



# Kortikoidy a operace

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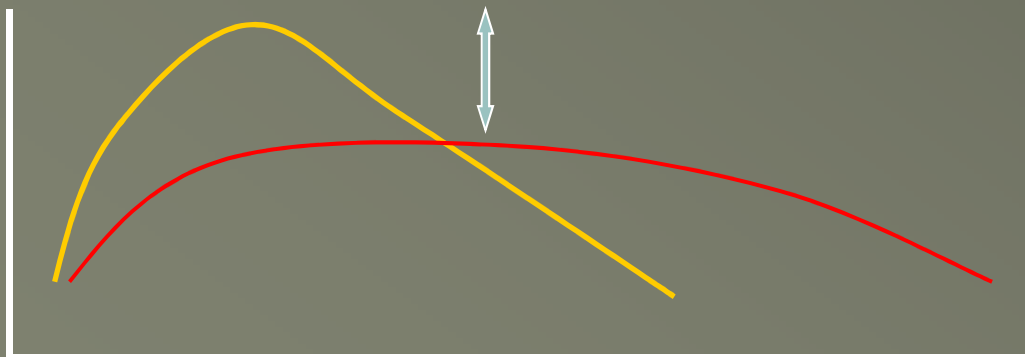
# Kortikoidy a operace

- ◆ Navýšení substituce ve stresu
- ◆ Stabilizace astmatu kolem operace
- ◆ Prevence pooperační nevolnosti
- ◆ **Regulace intenzity SIRS**
  - X
  - ◆ Riziko zhoršení hojení

# Intervence chirurgicky rizikového pacienta

1. Předoperační nutriční podpora a kondiční trénink
2. Nutriční imunomodulace
3. Vysokoproteinová dieta
4. Perioperační hemodynamická optimalizace „early goal directed“
5. Stabilní normoglykémie

Je přínosné mírnění zánětové reakce?



## Pro-inflammatory cytokines after different kinds of cardio-thoracic surgical procedures: is what we see what we know?

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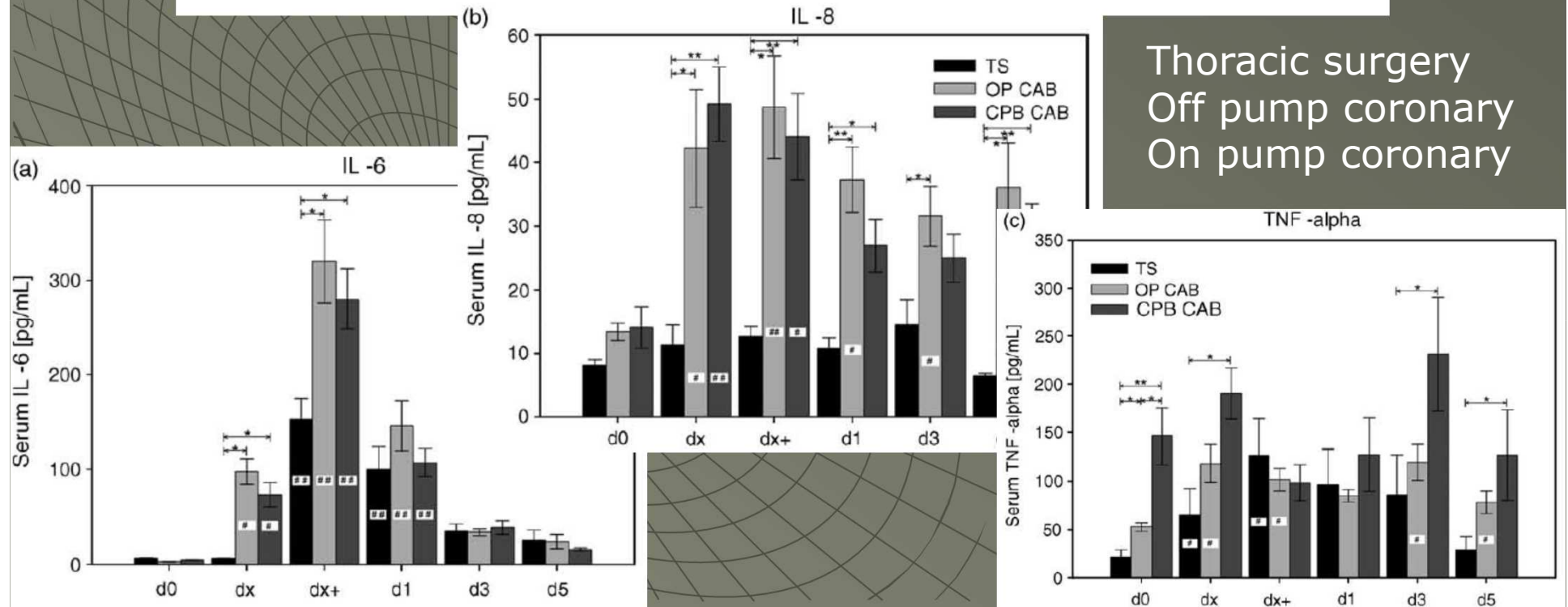
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Thoracic surgery  
Off pump coronary  
On pump coronary



*Fillinger MP, Rassias AJ, Futre PM, et al.*

## ***Glucocorticoid Effects on the Inflammatory and Clinical Response to Cardiac Surgery.***

*Journal of Cardiothoracic and Vascular Anesthesia 2002;  
16(2):163-169.*

- Randomizovaná, prospektivním dvojitě slepá, placebem kontrolovaná studie
- Koronární bypass v extrakorporálním oběhu
- Methylpredisolon 15mg/kg 1 hod. před operací, 0,3mg/kg a 6 hod. 4x
- Významné snížení IL-6, glykemie
- Podstatné snížení pooperační nevolnosti (0 versus 30%)
- Žádný klinický efekt na ventilaci, komplikace, délku pobytu na JIP a v nemocnici



# Requirement of Perioperative Stress Doses of Corticosteroids

## A Systematic Review of the Literature

Paul E. Marik, MD; Joseph Varon, MD

**Objective:** To determine the requirement for perioperative supplemental (stress) doses of corticosteroids in patients receiving long-term corticosteroid therapy and undergoing a surgical procedure. Corticosteroids are among the most commonly prescribed medications and will predictably result in suppression of the hypothalamic-pituitary-adrenal axis with long-term use. Patients receiving therapeutic dosages of corticosteroids frequently require surgery; these patients are almost universally treated with stress doses of corticosteroids during the perioperative period.

**Data Sources:** MEDLINE, EMBASE, Cochrane Register of Controlled Trials, and citation review of relevant primary and review articles.

**Study Selection:** Randomized controlled trials (RCTs) comparing stress doses of corticosteroids with placebo and cohort studies that followed up patients after surgery in which perioperative stress doses of corticosteroids were not administered.

**Data Extraction:** Data were abstracted on the study design, study size, study setting, patient population, dosage and duration of previous corticosteroid therapy, adrenal function testing results, surgical intervention, corticosteroid dosing regimen, intraoperative and postoperative hemodynamic profile, and incidence of adrenal crisis.

### Data Synthesis:

Patients, including 2 RCTs, enrolled a total of 100 patients in 5 cohort studies in their usual daily dose of corticosteroids before surgery development of these patients' adrenal function after administration.

### Conclusions:

Patients receiving corticosteroids who undergo surgery routinely require stress doses of corticosteroids so long as they continue to receive their usual daily dose of corticosteroid. Adrenal function testing is not required in these patients because the test is overly sensitive and does not predict which patient will develop an adrenal crisis. Patients receiving physiologic replacement doses of corticosteroids owing to primary disease of the hypothalamic-pituitary-adrenal axis, however, require supplemental doses of corticosteroids in the perioperative period.

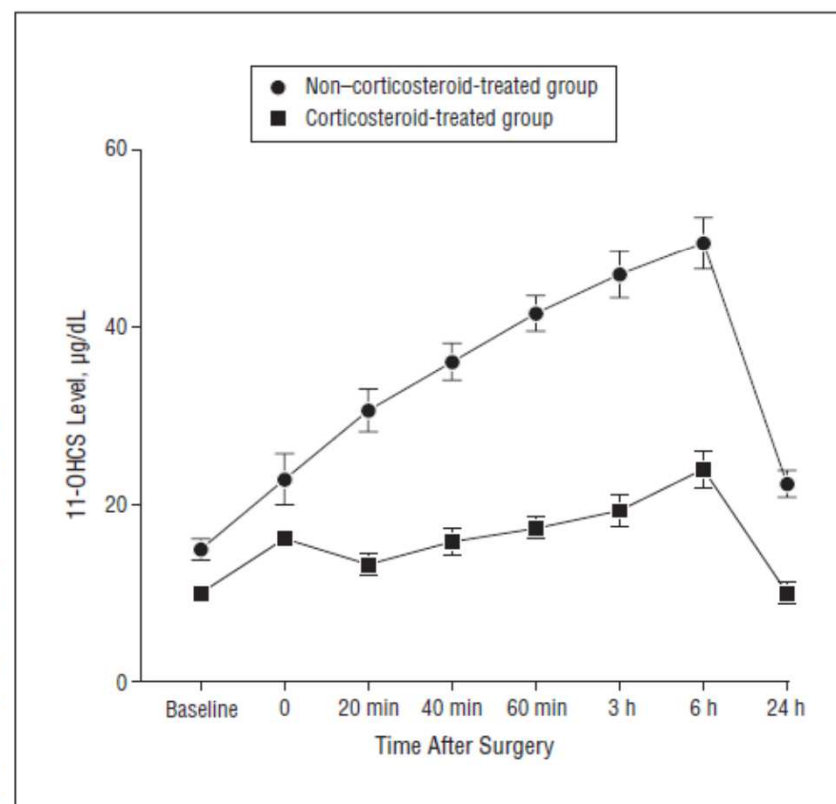


Figure. Plasma 11-hydroxycorticosteroid (11-OHCS) response to surgery in non-corticosteroid- and corticosteroid-treated patients with rheumatoid arthritis. Data from Jasani et al.<sup>10</sup>

# Perioperative intravenous corticosteroids reduce incidence of atrial fibrillation following cardiac surgery: a randomized study

*Corticosteroides intravenosos no perioperatório reduzem a incidência de fibrilação atrial após cirurgia cardíaca: estudo randomizado*

Monir Abbaszadeh<sup>1</sup>, Zahid Hussain Khan<sup>2</sup>, Fariborze Mehrani<sup>3</sup>, Hammid Jahanmehr<sup>4</sup>

## *Abstract*

**Objective:** Corticosteroids decrease side effects after noncardiac elective surgery. A randomized, double blinded, placebo-controlled study was plan to test the hypothesis that standard doses of dexamethasone (6X2) would decrease the incidence of atrial fibrillation (AF) following cardiac surgery.

**Methods:** A total of 185 patients undergoing coronary revascularization surgery were enrolled in this clinical study. The anesthetic management was standardized in all patients. Dexamethasone (6 mg/ml) or saline (1 ml) was administered after the induction of anesthesia and a second dose of the same study drug was given on the morning after surgery. The incidence of AF was determined by analyzing the first 72 hours of continuously recorded electrocardiogram records after cardiac surgery, to determine the incidence and severity of postoperative side effects.

**Results:** The incidence of 48 hours postoperative AF was significantly lower in the Dexamethasone group (21/92[37.5%]) than in the placebo group (35/92 [62.5%], adjusted hazard ratio, 2.07; 95% confidence interval, 1.09-3.95 ( $P<0.05$ ). Compared with placebo, patients receiving

dexamethasone did not have higher rates of superficial or deep wound infections, or other major complications.

**Conclusions:** Prophylactic short-term dexamethasone administration in patients undergoing coronary artery bypasses grafting significantly reduced postoperative atrial fibrillation.

**Descriptors:** Atrial fibrillation. Cardiac surgical procedures. Dexamethasone.

## *Resumo*

**Objetivo:** Os efeitos colaterais dos corticosteroides diminuem após a cirurgia eletiva não cardíaca. Este estudo randomizado, duplo cego, placebo-controlado foi planejado para testar a hipótese de que as doses-padrão de dexametasona (6 X 2) diminuiriam a incidência de fibrilação atrial (FA) após cirurgia cardíaca.

**Métodos:** Um total de 185 pacientes submetidos à cirurgia de revascularização coronária foram incluídos neste estudo clínico. O manuseio anestésico foi padronizado em todos os pacientes. Dexametasona (6 mg/ml) ou salina (1 ml) foram



## Anastomotic Leakage is Associated with Poor Long-Term Outcome in Patients After Curative Colorectal Resection for Malignancy

Wai Lun Law · Hok Kwok Choi · Yee Man Lee ·  
Judy W. C. Ho · Chi Leung Seto

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- Kratší přežití
- Vyšší rekurence nádoru
- Zvýšení nákladů
- Výskyt až ve 30%
- Větší riziko distálně a u akutní operace

cancer has not  
nor recurrence  
patients (904  
orectal cancer  
Kaplan Meier  
analysis. The  
occurred in 60  
s with surgery  
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spectively ( $p$ =  
val ( $p$ =0.043,  
1.23–3.06,  $p$ =

0.004) on multivariate analysis. In rectal cancer, anastomotic leakage was an independent factor for a higher local recurrence rate (hazard ratio: 2.55, 95% CI: 1.07–6.06,  $p$ =0.034). In conclusion, anastomotic leakage is associated with a poor survival and a higher tumor recurrence rate after curative resection of colorectal cancer. Efforts should be undertaken to avoid this complication to improve the long-term outcome.



# Kortikoidy a hojení

FOLIA HISTOCHEMICA  
ET CYTOBIOLOGICA  
Vol. 49, No. 1, 2011  
pp. 80–89

ORIGINAL STUDY



## The use of morphometric and fractal parameters to assess the effects of 5-fluorouracil, interferon and dexamethasone treatment on colonic anastomosis healing: an experimental study in rats

Katarzyna Łętowska-Andrzejewicz<sup>1</sup>, Anna Torres<sup>1</sup>, Kamil Torres<sup>1,2</sup>, Piotr Dobrowolski<sup>3</sup>, Tomasz Piersiak<sup>3</sup>, Ryszard Maciejewski<sup>1,4</sup>, Antoni Gawron<sup>3</sup>, Grzegorz Staśkiewicz<sup>1</sup>, Zbigniew Plewa<sup>5</sup>

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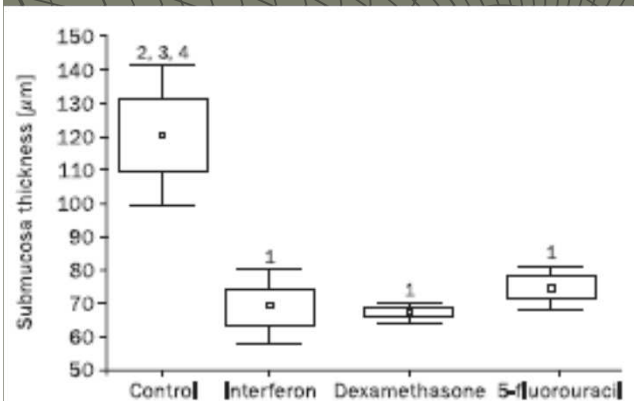
<sup>5</sup>Department of General Surgery, Military Hospital, Lublin, Poland

Dexametazon 0,5mg/den, 1. – 6. den  
(zvířata 250-350g)

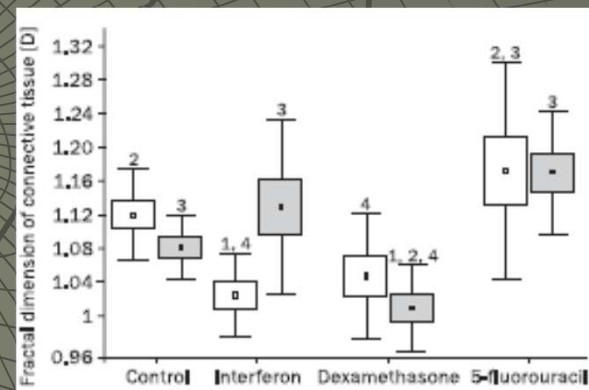
(1,5mg/kg ... 120mg/80kg ... cca 600mg Prednisonu)

3 z 15 zvířat měla leak v anastomóze na tlustém střevě  
7. den

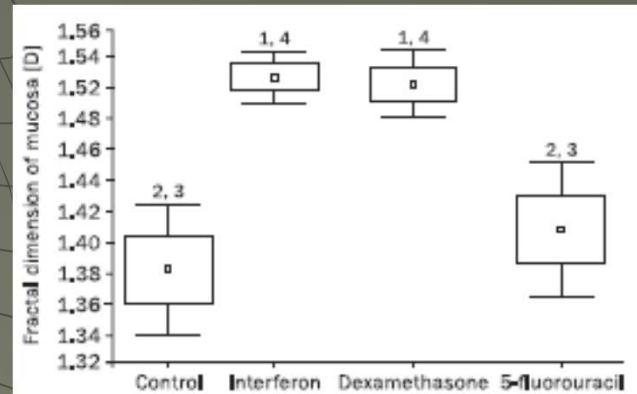
- Menší otok submukózy
- Méně pojiva
- Odložení hojení



**Figure 1.** Thickness of submucosa on the fourth post-operative day. Numbers above boxplots indicate statistically significant differences ( $p < 0.05$ ): 1. vs. control group; 2. vs. interferon group; 3. vs. dexamethasone group; 4. vs. 5-fluorouracil group



**Figure 2.** Fractal dimensions of connective tissue of large intestine on seventh (white boxes) and fourteenth (grey boxes) post-operative days. Numbers above boxplots indicate statistically significant differences ( $p < 0.05$ ): 1. vs. control group; 2. vs. interferon group; 3. vs. dexamethasone group; 4. vs. 5-fluorouracil group



**Figure 3.** Fractal dimensions of mucosa of large intestine on the seventh post-operative day. Numbers above boxplots indicate statistically significant differences ( $p < 0.05$ ): 1. vs. control group; 2. vs. interferon group; 3. vs. dexamethasone group; 4. vs. 5-fluorouracil group



# Long-term and Perioperative Corticosteroids in Anastomotic Leakage

## *A Prospective Study of 259 Left-Sided Colorectal Anastomoses*

Juliette C. Slieker, MD; Niels Komen, MD; Guido H. Mannaerts, MD, PhD; Tom M. Karsten, MD, PhD; Paul Willemsen, MD; Magdalena Murawska, MS; Johannes Jeekel, MD, PhD; Johan F. Lange, MD, PhD

- Akutní podání 5 dnů před operací
- 30 mg prednisonu 7 dnů
- Akutní i chronická terapie zvyšuje riziko leaku
- Ale vysoké riziko u plicní

went left-sided colorectal anastomoses.

**Intervention:** Corticosteroids taken as long-term medication for underlying disease or perioperatively for the prevention of postoperative pulmonary complications.

**Main Outcome Measures:** Prospective evaluations for risk factors for symptomatic AL.

**Results:** In 23% of patients, a defunctioning stoma was constructed. The incidence of AL was 7.3%. The clinical course of patients with AL showed that in 21% of leaks, the drain indicated leakage; in the remaining patients, com-

puted tomography or laparotomy resulted equally often in the detection of AL. In 50% of patients with AL, a Hartmann operation was needed. The incidence of AL was significantly higher in patients with pulmonary comorbidity (22.6% leakage), patients taking corticosteroids as long-term medication (50% leakage), and patients taking corticosteroids perioperatively (19% leakage). Perioperative corticosteroids were prescribed in 8% of patients for the prevention of postoperative pulmonary complications.

**Conclusions:** We found a significantly increased incidence of AL in patients treated with long-term corticosteroids and perioperative corticosteroids for pulmonary comorbidity. Therefore, we recommend that in this patient category, anastomoses should be protected by a diverting stoma or a Hartmann procedure should be considered to avoid AL.

**Trial Registration:** trialregister.nl Identifier: NTR1258

*Arch Surg.* 2012;147(5):447-452. Published online January 16, 2012. doi:10.1001/archsurg.2011.1690

# Kortikosteroidy zhoršují hojení

1. Snížená syntéza kolagenu
2. Inhibice angiogeneze
3. Stabilizace lysozomální membrány leukocytů
4. Ochrnutí migrace zánětlivých buněk
5. Invaze bakteriální flory





# Fáze hojení rány

1. Hemostáza
2. Reaktivita – záněť – kapilární propustnost
3. Lýza - 72 hodin
4. Proliferace – angiogeneze, fibroplázie, epitelizace
5. Remodelace

*Marjanovic G, Hopt UT. Physiology of anastomotic healing. Chirurg 2011;82:41-47*



## Predictive Factors for Anastomotic Leakage after Simultaneous Resection of Synchronous Colorectal Liver Metastasis

Kentaro Nakajima · Shinichiro Takahashi ·  
Norio Saito · Masahito Kotaka · Masaru Konishi ·  
Naoto Gotohda · Yuichiro Kato · Taira Kinoshita

Velké operační trauma (délka operace, velikost, ztráta krve) vyvolává silnou zánětovou reakci, která je spojena s poruchou hojení anastomózy.

### Abstract

**Background** The optimal surgical strategy for resectable, synchronous, colorectal liver metastases remains unclear. The objective of this study was to determine which patients could benefit from staged resections instead of simultaneous resection by identifying predictive factors for postoperative morbidity and anastomotic leakage after simultaneous resection of synchronous, colorectal liver metastases and the primary colorectal tumor.

**Methods** This study involved 86 patients with synchronous colorectal liver metastases who underwent simultaneous resection of the primary colorectal tumor and the hepatic tumor. Postoperative mortality, morbidity, and other surgical outcomes, including survival and hospitalization, were assessed. Predictive factors for postoperative morbidity and for anastomotic leakage were evaluated.

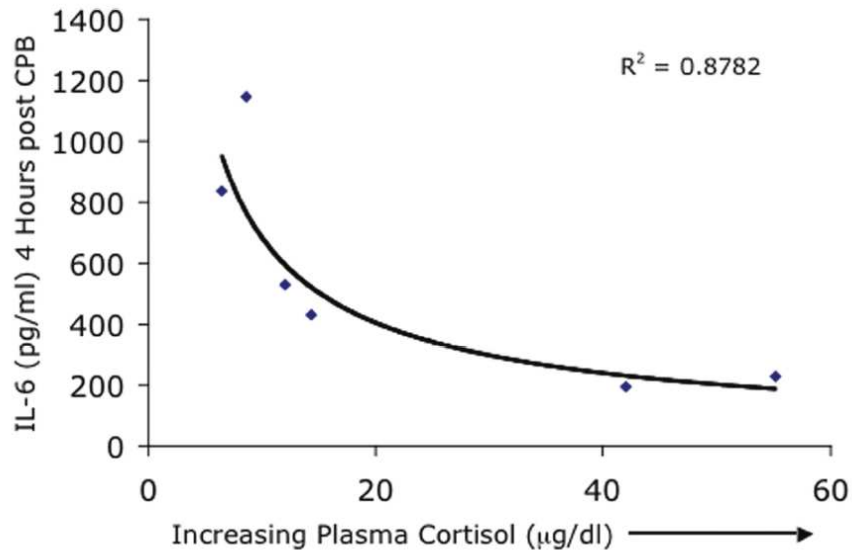
**Results** Postoperative morbidity and anastomotic leakage were found in 55 (64%) and 18 (21%) patients. Predictive factors for postoperative morbidity and for anastomotic leakage were intraoperative blood loss and operation time >8 h, respectively. The overall 5-year survival rate was 45%.

**Conclusions** The frequency of morbidity and that of anastomotic leakage seemed to be high after simultaneous resection for synchronous colorectal liver metastases, especially when intraoperative blood loss or operation time increased greatly. Staged resections should be considered in cases in which excessive surgical stress from simultaneous resection of synchronous colorectal liver metastases would be expected.

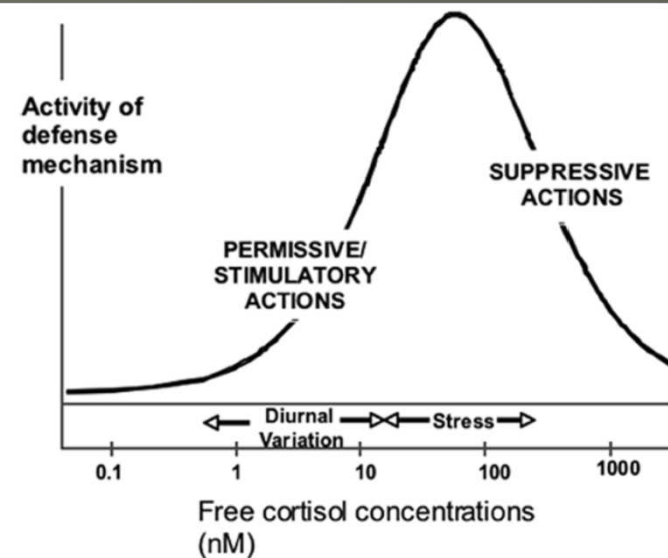
## CORTISOL EXERTS BI-PHASIC REGULATION OF INFLAMMATION IN HUMANS

**Mark P. Yeager, MD** □ Department of Anesthesiology and Critical Care Medicine, Dartmouth-Hitchcock Medical Center

**Patricia A. Pioli, PhD, Paul M. Guyre, PhD** □ Department of Physiology, Dartmouth Medical School



**FIGURE 4.** Cardiac surgical patients (n=60) were randomly divided into 6 groups before surgery. Treatment groups received intravenous etomidate during surgery to suppress endogenous cortisol synthesis. Varying doses of cortisol were then administered for 6 hours before and during surgery to regulate plasma cortisol concentrations over the physiologic range. Plasma cortisol concentration at the end of the cortisol infusion is plotted against peak plasma IL-6 concentrations that were observed 4 hours after surgery. The results show a classic dose-response relationship between the pro-inflammatory cytokine, IL-6, and the acute plasma cortisol concentration.



**FIGURE 1.** The figure shows a bi-phasic model of GC regulation of *in vivo* defense mechanisms, including innate immune inflammation. According to this model, basal concentrations of cortisol are not anti-inflammatory but exert a supportive (permissive) action on various defense mechanisms. As cortisol concentrations increase to those associated with systemic stress or pharmacological administration of cortisol, a bi-phasic relationship is observed, especially when there is a time delay between the increase in cortisol concentration and the inflammatory stimulus.



## Effect of Preoperative Single-Dose Corticosteroid Administration on Postoperative Morbidity Following Esophagectomy

Edgard Engelman • Cécile Maeyens

Received: 16 November 2009  
© 2010 The Society of

### Abstract

**Background** Esophagectomy is a major operation in order to decrease postoperative morbidity and mortality associated morbidity. **Method** A meta-analysis of randomized controlled studies, a Bayesian analysis was performed. **Results** The end point was the incidence of postoperative morbidity (OR=0.37), liver dysfunction (OR=0.37), and mortality (OR=0.37). **Conclusion** We conclude that, in the absence of a randomized controlled trial, the best option would be the planning of a large multicenter prospective randomized study.

- Metaanalýza 8 studií
- Neprůkazný závěr
- Nízká kvalita studií
- Snaha autorů prospěšnost obhájit
- Potřeba kvalitnější studie

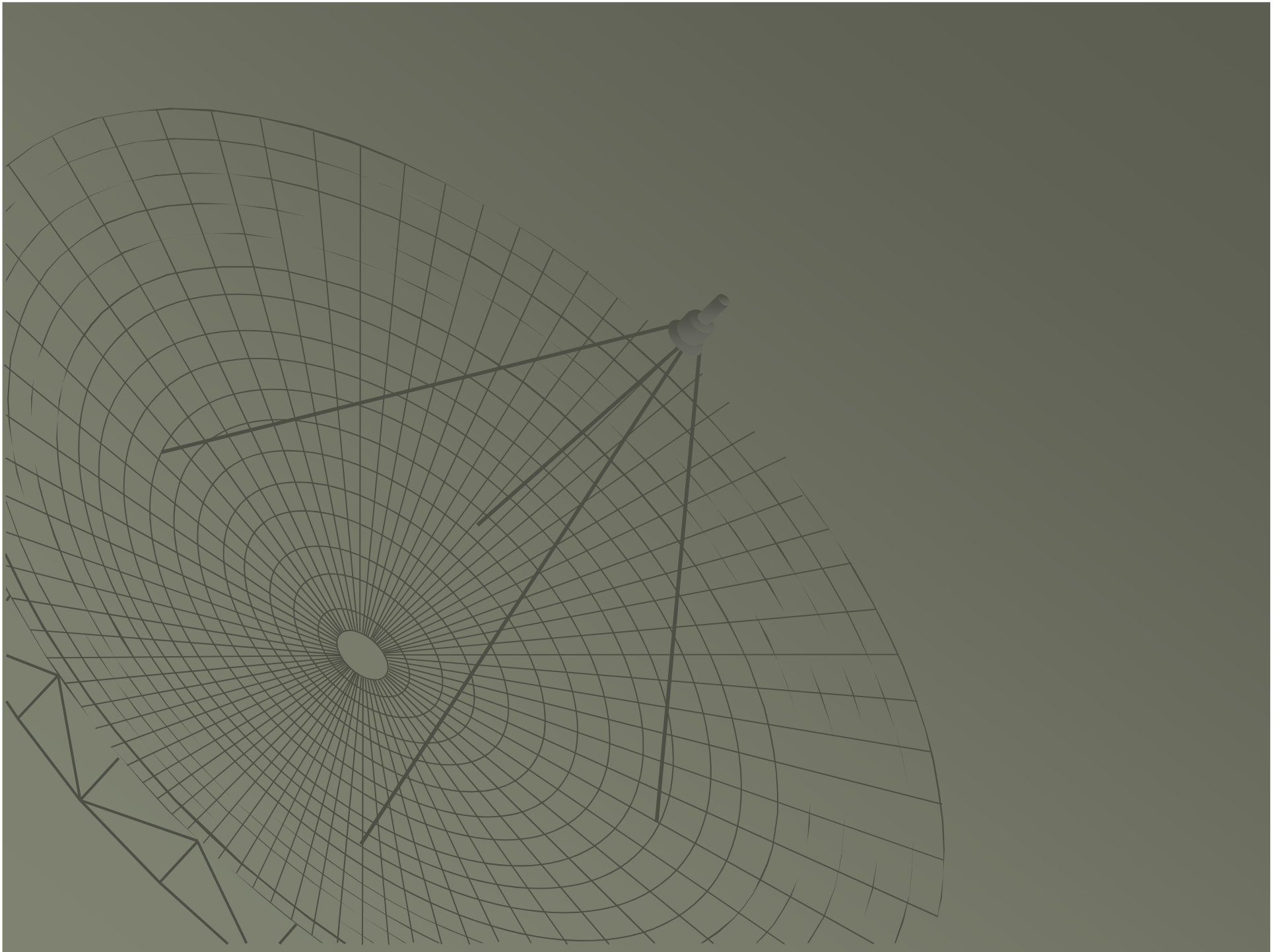
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# Závěr

1. Glukokortikoidy efektivně snižují intenzitu pooperační stresové reakce
2. Podání glukokortikoidů je spojeno s rizikem poruchy hojení a bakteriální invazí
3. Intenzivní SIRS je též spojen s poruchou hojení a rizikem pooperačních komplikací
4. Podání kortikoidů po operacích na střevě nemá bezpečný návod
5. Jednorázové či krátkodobé pooperační podání glukokortikoidů může u rizikových osob příznivě ovlivnit SIRS a zlepšit pooperační průběh.

**Děkuji za pozornost**







**Tabulka 3. Účinnost a další vlastnosti jednotlivých kortikosteroidních látek (přirozených a syntetických derivátů)**

preparát	protizánětlivý účinek	odpovídající dávka (mg)	retence sodíku	biologický poločas (hod)	odpovídající poločas (min)
Hydrokortizon	1	20	2+	8–12	90
Kortizon	0,8	25	2+	8–12	30
Prednizon	3,5	5	1+	12–36	60
Prednizolon	4	5	1+	12–36	200
Metylprednizon	5	4	0	12–36	180
Triamcinolon	6	4	0	24–48	300
Parametazon	10	2	0	36–54	—
Dexametazon	30	0,75	0	36–54	100–300
Betametazon	25	0,80	0	36–54	100–300
Beclometazon	40	0,50	0	—	—

Klin Farmakol Farm 2004; 18: 30–37