Gestione dell’ iperglicemia in chirurgia one-day e Fast-Track

L. Pellegrino

S.C. CHIRURGIA GENERALE
Direttore: dott. F. Borghi
Azienda Ospedaliera S. Croce e Carle - Cuneo
Ente di rilievo nazionale e di alta specializzazione
Blood glucose increases after surgery and post-operative hyperglycemia induces an increased risk of infections (SSI), not related to diabetic status.


Surgical stress is the primary source of perioperative hyperglycemia also in non-diabetic patients, followed by “iatrogenic causes” (discontinuation of hypoglycemic medications or preoperative poorly controlled diabetic) in diabetic patients.
Physiopathology of surgical stress
Physiopathology of surgical stress

**ENDOCRINE MODIFICATIONS INDUCED BY SURGICAL STRESS**

- Increased release in catabolic hormones
  - Catecholamines (adrenalin and noradrenalin)
  - ACTH and cortisol
  - GH
  - Glucagon
  - TSH
  - ADH

**METABOLIC MODIFICATIONS BY SURGICAL STRESS**

- Increased energetic resources
- Proteolysis and gluconeogenesis
- Insulin-resistance and muscle impaired glucose tolerance (GLUT4)
Insulin-resistance and surgical stress

Insulin-resistance and surgical stress

Elective abdominal surgery (open cholecystectomy) causes a marked, transient reduction in insulin sensitivity.

The reduction in insulin sensitivity is related to the magnitude of surgery.

Hyperglycemia and one day surgery


Diabetes Mellitus
- Diagnosed
- Undiagnosed

Stress Hyperglycemia

IFG
- impaired fasting glucose

IGT
- impaired glucose tolerance
Hyperglycemia and one day surgery

The literature on perioperative glycemic control for patients undergoing day surgery procedures is limited.

Anesth Analg 2010;111:1378 –87

Clinical recommendations are available for the management of hyperglycemia in hospitalized patients, including the critically ill and those undergoing major surgical procedures.

There is **insufficient evidence** regarding preoperative management of oral antidiabetics and insulin in **one day surgery**.
Hyperglycemia and one day surgery

To reduce the risks of hyperglycemia is important the optimization of pre-operative status and a minimal disruption in the patients’ antidiabetic therapy (avoid iatrogenic hyperglycemia).

Anesth Analg 2010;111:1378–87

There are no RCTs evaluating the effects of preoperative glycemic control on postoperative infection in ambulatory surgical procedures.

For ambulatory surgery, not discontinue oral antidiabetics the day before surgery (LoE 2A), but only metformin (24 - 48h before surgery) in patients with renal dysfunction or if receive IV contrast (LoE 2A).

Anesth Analg 2010;111:1378–87

And also, there is no evidence that metformin is associated with an increased risk of perioperative lactic acidosis (LoE 1).

Salpeter SR et al. Cochrane Database Syst Rev 2010 Jan 20;::CD002967
### Table 5. Instructions to Patient Regarding Preoperative Insulin and Noninsulin Injectable Administration

<table>
<thead>
<tr>
<th>Insulin regimen</th>
<th>Day before surgery</th>
<th>Day of surgery</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Insulin pump</td>
<td>No change</td>
<td>No change</td>
<td>Use &quot;sick day&quot; or &quot;sleep&quot; basal rates.</td>
</tr>
<tr>
<td>Long-acting, peakless insulins</td>
<td>No change</td>
<td>75%–100% of morning dose</td>
<td>Reduce nighttime dose if history of nocturnal or morning hypoglycemia.</td>
</tr>
<tr>
<td>Intermediate-acting insulins</td>
<td>No change in the daytime dose, 75% of dose if taken in the evening</td>
<td>50%–75% of morning dose</td>
<td>On the day of surgery, the morning dose of basal insulin may be administered on arrival to the ambulatory surgery facility.</td>
</tr>
<tr>
<td>Fixed combination insulins</td>
<td>No change</td>
<td>50%–75% of morning dose of intermediate-acting component</td>
<td>See the comments for long-acting insulins.</td>
</tr>
<tr>
<td>Short- and rapid-acting insulin</td>
<td>No change</td>
<td>Hold the dose</td>
<td>Lispro-proteamine only available in combination; therefore use NPH instead on day of surgery.</td>
</tr>
<tr>
<td>Noninsulin Injectables</td>
<td>No change</td>
<td>Hold the dose</td>
<td>See the comments for long-acting insulins.</td>
</tr>
</tbody>
</table>

LoE 2A

Anesth Analg 2010;111:1378 –87
Avoid overnight preoperative admission to hospital and prolonged fasting is important for reducing the risk of hyperglycemia. Patients with diabetes should be prioritized on the operating list.

Oral antidiabetics and insulin should be taken on the day of surgery (LoE 2A) if a normal food intake is resumed (aggressive PONV prophylaxis).

Anesth Analg 2010;111:1378 –87
Hyperglycemia and major surgery

Diabetes Mellitus
  - Diagnosed
  - Undiagnosed

Stress Hyperglycemia

IFG
  - impaired fasting glucose
   /  
IGT
  - impaired glucose tolerance

Stress hyperglycemia and surgery

Stress-induced hyperglycemia: inpatient hyperglycemia that normalizes when the excessive pro-inflammatory state abate.


Stress-induced hyperglycemia is different than hyperglycemia secondary to diabetes in that it confers an increased risk of mortality.

In colorectal surgery, post-operative serum glucose level > 140 mg/dL is the only significant predictor of SSI (20.6% vs 7.6%).


In nondiabetic patients, a single postoperative elevated glucose value is adversely associated with morbidity and mortality; this risk is related to the degree of glucose elevation.

Hyperglycemia and major surgery

**Figure 1.** Relationship between postoperative hyperglycemia and risk of postoperative infection (POI).

Patients with HbA1c > 6% had higher post-operative glycemia than patients with a normal HbA1c level (<6%) in colorectal surgery, and higher post-operative infections rate.


Several stress reducing interventions should be introduced in routine clinical perioperative practice in order to attenuate the risk of postoperative hyperglycemia.

Optimize the preoperative metabolic status of our patients (HbA1c) and introduce Fast Track program (or Enhanced Recovery After Surgery = ERAS) are the most important aspects.
Definition of Fast-Track program

Multimodal program created to reduce post-operative stress, including attenuation of postoperative insulin resistance, maintain physiological function and enhance post-operative recovery.

Bari, 7-10 novembre 2013

FT in colorectal surgery: metanalysis

<table>
<thead>
<tr>
<th>Author</th>
<th>Year</th>
<th>N°RCT (pts) FT vs non-FT</th>
<th>N°CCT (pts) FT vs non-FT</th>
<th>LOS</th>
<th>Morbidity</th>
</tr>
</thead>
<tbody>
<tr>
<td>Wind</td>
<td>2006</td>
<td>3 (64 vs 64)</td>
<td>3 (191 vs 195)</td>
<td>-1.56 (-2.61, -0.50) p=0.004</td>
<td>0.54 (0.42, 0.69) p&lt;0.001</td>
</tr>
<tr>
<td>Gouvas</td>
<td>2009</td>
<td>4 (99 vs 101)</td>
<td>7 (447 vs 416)</td>
<td>-2.46 (-3.43, -1.48) p&lt;0.00001</td>
<td>0.56 (0.45, 0.69) p&lt;0.00001</td>
</tr>
<tr>
<td>Eskicioglu</td>
<td>2009</td>
<td>4 (198)</td>
<td>/</td>
<td>/</td>
<td>0.61 (0.42, 0.88) p=0.009</td>
</tr>
<tr>
<td>Walter</td>
<td>2009</td>
<td>2 (33 vs 31)*</td>
<td>2 (153 vs 159)</td>
<td>-3.64 (-4.98, -2.29) p&lt;0.00001</td>
<td>0.63 (0.39, 1.02) p=0.06*</td>
</tr>
<tr>
<td>Varadhan</td>
<td>2010</td>
<td>6 (226 vs 226)</td>
<td>/</td>
<td>-2.51 (-3.54, -1.47) p&lt;0.00001</td>
<td>0.53 (0.41, 0.69) p&lt;0.00001</td>
</tr>
<tr>
<td>Spanjersberg</td>
<td>2011</td>
<td>4 (119 vs 118)</td>
<td>/</td>
<td>-2.94 (-3.69, -2.19) p&lt;0.00001</td>
<td>0.52 (0.38, 0.71) p&lt;0.00001</td>
</tr>
<tr>
<td>Adamina</td>
<td>2011</td>
<td>6 (226 vs 226)</td>
<td>/</td>
<td>-2.5 (-3.92, -1.11) p&lt;0.00001</td>
<td>0.52 (0.36, 0.73) p&lt;0.00001</td>
</tr>
</tbody>
</table>

S.C. Chirurgia Generale - Cuneo
Fast-Track program

**Pre-operative**
- Pre-operative information
- No mechanical bowel preparation
- No pre-anesthetic medication
- No pre-operative fasting
  - CHO

**Intra-operative**
- Minimally invasive surgery
- Normothermia
- Multimodal Analgesia (CPD-no morphine)
- Remifentanil
- Prevention PONV
- Goal-directed fluid therapy
- Iperoxigenation

**Post-operative**
- No abdominal drainage
- No urinary drainage and no NG intubation
- Early Mobilization (d0)
- Prophylaxis against thromboembolism
  - Use of laxative
- Early Enteral feeding (d0)
- Early discharge (d2-d3 after surgery)

S.C. Chirurgia Generale - Cuneo
Fast-Track program in colorectal surgery

**Pre-operative**
- Pre-operative information
- No mechanical bowel preparation
- No pre-anesthetic medication
- No pre-operative fasting
- CHO

**Intra-operative**
- Minimally invasive surgery
- Normothermia
- Multimodal Analgesia (CPD-no morphine)
- Remifentanil
- Prevention PONV
- Goal-directed fluid therapy
- Iperoxigenation

**Post-operative**
- No abdominal drainage
- No urinary drainage and no NG intubation
- Early Mobilization (d0)
- Prophylaxis against thromboembolism
- Use of laxative
- Early Enteral feeding (d0)
- Early discharge (d2-d3 after surgery)

S.C. Chirurgia Generale - Cuneo
Preoperative fasting

Anesthesiology 1999; 90: 896-905.

Patients benefit from avoiding preoperative fasting, instead of overnight fasting (diabetic patients with neuropathy may have delayed gastric emptying for solids).
Preoperative carbohydrates

By providing a clear fluid containing a defined (12 %) concentration of complex carbohydrates up until 2 h before anesthesia, patients can undergo surgery in a metabolically fed state.


This treatment reduces the prevalence of preoperative thirst, hunger, anxiety, and nitrogen losses. In addition, postoperative insulin resistance is reduced by 50 %.

Preoperative carbohydrates

FT Program recommends the administration of high-carbohydrate drinks prior to surgery. This may compromise blood glucose control and is not recommended for people with insulin-treated diabetes.

Fast-Track program in colorectal surgery

**Pre-operative**
- Pre-operative information
- No mechanical bowel preparation
- No pre-anesthetic medication
- No pre-operative fasting
- CHO

**Intra-operative**
- Minimally invasive surgery
- Normothermia
- Multimodal Analgesia (CPD-no morphine)
- Remifentanil
- Prevention PONV
- Goal-directed fluid therapy
- Iperoxigenation

**Post-operative**
- No abdominal drainage
- No urinary drainage and no NG intubation
- Early Mobilization (d0)
- Prophylaxis against thromboembolism
- Use of laxative
- Early Enteral feeding (d0)
- Early discharge (d2-d3 after surgery)

S.C. Chirurgia Generale - Cuneo
Insulin-resistance and laparoscopy

Laparoscopy improves short-term outcomes (wound morbidity, time to first bowel movement and discharge) and decrease the surgical stress and the insulin resistance.

The anaesthetist is responsible for three key elements in affecting outcome after surgery: stress reactions to the surgery, fluid therapy, and analgesia ("trimodal approach").

Attenuation of the hyperglycemic response with epidural anesthesia and analgesia is due to the sympathetic blockade, lower peak cortisol levels, and a less pronounced glucagon effect.

Epidural analgesia
The epidural anesthesia followed by post-operative epidural analgesia blocks the inhibitory sympathetic fibres contributing to ileus, conserving the excitatory parasympathetic fibres to the gut.


The use of epidural analgesia avoid the use of opioids in post operative, (disturbing bowel movements), facilitating early enteral intake and mobilization on the day of surgery.

The pharmacological prophylaxis (evaluation of the risk factors) and treatment of PONV is necessary to support the early nutritional intake, avoiding ileus and fasting.

**Characteristics**

<table>
<thead>
<tr>
<th>Score</th>
<th>Characteristics</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Female sex</td>
</tr>
<tr>
<td>1</td>
<td>History of motion sickness or PONV</td>
</tr>
<tr>
<td>1</td>
<td>Nonsmoker</td>
</tr>
<tr>
<td>1</td>
<td>Postoperative opioid treatment is planned</td>
</tr>
<tr>
<td></td>
<td><strong>TOTAL</strong></td>
</tr>
</tbody>
</table>

Score Probability of PONV (%):

- score 0 = 10%
- points 1: 21%
- score 2: 39%
- score 3: 61%
- score 4: 78%
It is standard practice to infuse volumes of intravenous fluids substantially in excess of actual peri-operative losses.


Balanced crystalloids should be preferred to 0.9 % saline and intravenous fluids should be discontinued as soon as is practicable.
# Fast-Track program in colorectal surgery

<table>
<thead>
<tr>
<th>Pre-operative</th>
<th>Intra-operative</th>
<th>Post-operative</th>
</tr>
</thead>
<tbody>
<tr>
<td>- Pre-operative information</td>
<td>- Minimally invasive surgery</td>
<td>- No abdominal drainage</td>
</tr>
<tr>
<td>- No mechanical bowel preparation</td>
<td>- Normothermia</td>
<td>- No urinary drainage and no NG intubation</td>
</tr>
<tr>
<td>- No pre-anesthetic medication</td>
<td>- Multimodal Analgesia (CPD-no morphine)</td>
<td>- Early Mobilization (d0)</td>
</tr>
<tr>
<td>- No pre-operative fasting</td>
<td>- Remifentanil</td>
<td>- Prophylaxis against thromboembolism</td>
</tr>
<tr>
<td>- CHO</td>
<td>- Prevention PONV</td>
<td>- Use of laxative</td>
</tr>
<tr>
<td></td>
<td>- Goal-directed fluid therapy</td>
<td>- Early Enteral feeding (d0), stop ev (d1)</td>
</tr>
<tr>
<td></td>
<td>- Iperoxigenation</td>
<td>- Early discharge (d2-d3 after surgery)</td>
</tr>
</tbody>
</table>

S.C. Chirurgia Generale - Cuneo
Early enteral feeding

There is no advantage in keeping patients ‘nil by mouth’ following GI surgery. Early feeding reduced both the risk of infection and the length of hospital stay without increasing the risk of anastomotic leakage.

Andersen HK Cochrane Database Syst Rev; 2006:CD004080

In the postoperative phase of FT program, patients can drink immediately after recovery from anaesthesia and then eat normal hospital food (from the day of surgery).

Several treatments in FT protocol affect insulin action/resistance and hence glucose levels directly or indirectly. None of these treatments carry the risk of hypoglycaemia.

FT protocol should be introduced in routine clinical practice.
Conclusions

Post-operative hyperglycemia is the most important risk factor for post operative SSI after abdominal surgery, and could be controlled:

1) In minor surgery (One day surgery), optimizing preoperative metabolic status and reducing «iatrogenic hyperglycemia» (avoiding prolonged discontinuation of anti-diabetic therapy).

2) In major surgery, optimizing preoperative metabolic status and reducing surgical stress/insulin resistance implementing the Fast Track program.