of evidence for ERAS in pediatric surgery
• Current evidence suggests that ERAS can be implemented safely
• At least in selected patients, ERAS can lead to shorter hospital stay