Update in endocrinologia clinica

Bari,
7-10 novembre 2013

12° Congresso Nazionale AME
Associazione Medici Endocrinologi
6th Joint Meeting with AACE
American Association of Clinical Endocrinologists

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

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S.C. CHIRURGIA GENERALE
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Ente di rilievo nazionale e di alta specializzazione

Introduction

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Blood glucose increases after surgery and post-operative hyperglycemia induces an increased risk of infections (SSI), not related to diabetic status.

Ramos M et al. Ann Surg 2008;248: 585–591

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

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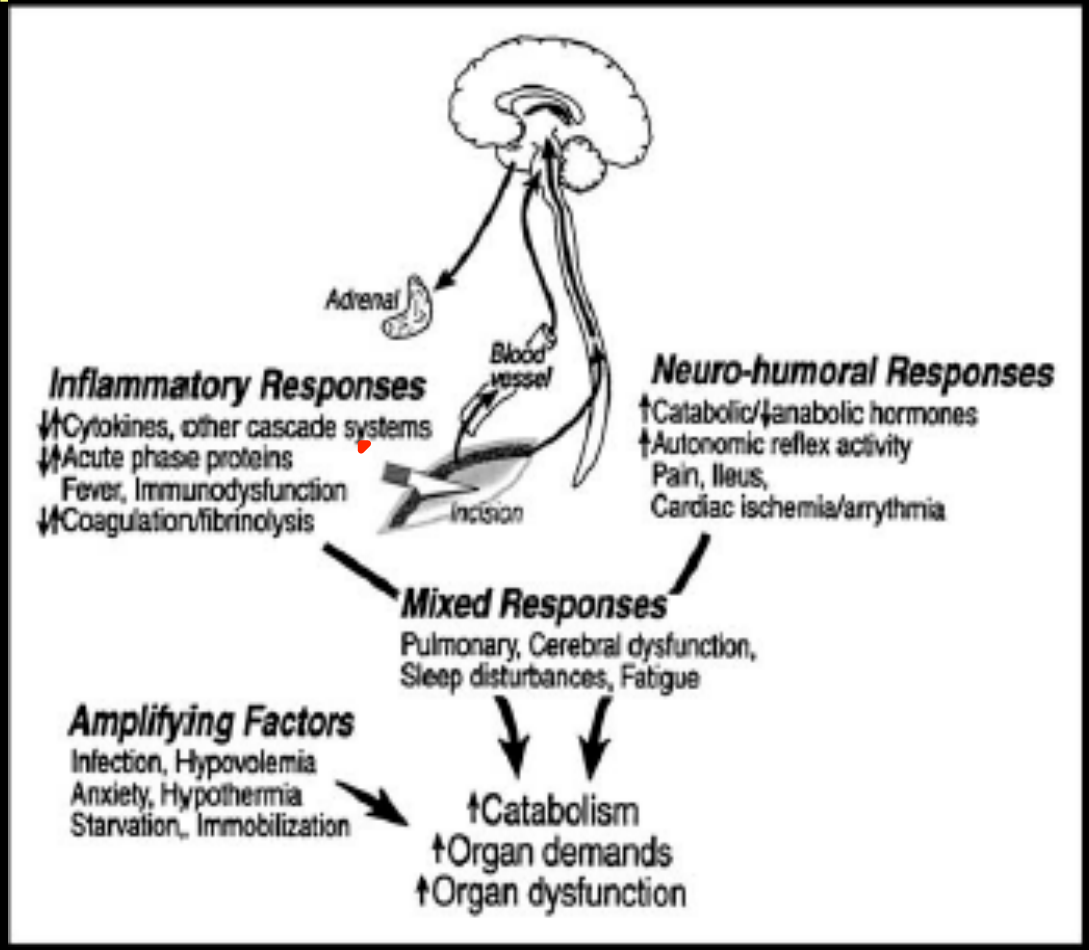

Physiopathology of surgical stress

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ENDOCRINE MODIFICATIONS INDUCED BY SURGICAL STRESS

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

METABOLIC MODIFICATIONS BY SURGICAL STRESS

- Increased energetic resourses
- Proteolisis and gluconeogenesis
- Insulin-resistance and muscle impaired glucose tolerance (GLUT4)

Insulin-resistance and surgical stress

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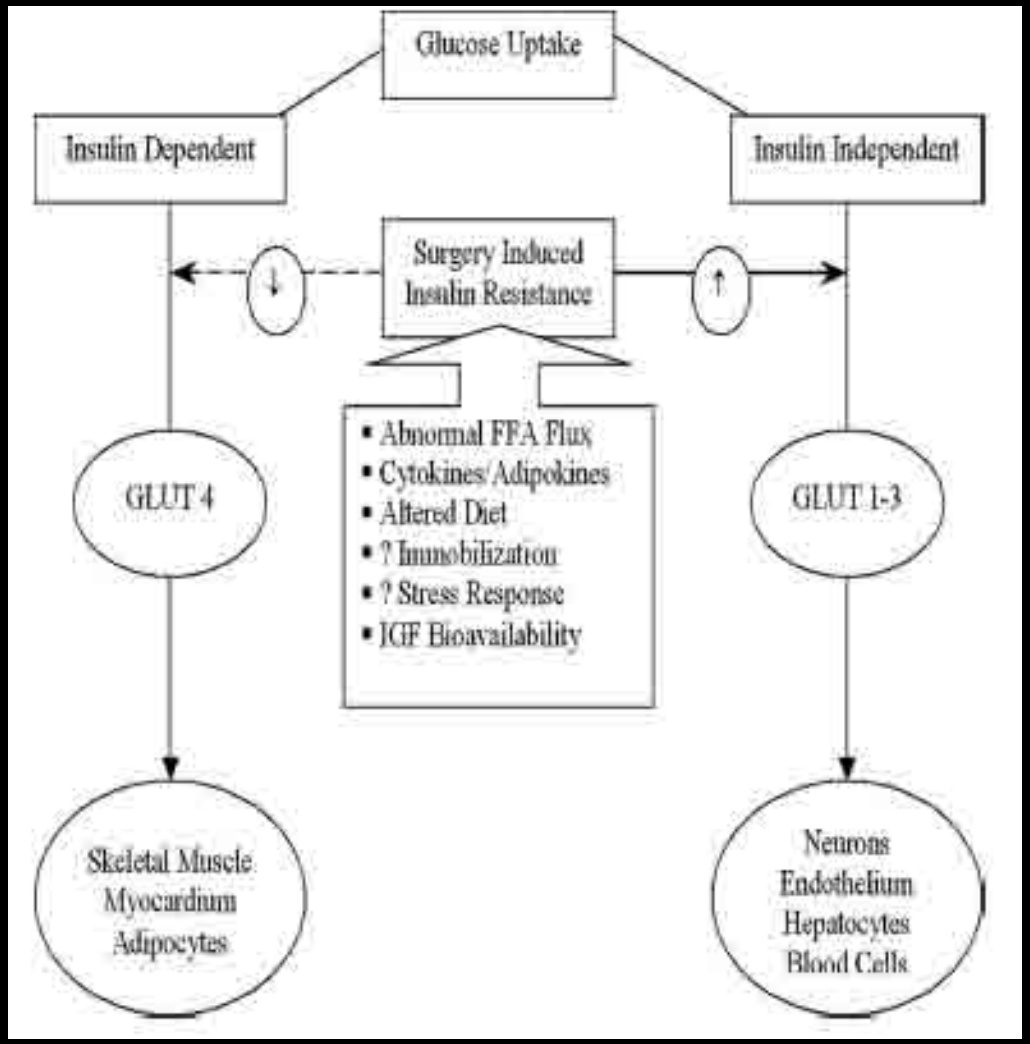

Bagry HS, et al. ANESTHESIOLOGY 2008; 108:506–23

Insulin-resistance and surgical stress

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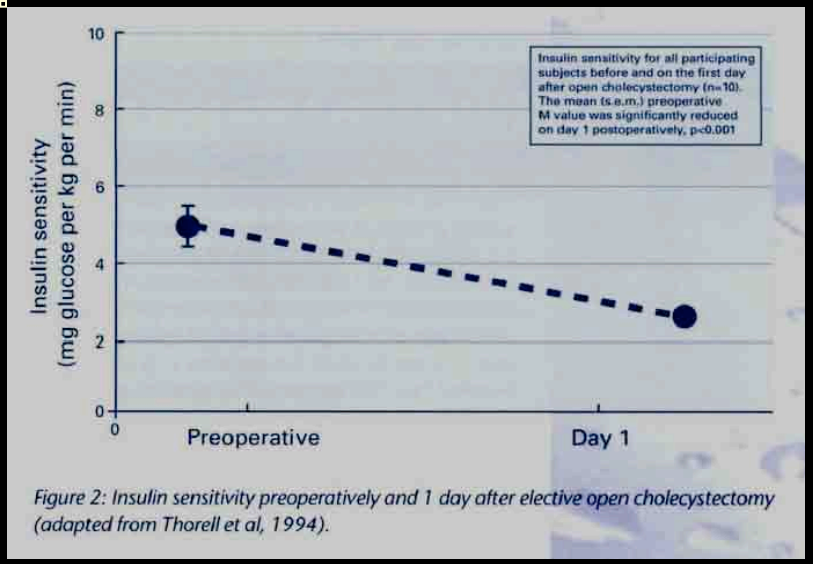
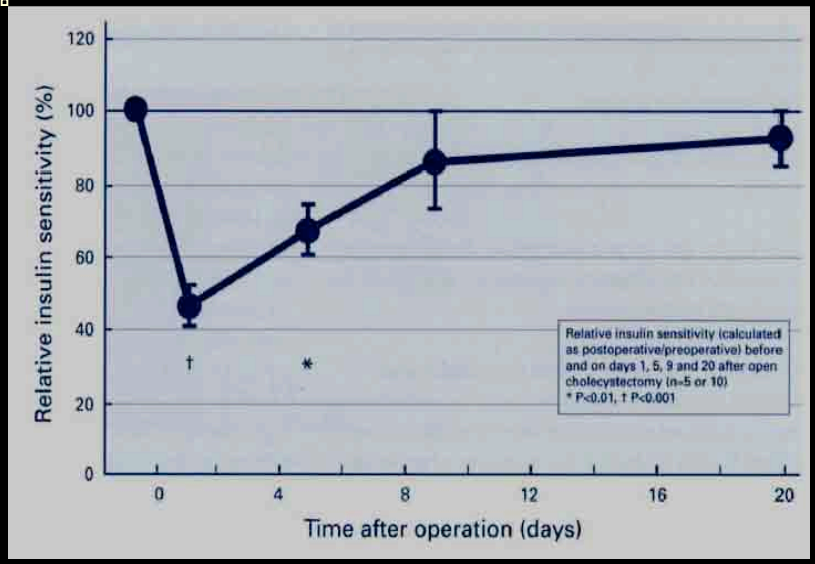


Figure 2: Insulin sensitivity preoperatively and 1 day after elective open cholecystectomy (adapted from Thorell et al, 1994).



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

A. Thorell, J. Nygren, O. Ljungqvist. Curr Opin Clin Nutr Metab Care, 1999: 69-78

Insulin-resistance and surgical stress

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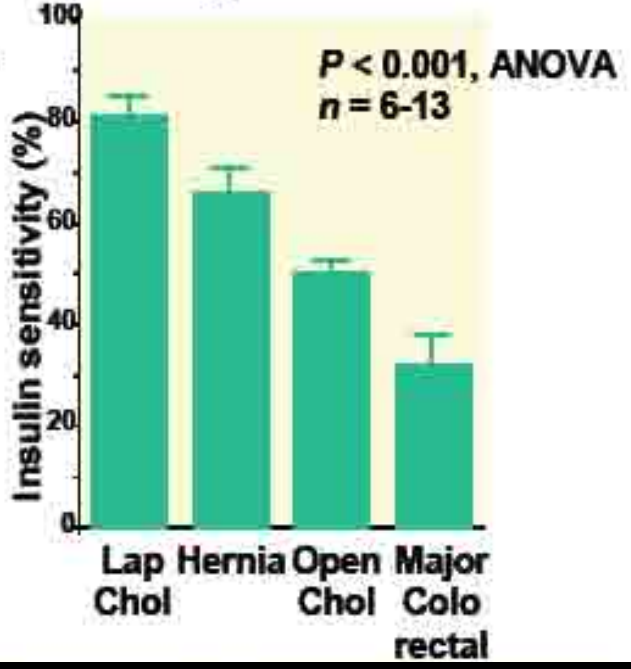
Insulin sensitivity and magnitude of operation

Factors that influence postoperative insulin resistance:

- The type of surgery
- Factors that did not affect postop IR:
- Gender
- Preop insulin sensitivity



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

A. Thorell et al. Curr Opin Clin Nutr Metab Care, 1999.

Hyperglycemia and one day surgery

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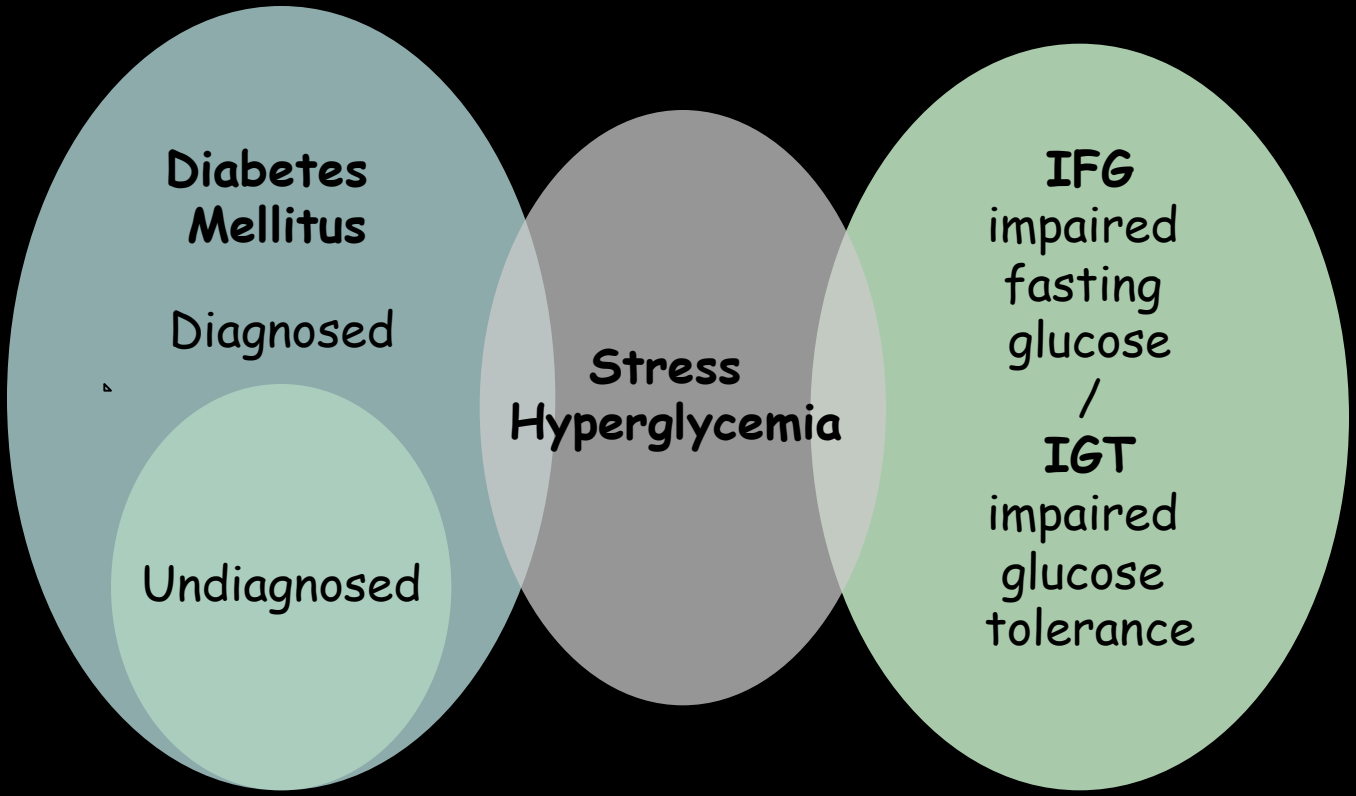

Clement S. et al. Diabetes Care. 2004;27(2):553–91

Hyperglycemia and one day surgery

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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.

K. Dhatariya et al. NHS Diabetes perioperative management guideline (2012)

Guidelines in one day surgery

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SPECIAL ARTICLE

Society for Ambulatory Anesthesia Consensus Statement on Perioperative Blood Glucose Management in Diabetic Patients Undergoing Ambulatory Surgery

Girish P. Joshi, MB, BS, MD, FFARSCI,* France
Shireen Ahmad, MD,§ Tong J. Gan, MD, FRCA,
and Rebecca Twersky, MD, MPH**

Studies selected for the review	10 records
- Systematic review on ambulatory surgery:	1 record
- Trials on ambulatory surgery	9 records
- RCT:	5 records

Anesth Analg 2010;111:1378 –87

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

Hyperglycemia and one day surgery

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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.

Vann MA. Curr Opin Anaesthesiol 2009; 22:718–724

Therapy management in one day surgery

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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

K. Dhatariya et al. NHS Diabetes perioperative management guideline (2012)

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

Therapy management in one day surgery

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Table 5. Instructions to Patient Regarding Preoperative Insulin and Noninsulin Injectable Administration

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

LoE 2A

Anesth Analg 2010;111:1378 –87

Strategy in one day surgery

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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

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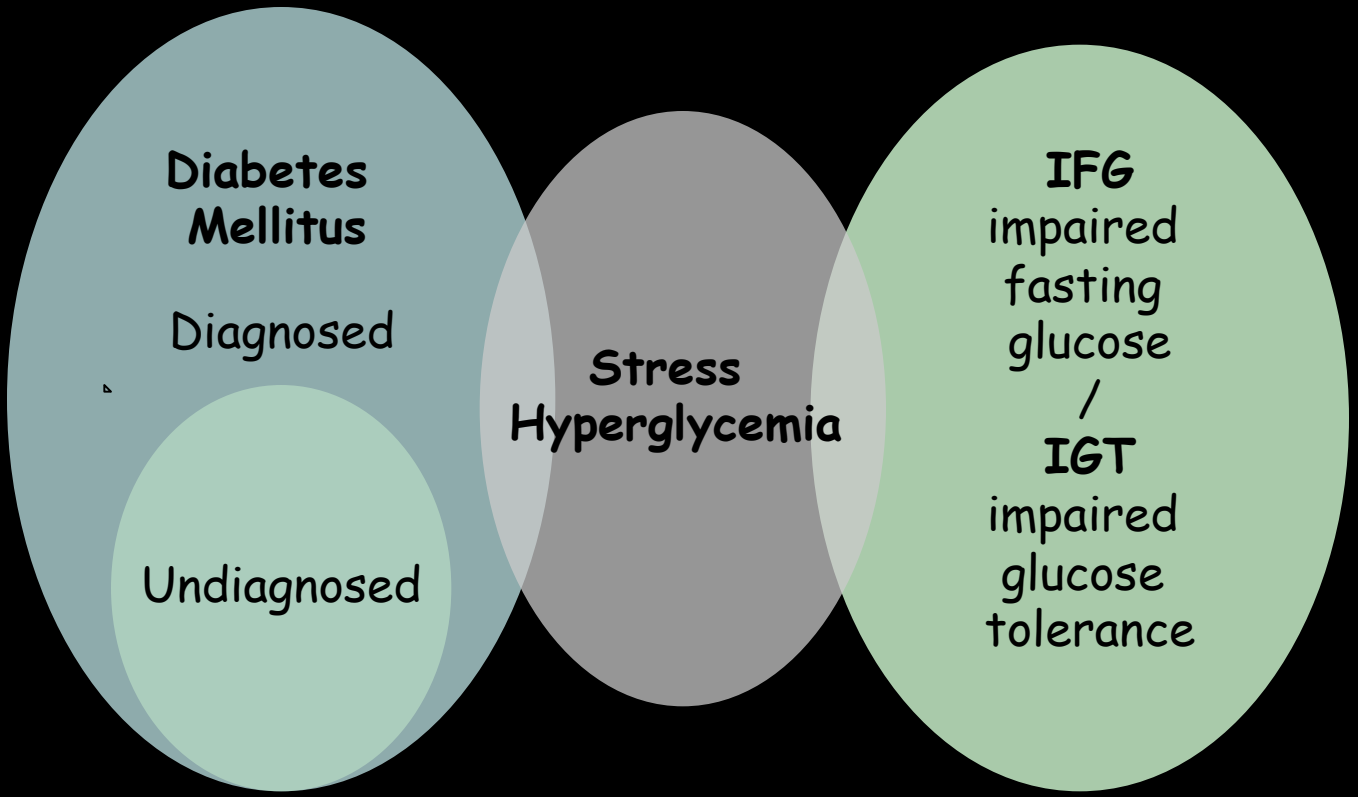

Clement S. et al. Diabetes Care. 2004;27(2):553–91

Stress hyperglycemia and surgery

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

Sheehy AM et al. J Diabetes Sci Technol 2009;3(6):1261-1269

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

Rady MY et al. Mayo Clin Proc. 2005;80(12):1558-67.

Hyperglycemia and major surgery

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

Ata A. et al. Am Surg 2010;76(7):697-702.

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.

Kiran RP et al. Ann Surg. 2013 Oct;258(4):599-605.

Hyperglycemia and major surgery

Bari,
7-10 novembre 2013

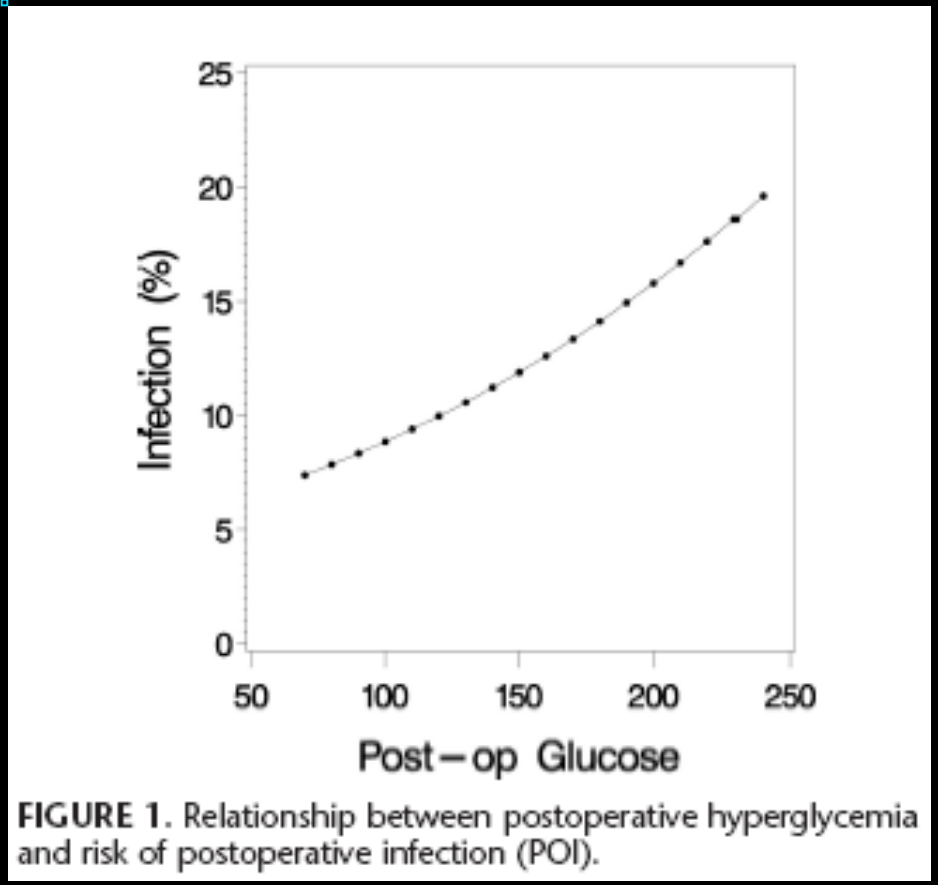

FIGURE 1. Relationship between postoperative hyperglycemia and risk of postoperative infection (POI).

Ramos M et al. Ann Surg 2008;248: 585–591

Colorectal surgery and HbA1c

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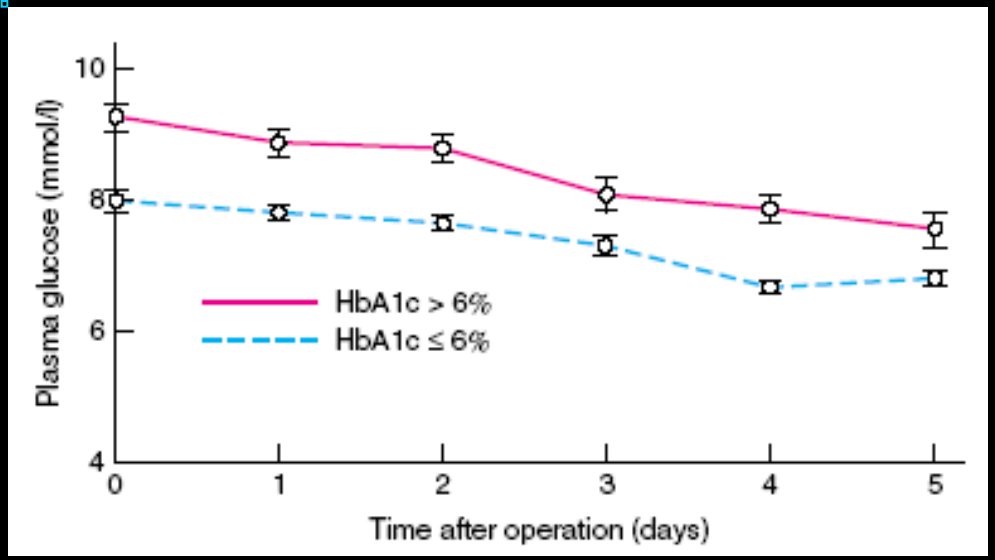

Patients with HbA1c > 6% had higher post-operative glycemia than patients with a normal HbA1c level (<6%) in colorectal surgery, and higher post-operative infections rate.

Gustafsson et al. British Journal of Surgery 2009; **96**: 1358–1364

Dronge AS. et al. Arch Surg. 2006;141:375-380

Insulin-resistance and Fast-Track

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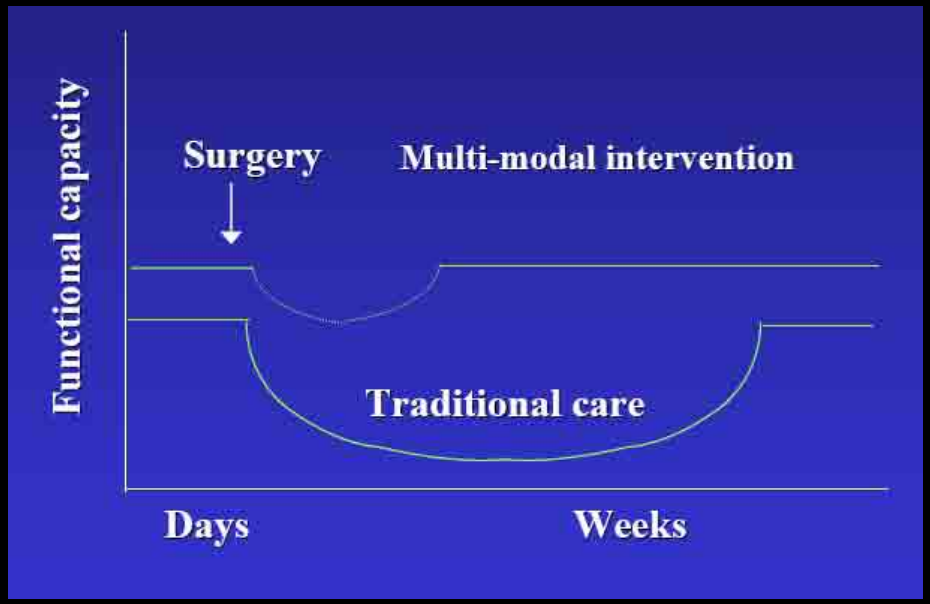
Several stress reducing interventions should be introduce in routine clinical perioperative practice in order to attenuate the risk of postoperative hyperglycemia.

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.

Kehlet H. Br J Anaesth 1997;78:606–17.



Field of application of Fast-Track

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World J Surg
DOI 10.1007/s00268-012-1772-0

World Journal of Surgery

Guidelines for Perioperative Care in Elective Colonic Surgery: Enhanced Recovery After Surgery (ERAS®) Society Recommendations

U. O. Gustafsson · M. J. Scott · W. Schwenk · N. Demartines · D. N. Francis · C. E. McNaught · J. MacFie · A. S. Liberman · M. Sc A. Hill · R. H. Kennedy · D. N. Lobo · K. Fearon · O. Ljungqvist

World J Surg
DOI 10.1007/s00268-012-1787-6

World Journal of Surgery

Guidelines for Perioperative Care in Elective Rectal/Pelvic Surgery: Enhanced Recovery After Surgery (ERAS®) Society Recommendations

J. Nygren · J. Thacker · F. Carli · K. C. H. Fearon · S. Norderval · D. N. Lobo · O. Ljungqvist · M. Soop · J. Ramirez

World J Surg
DOI 10.1007/s00268-012-1771-1

Guidelines for Perioperative Care for Pancreaticoduodenectomy: Enhanced Recovery After Surgery (ERAS®) Society Recommendations

Kristoffer Lassen · Marielle M. E. Coolsen · Karem Slim · Francesco Carli · José E. de Aguilar-Nascimento · Markus Schäfer · Rowan W. Parks · Kenneth C. H. Fearon · Dileep N. Lobo · Nicolas Demartines · Marco Braga · Olle Ljungqvist · Cornelis H. C. Dejong

FT in colorectal surgery: metanalysis

Bari,
7-10 novembre 2013

Author	Year	N°RCT (pts) FT vs non-FT	N°CCT (pts) FT vs non-FT	LOS	Morbidity
Wind	2006	3 (64 vs 64)	3 (191 vs 195)	-1·56 (-2·61, -0·50) p=0.004	0·54 (0·42, 0·69) p<0.001
Gouvas	2009	4 (99 vs 101)	7 (447 vs 416)	-2.46 (-3.43,-1.48) p<0.00001	0.56 (0.45, 0.69) p<0.00001
Eskicioglu	2009	4 (198)	/	/	0.61 (0.42, 0.88) p=0.009
Walter	2009	2 (33 vs 31)*	2 (153 vs 159)	-3.64 (-4.98, -2.29) p<0.0001	0.63 (0.39, 1.02) p=0.06*
Varadhan	2010	6 (226 vs 226)	/	-2.51(-3.54, -1.47) p<0.00001	0.53 (0.41, 0.69) p<0.00001
Spanjersberg	2011	4 (119 vs 118)	/	-2.94 (-3.69, -2.19) p<0.00001	0.52 (0.38,0.71) p<0.0001
Adamina	2011	6 (226 vs 226)	/	-2.5 (-3.92, -1.11) p<0.00001	0.52 (0.36,0.73) p<0.00001

Fast-Track program

Bari,
7-10 novembre 2013

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)

Fast-Track program in colorectal surgery

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7-10 novembre 2013

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Preoperative fasting

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Country	Fasting time before anaesthesia (h)		Exclusions from guidelines (i.e. fast)	Patients for whom individual modifications are needed
	Clear fluids	Solids		
UK	3	6	Emergency operation, gastrointestinal disease or intake of drugs likely to slow gastric emptying	–
Canada	2	6–8		
Norway	2	6	Emergency operation	Known delay in gastric emptying
Sweden	2–3	Fast from midnight for solids, 4 h for yoghurt or clear soup	Emergency operation	Reflux, regurgitation, full stomach, slow gastric motility, difficult airway
USA	2	6 ('light meal')	Women in labour, emergency operation	Conditions affecting gastric emptying and patients with airway problems

Anestesiology 1999; 90: 896905.

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

Preoperative carbohydrates

Bari,
7-10 novembre 2013

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.

Brady M, et al. Cochrane Database Syst Rev 2009; 7(4):CD005285

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

Nygren J Best Pract Res Clin Anaesthesiol 2008; 20:429–438

Wang Z.G. et al British Journal of Surgery 2010; **97**: 317–327

Preoperative carbohydrates

Bari,
7-10 novembre 2013

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.

K. Dhatariya et al. NHS Diabetes perioperative management guideline (2012)

Fast-Track program in colorectal surgery

Bari,
7-10 novembre 2013

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Insulin-resistance and laparoscopy

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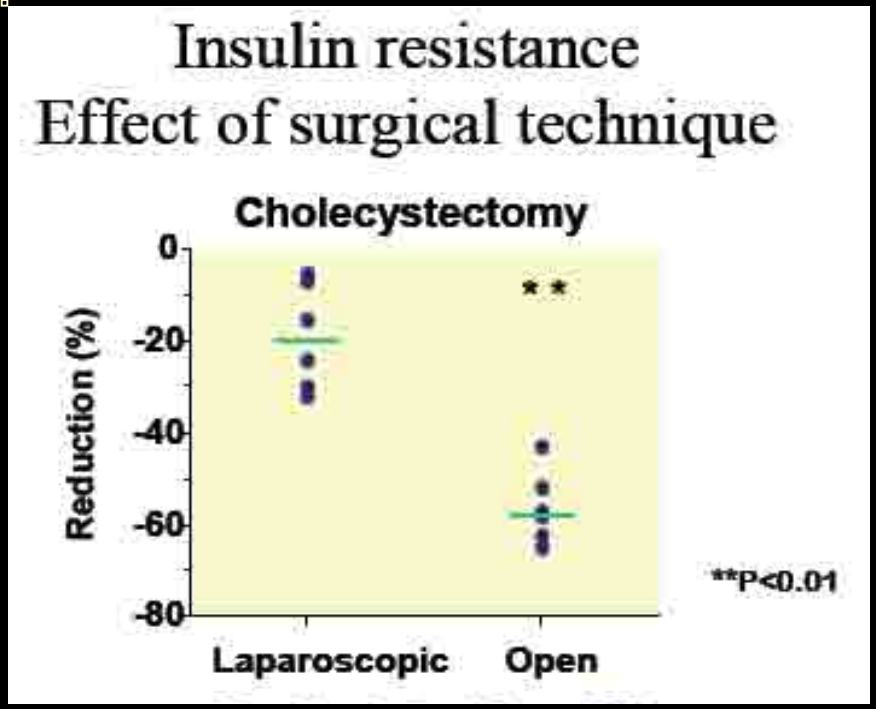
Laparoscopy improves short-term outcomes (wound morbidity, time to first bowel movement and discharge) and decrease the surgical stress and the insuline resistance.



Tjandra JJ , Chan MK. Colorectal Dis 2006; 8: 375-388.

A. Thorell et al. Eur J Surg, 1995.

Epidural anesthesia and analgesia

Bari,
7-10 novembre 2013

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.

Bouwmeester NJ et al. Br J Anaesth 2001;87:390 –9.

Epidural analgesia





Epidural anesthesia and analgesia

Bari,
7-10 novembre 2013

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.

Wu CL, et al. Anesthesiology 2005;103:1079-88

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.

Marret E. Br J Surg. 2007; 94 (6): 665-673.

PONV and FT

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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	Score
Female sex	1
History of motion sickness or PONV	1
Nonsmoker	1
Postoperative opioid treatment is planned	1
TOTAL	_____

Score Probability of PONV (%):
score 0=10%; points1: 21%; score 2: 39%; score 3: 61%; score 4: 78%

Fluid management

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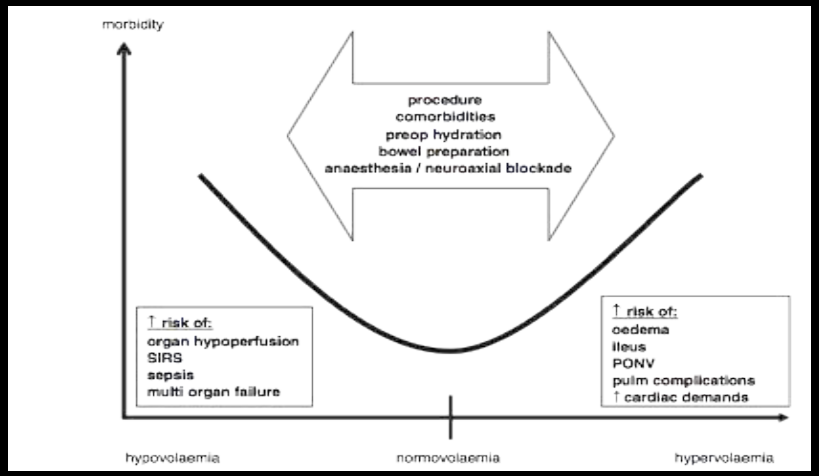
7-10 novembre 2013

It is standard practice to infuse volumes of intravenous fluids substantially in excess of actual peri-operative losses.

Lobo DN, et al. Lancet. 2002;359(9320):1812-1818.



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

Bari,
7-10 novembre 2013

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-Early Mobilization (d0)

-Prophylaxis against thromboembolism

-Use of laxative

-Early Enteral feeding (d0), stop ev (d1)

-Early discharge (d2-d3 after surgery)

Early enteral feeding

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7-10 novembre 2013

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).

U. O. Gustafsson et al. W J Surg 2013.

Fast-Track program

Bari,
7-10 novembre 2013

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

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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 implementating the Fast Track program.