SYSTÉMOVÉ FAKTORY HOJENÍ RAN

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UDRŽOVÁNÍ HOMEOSTÁZY

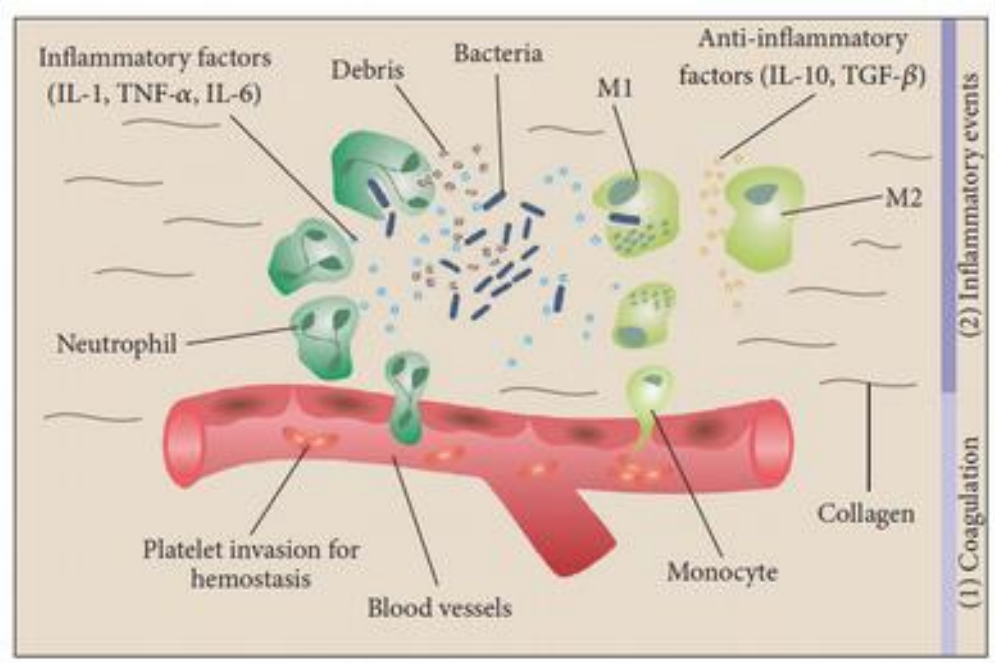
– základní charakteristika živého organizmu

- Rána narušuje homeostázu – narušení přirozeného metabolizmu tkání
  - otevření prostoru pro invazi predátorů
- Imunitní systém – strážce homeostázy
- Hojení rány – složka lokální a složka systémová

LOKÁLNÍ SLOŽKA HOJENÍ RAN

1. Inflamace
2. Proliferace
3. Remodelace

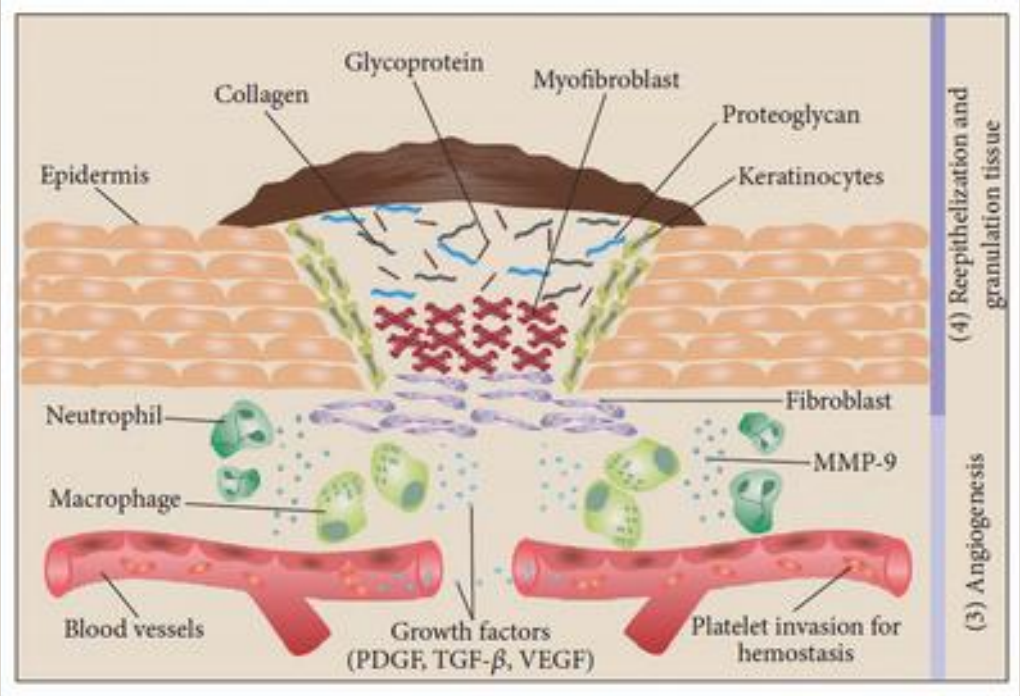
I. INFLAMACE (+ HEMOSTÁZA)



- **Infiltrace neutrofily** (útok na mikroby a rozpadlé buňky)
- **Infiltrace monocyty** s přeměnou na makrofágy (produkce cytokinů, likvidace apoptotických buněk včetně neutrofilů)
- **Infiltrace lymfocyty** (T-lymfocyty – dendritické bb. – růstové faktory pro keratinocyty, fibroblasty, IGF-1)

Serra MD et al. Hindawi International J of Inflammation, Volume 2017, Article ID 3406215, https://doi.org/10.1155/2017/3406215

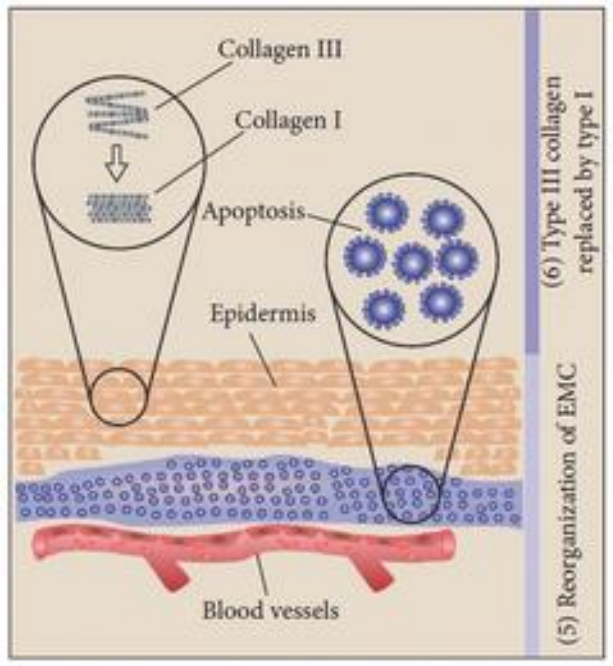
2. PROLIFERACE – provizorní výplň



- Reepitelizace – epitel a fibroblasty
- Angiogeneze - endotel
- Syntéza kolagenu
- Tvorba extracelulární matrix – fibroblasty produkují proteoglycany a glycosaminoglycany

Serra MD et al. Hindawi International J. of Inflammation, Volume 2017, Article ID 3406215, https://doi.org/10.1155/2017/3406215

3. REMODELACE



- Remodelace kolagenu
- Vaskulární regrese

Většina chronických ran jsou vředy z důvodu ischemie, diabetu, venostázy, tlaku.

Serra MD et al. Hindawi International J of Inflammation, Volume 2017, Article ID 3406215, https://doi.org/10.1155/2017/3406215

HYPOXIE A INFEKCE
– jsou základní lokální faktory poruchy hojení

- Hypoxie nahrává bakteriálnímu růstu, snižuje angiogenezi proliferační aktivity hojení
- Infekce prodlužuje inflamační fázi hojení (IL-1, TNF-α), proteázy rozpouští extracelulární matrix,
- Biofilm bakterií chrání bakterie a brání hojení

→ Perfuze a oxygenace tkání je systémovým opatřením pro hojení ran, (+význam zmírnění inflamační intenzity)

SYSTÉMOVÉ FAKTORY HOJENÍ RAN

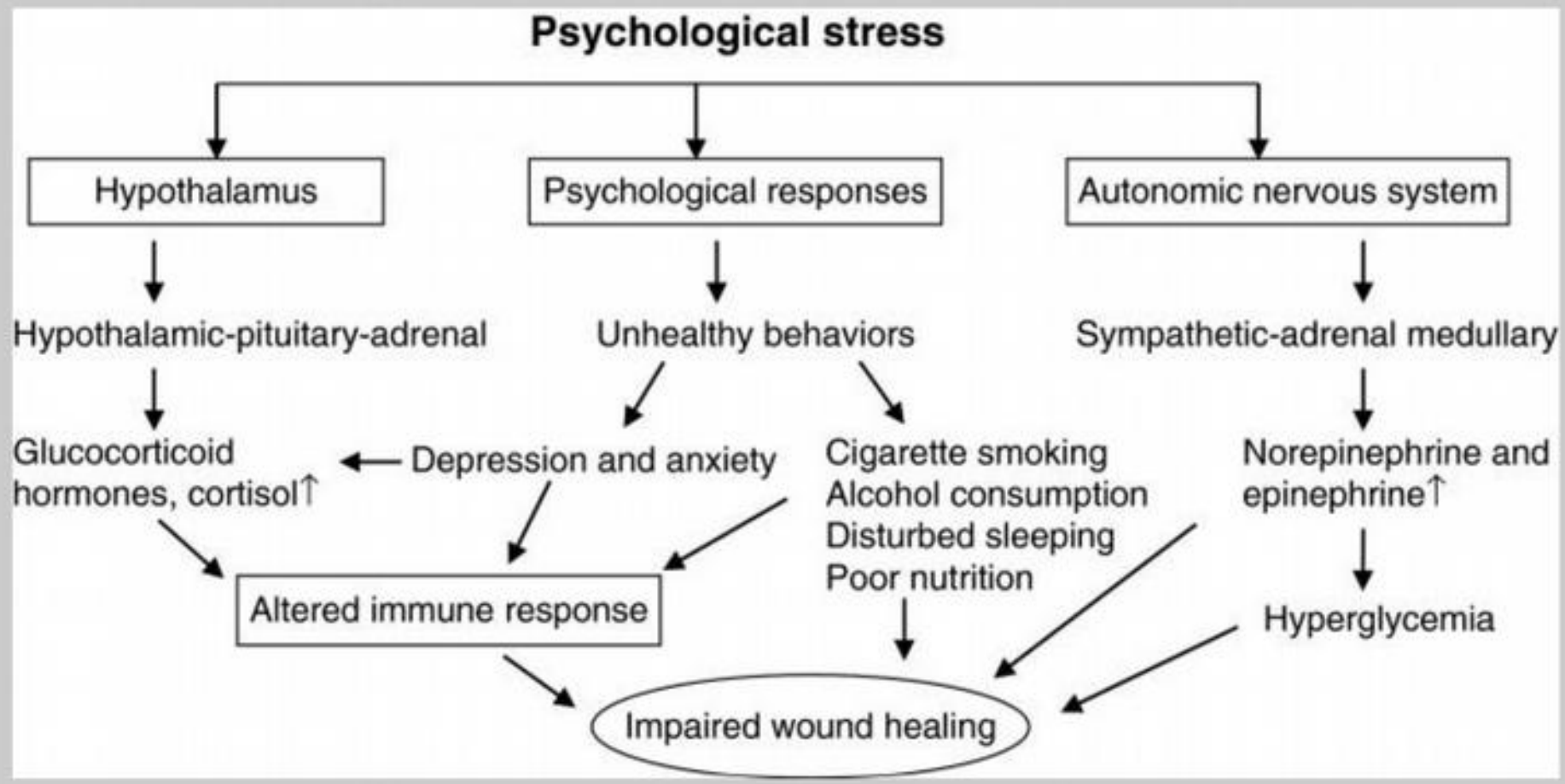
1. **Věk** – nikoliv schopnost hojení ale snížení rychlosti procesu hojení. Cvičení zvyšuje tkáňovou regeneraci, snížení zánětu v ráně.

Keylock KT, Vieira VJ, Wallig MA, DiPietro LA, Schrementi M, Woods JAExercise accelerates cutaneous wound healing and decreases wound inflammation in aged mice. Am J Physiol Regul Integr Comp Physiol. 2008 Jan; 294(1):R179-84.

2. **Pohlaví** – estrogeny zlepšují hojení ran u žen i mužů

Gilliver SC, Ashworth JJ, Ashcroft GS. The hormonal regulation of cutaneous wound healing. Clin Dermatol. 2007 Jan-Feb; 25(1):56-62.

3. **Stress** – nejen hormonální změny



Guo S, Dipietro LA. Factors affecting wound healing. *J Dent Res*.2010;89(3):219-29.

van Genderen et al. Critical Care 2014, 18:R114
http://ccforum.com/content/18/3/R114

CRITICAL CARE

RESEARCH Open Access

Clinical assessment of peripheral perfusion to predict postoperative complications after major abdominal surgery early: a prospective observational study in adults

Michel E van Genderen[1], Jorden Paauwe[1], Jeroen de Jonge[2], Ralf JP van der Valk[3,4], Alexandre Lima[1], Jan Bakker[1] and Jasper van Bommel[1*]

- CRT – capilary refeal time (>4,5s)
- PPI – periheral perfusion index (MASIMO, <1,4)
- $T_{skin-diff.}$ - rozdíl teploty kůže předloktí a prstu (>2st.C)

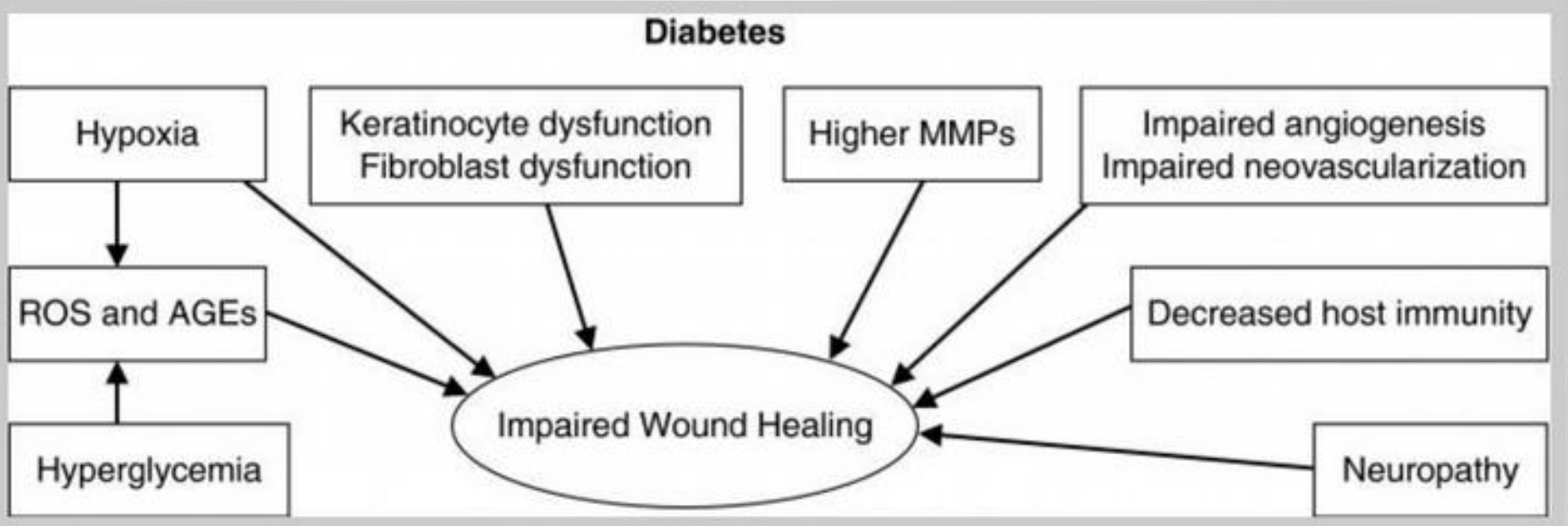
Table 4 Peripheral perfusion paramete

Measurement parameters	Baseline		D2		D3	
	Nonsevere complications	Severe complications	Nonsevere complications	Severe complications	Nonsevere complications	Severe complications
CRT (s)	2.4 (0.1)	2.8 (0.2)	2.7 (0.1)	5.9 (0.6)[b]	2.8 (0.2)	5.7 (0.7)[b]
PPI (a.u.)	3.9 (0.3)	2.9 (0.3)	3.9 (0.3)	1.7 (0.4)[b]	4.4 (0.3)	2.2 (0.5)[b]
$T_{skin-diff}$ (°C)	2.1 (0.2)	2.5 (0.5)	2.2 (0.2)	3.9 (0.6)[b]	2.2 (0.2)	3.6 (0.7)[b]

[a]a.u., Arbitrary units; Baseline, Prior to surgery; CRT, Ond postoperative day; D3, Third postoperative day; PPI, Peripheral perfusion index; $T_{skin-diff}$, Forearm-to-fingertip skin temperature gradiemplications. Severe complications category comprises grades III to V complications. Data are presented as mean ± SE for the total patient specific time point by linear mixed-model analysis.

Citlivější, ve srovnání s klasickými hemodynamickými parametry.

4. **Diabetes –** hypoxie z poruchy perfuze a angiogeneze



MMP= matrix metalloprotease , ROS= reactive oxygen species, AGE= advanced glycation end-product

Guo S, Dipietro LA. Factors affecting wound healing. *J Dent Res*. 2010;89(3):219-29.

5. Obezita

lokální charakter rány, komorbidita, hormonální a cytokinová aktivita

Local Wound Conditions	Associated Diseases and Conditions	Factors Altering Immune and Inflammatory Responses
1. decreased vascularity in adipose tissue	1. hard to reposition	1. adipokines: leptin, adiponectin, resistin
2. skin folds harbor micro-organisms	2. coronary heart disease	2. cytokines: TNF-alpha, IL-1, IL-6, IL-8, IL-10
3. friction caused by skin on skin	3. atherosclerosis	3. chemokines: IL-8, MCP-1, IP-10
4. increased wound tension	4. type 2 diabetes	
5. increased tissue pressure	5. cancer	
6. hematoma and seroma formation	6. hypertension	
7. venous hypertension	7. dyslipidemia	
	8. stroke	
	9. respiratory problems	

MCP, monocyte chemoattractant protein-1; IP-10 interferon-gamma-inducible protein 10.

Guo S, Dipietro LA. Factors affecting wound healing. *J Dent Res*. 2010;89(3):219-29.

6. Alkohol – zvýšené riziko infekcí (chronický abusus)

- snížená reaktivita hojení – akutní vliv alkoholu – snížená tvorba zánětových cytokinů, snížená kumulace neutrofilů a jejich snížena fagocytární aktivita, snížená angiogeneze ….

7. Kouření – vasokonstrikce, tkáňová ischemie, infekce

- snížená aktivita leukocytů, IL-1, proliferace fibroblastů, tvorby matrix

- předoperační přerušení kouření, případně použití náplastí zlepšuje hojení

- existují i práce, kde malá dávka nikotinu zvyšuje angiogenezi a zlepšuje hojení.

Sorensen LT, Jorgensen LN, Zillmer R, Vange J, Hemmingsen U, Gottrup F (2006). Transdermal nicotine patch enhances type I collagen synthesis in abstinent smokers. *Wound Repair Regen* 14:247-251.
Morimoto N, Takemoto S, Kawazoe T, Suzuki S (2008). Nicotine at a low concentration promotes wound healing. *J Surg Res* 145:199-204.

8. Léky - antikoagulace, antiinflamace, antiproliferace

- glukokortikoidy systémové

x glukokortikoidy lokální – malé dávky u chronických ran akcelerují hojení (redukce exsudátu, bolesti, hypergranulací)

- nesteroidní antirevmatika

- chemoterapeutika včetně biologické léčby (inhibice angiogeneze)

9. Výživa – energetické substráty, vitamíny, stopové prvky, minerály

- obecně zaměření na protein, glukózu, polynenasycené mastné kyseliny, K, P, Mg, vitaminy A,C, E, D, zinek, měď železo

Nonsteroidal anti-inflammatory drugs and the risk of anastomotic leakage after anterior resection for rectal cancer☆

D. Kverneng Hultberg [a,*], E. Angenete [b], M.-L. Lydrup [c], J. Rutegård [a], P. Matthiessen [d], M. Rutegård [a]

[a] *Department of Surgical and Perioperative Sciences, Surgery, Umeå University, Umeå, Sweden*
[b] *Department of Surgery, Institute of Clinical Sciences, SSORG – Scandinavian Surgical Outcomes Research Group, Sahlgrenska Academy at University of Gothenburg, Sahlgrenska University Hospital/Östra, Gothenburg,*

Abstract

Background: Nonsteroidal anti-inflammatory drugs (NSAIDs) have been widely used in colorectal surgery due to their opioid-sparing effect. However, several studies have indicated an increased risk of anastomotic leakage following NSAID treatment, although conflicting results exist. The primary goal of this study was to further examine whether postoperative NSAIDs are independently associated with anastomotic leakage after anterior resection for rectal cancer.

Methods: Patients who underwent anterior resection for rectal cancer during 2007–2013 in 15 different hospitals in three healthcare regions in Sweden were included in the study. Registry data and information from patient records were retrieved. The association between NSAID treatment (for at least two days in the first postoperative week) and symptomatic anastomotic leakage (within 90 days) was evaluated with multiple logistic regression, with adjustment for pertinent confounding factors.

Results: Some 1495 patients were included in the study. Of these, 27% received postoperative NSAIDs for at least two days in the first postoperative week. Symptomatic anastomotic leakage occurred in 11% and 14% in the NSAID and non-NSAID group, respectively. With adjustment for confounders, the odds ratio for leakage among patients who received NSAIDs compared with those who did not was 0.88 (95% CI 0.65–1.20). No differences were seen between non-selective and COX-2-selective NSAIDs.

Conclusion: Postoperative NSAID treatment does not seem to increase the risk of symptomatic anastomotic leakage after anterior resection for rectal cancer. NSAID use appears to be safe, but a well-powered randomized clinical trial is warranted.

. Kverneng Hultberg et al. / EJSO, October 217, Volume 43, Issue 10, Pages 1908–1914

Systematic Review and Meta-Analysis

Medicine

OPEN

Perioperative intravenous glucocorticoids can decrease postoperative nausea and vomiting and pain in total joint arthroplasty

A meta-analysis and trial sequence analysis

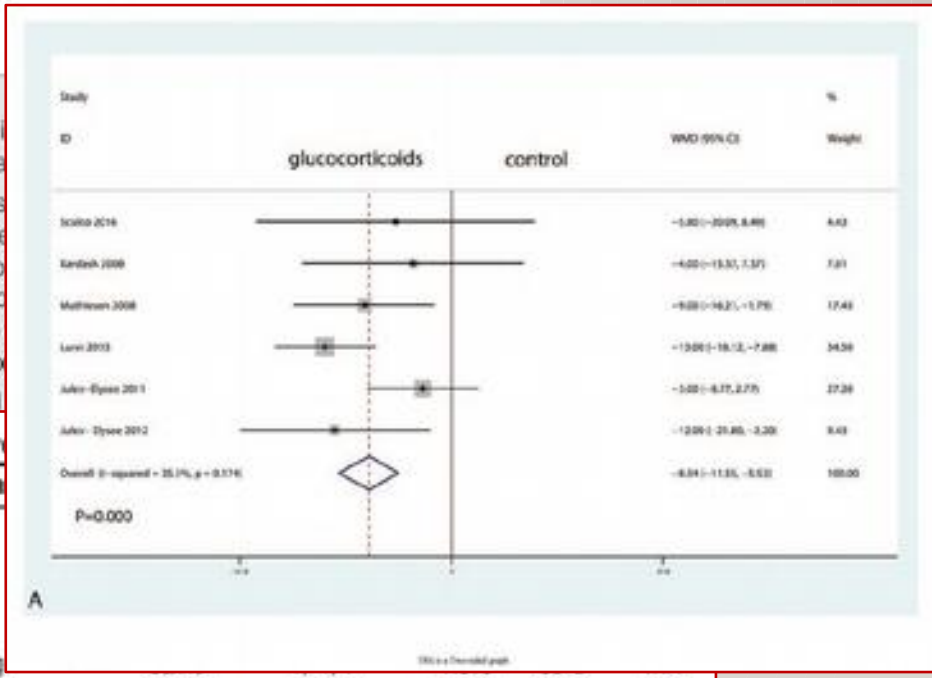
Ping Chen, MM[a], Xiwen Li, MM[b], Lili Sang, MM[c], Jiangfa Huang, MM[a,*]

Abstract

Background: This meta-analysis aimed to demonstrate the efficacy and safety of i
intensity and postoperative nausea and vomiting (PONV) in patients undergoing tota

Methods: PubMed, Embase, the Cochrane Central Register of Controlled Trials
databases were searched for randomized controlled trials (RCTs) comparing intrave
glucocorticoids or sham for patients undergoing TJA. Outcomes included visual analo
the occurrence of PONV; length of hospital stay; the occurrence of infection; and bloo
risk ratios (RR) with a 95% confidence interval (CI) for dichotomous outcomes and the
CI for continuous outcomes. Trial sequential analysis was also used to verify the po

Results: Thirteen clinical trials involving 821 patients were ultimately included



Reference	No. of patients		Male, %	Mean age, y	Anesthesia	Interv				
	Intervention	Control				Equivalency to dexa				
Sculco 2016	14	13	44	66	SA/EA	7.5 mg				
Kardash 2008	25	25	50	68	SA	40 mg				
Bergeron 2009	25	25	NS	NS	SA	40 mg				
Mathiesen 2008	40	40	50	67	SA	8 mg				
Lunn 2013	24	24	44	66	SA	23.43 mg				
Lunn 2011	24	24	NS	66	SA	25 mg	Saline	2, 3,4,	RCTs	1 mo	TKA
Fujii 2005	20	10	53	58	EA	4, 8 and 16 mg	Saline	4	RCTs	1 d	TKA
Koh 2013	135	134	51	72	SA	10 mg	Placebo	2, 3, 4, 7	RCTs	3 d	TKA
Jules-Elysee 2011	15	15	62	68	SA/EA	11.3 mg	Saline	1, 2, 3, 4, 5, 6, 7	RCTs	2 d	TKA
Jules- Elysee 2012	17	17	48	68	SA/EA	11.3 mg	Saline	1, 2, 3, 4, 5, 6, 7	RCTs	3 d	TKA
McLawhorn 2016	11	12	51	67	SA/EA	11.3 mg	Placebo	2, 6	RCTs	2 d	TKA
Morales-Munoz 2016	27	27	50	68.8	SA	8 mg	Saline	3, 4, 7	RCTs	2 d	TKA
Backes 2013	41	37	56.8	66	SA	10 mg	Placebo	1, 2, 3, 4, 5, 7	RCTs	3 d	TJA

1 = VAS at 12 h, 2 = VAS at 24 h, 3 = VAS at 48 h, 4 = the occurrence of nausea and vomiting, 5 = length of hospital stay, 6 = the blood glucose, 7 = the occurrence of infection, EA = epidural anesthesia, NS = not stated, RCTs = randomized controlled trials, SA = spinal anesthesia, THA = total hip arthroplasty, TJA = total joint arthroplasty, TKA = total knee arthroplasty.

Wu et al. BMC Cardiovascular Disorders (2016) 16:59
DOI 10.1186/s12872-016-0234-2

BMC Cardiovascular Disorders

RESEARCH ARTICLE Open Access

Postoperative glucocorticoid enhances recovery after endovascular aortic repair for chronic type B aortic dissection: a single-center experience

Mengtao Wu[1,2†], Lei Zhang[1†], Junmin Bao[1†], Zhiqing Zhao[1], Qingsheng Lu[1], Rui Feng[1], Chao Song[1], Jian Zhou[1*] and Zaiping Jing[1*]

Dexamethason 5mg/den 3 dny

Table 2 Postoperative outcomes

Outcomes	DXM ($n = 52$)	N-DXM ($n = 40$)	P
Pain score on the second day	3.60 ± 0.21	4.83 ± 0.32	0.001
Postoperative hospital stay, days	6.21 ± 0.44	6.48 ± 0.36	0.658
Postoperative adverse events, *n* (%)			0.313
Adverse cardiac events	0	3 (7.5)	
Adverse cerebrovascular events	1 (1.9)	0	
3-month follow-up, *n* (%)			0.718
Type I endoleak	0	1 (2.5)	
Type II endoleak	1 (1.9)	1 (2.5)	

DXM dexamethasone group, *N-DXM* non-dexamethasone group

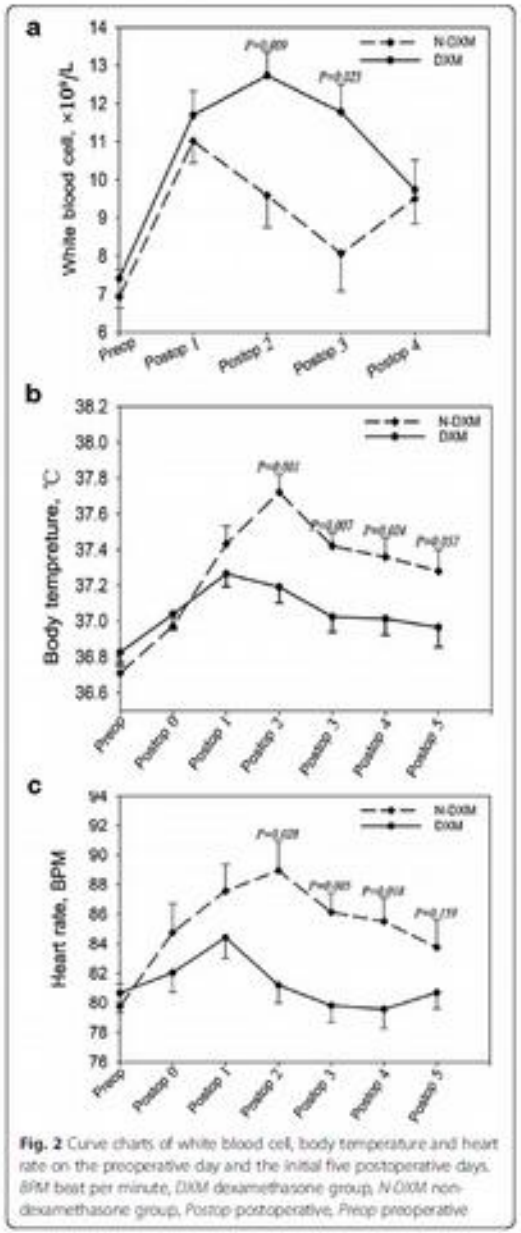


Fig. 2 Curve charts of white blood cell, body temperature and heart rate on the preoperative day and the initial five postoperative days. *BPM* beat per minute, *DXM* dexamethasone group, *N-DXM* non-dexamethasone group, *Postop* postoperative, *Preop* preoperative

BMJ Open

Preadmission glucocorticoid use and anastomotic leakage after colon and rectal cancer resections: a Danish cohort study

Eva Bjerre Ostenfeld,[1,2] Rune Erichsen,[1] John A Baron,[1,3] Ole Thorlacius-Ussing,[2] Lene Hjerrild Iversen,[4] Anders H Riis,[1] Henrik Toft Sørensen,[1] on behalf of the Danish Colorectal Cancer Group

Riziko leaku záleží na podání kortikoidů, ale není významné.

Table 3 Absolute and relative risk (ORs) associating use of glucocorticoids and anastomotic leakage after colon cancer resection, Denmark, 2001–2011

Glucocorticoid use	Study population, N=18 190 n (%)	Leakage, N=1184 n (%)	Leakage risk, % (95% CI)	Risk difference,* % (95% CI)	Unadjusted OR (95% CI)	Adjusted OR† (95% CI)
No use	14 041 (77.2)	897 (75.8)	6.4 (6.0 to 6.8)	Referent	Referent	Referent
Any use	4149 (22.8)	287 (24.2)	6.9 (6.0 to 6.8)	0.5 (−0.3 to 1.4)	1.09 (0.95 to 1.25)	1.05 (0.89 to 1.23)
Oral use						
Current use	345 (1.9)	26 (2.2)	7.5 (5.1 to 10.7)	1.1 (−1.7 to 4.0)	1.19 (0.80 to 1.79)	1.24 (0.82 to 1.88)
Recent use	207 (1.1)	18 (1.5)	8.7 (5.4 to 13.1)	2.3 (−1.6 to 6.2)	1.40 (0.86 to 2.27)	1.43 (0.87 to 2.34)
Former use	948 (5.2)	53 (4.5)	5.6 (4.3 to 7.2)	−0.8 (−2.3 to 0.7)	0.87 (0.65 to 1.15)	0.90 (0.67 to 1.20)
Inhaled use						
Current use	434 (2.4)	32 (2.7)	7.4 (5.2 to 10.1)	1.0 (−1.5 to 3.5)	1.17 (0.81 to 1.68)	1.04 (0.70 to 1.53)
Recent use	252 (1.4)	16 (1.4)	6.3 (3.8 to 9.9)	−0.0 (−3.1 to 3.0)	0.99 (0.60 to 1.66)	0.96 (0.57 to 1.62)
Former use	742 (4.1)	51 (4.3)	6.9 (5.2 to 8.9)	0.5 (−1.4 to 2.3)	1.08 (0.81 to 1.45)	1.06 (0.78 to 1.44)
Intestinal acting use	54 (0.3)	5 (0.4)	9.3 (3.6 to 19.1)	2.9 (−4.9 to 10.6)	1.50 (0.59 to 3.76)	1.47 (0.56 to 3.84)
Mixed use	1167 (6.4)	86 (7.3)	7.4 (6.0 to 9.0)	1.0 (−0.6 to 2.5)	1.17 (0.93 to 1.47)	1.02 (0.78 to 1.35)

Values in parentheses are 95% CIs unless otherwise indicated.
*Calculated by subtracting the estimate for never-use from that for glucocorticoid users.
†Adjusted for sex, age, Charlson Comorbidity Index score, American Society of Anesthesiologists' Physical Status Classification (ASA) score, inflammatory bowel disease, alcoholism, smoking status, chronic obstructive pulmonary disorder medications and non-steroidal anti-inflammatory drugs.

Ostenfeld EB et al. BMJ Open 2015;5

BMJ Open

Preoperative single-dose methylprednisolone versus placebo after major liver resection in adults: protocol for a randomised controlled trial

Alexsander K Bressan,[1] Derek J Roberts,[1,2] Sana U Bhatti,[1] Elijah Dixon,[1] Francis R Sutherland,[1] Oliver F Bathe,[1] Chad G Ball[1]

Strengths and limitations of this study

- This randomised controlled trial will evaluate the effect of a single preoperative dose of methylprednisolone on the incidence of postoperative complications and other patient-important outcomes instead of surrogate outcome measures.
- Surgical team members, participants, and outcome assessors will be blinded to study allocation status.
- This is a single-centre study.

ABSTRACT

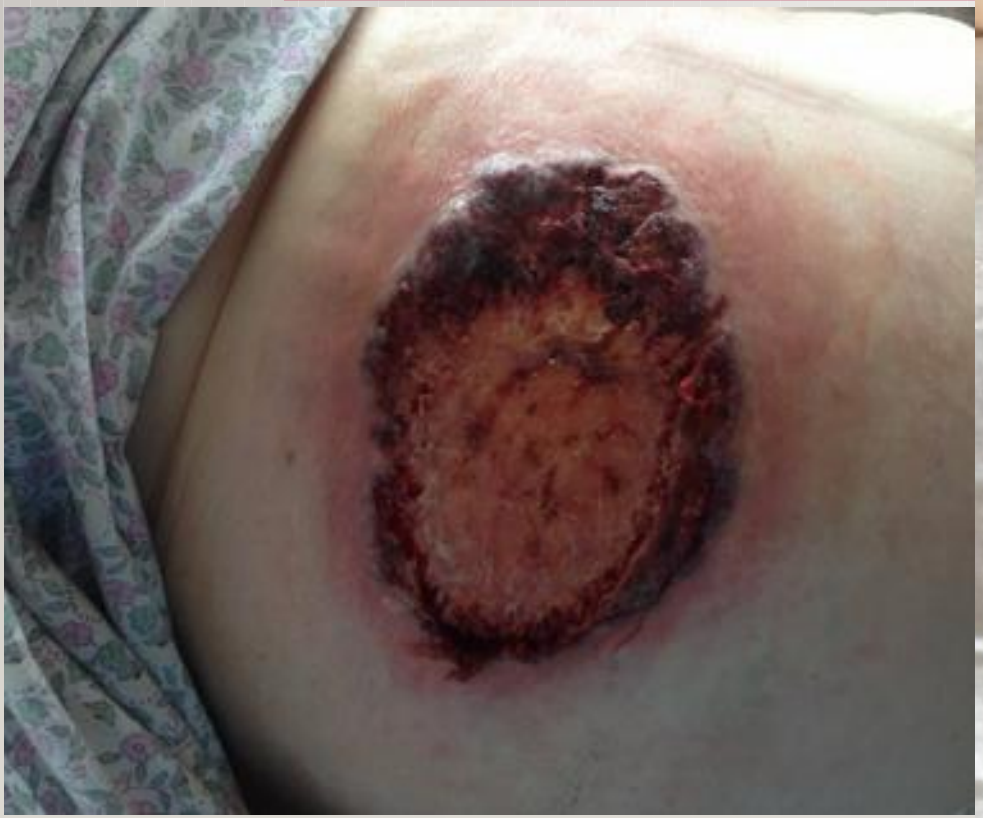
Introduction: Although randomised controlled trials have demonstrated that preoperative glucocorticoids may improve postoperative surrogate outcomes among patients undergoing major liver resection, evidence supporting improved patient-important outcomes is lacking. This superiority trial aims to evaluate the effect of administration of a bolus of the glucocorticoid methylprednisolone versus placebo during induction of anaesthesia on postoperative morbidity among adults undergoing elective major liver resection.

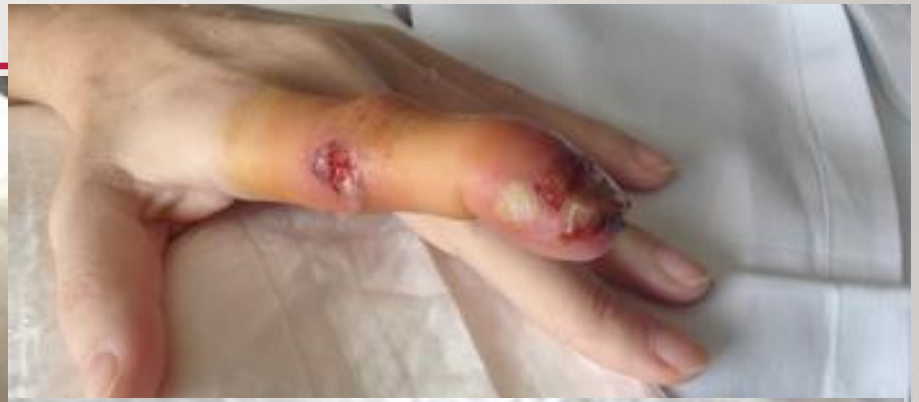
Methods and analysis: This will be a randomised, dual-arm, parallel-group, superiority trial. All consecutive adults presenting to a large Canadian tertiary care hospital who consent to undergo major liver resection will be included. Patients aged <18 years and those currently receiving systemic corticosteroid therapy will be excluded. We will randomly allocate participants to a preoperative 500 mg intravenous bolus of methylprednisolone versus placebo. Surgical team members and outcome assessors will be blinded to treatment allocation status. The primary outcome measure will be postoperative complications. Secondary outcome measures will include mortality, the incidence of several specific postoperative complications, and blood levels of select proinflammatory cytokines, acute-phase proteins, and laboratory liver enzymes or function tests on postoperative days 0, 1, 2 and 5. The incidence of postoperative complications and mortality will be compared using Fisher's exact test, while the above laboratory measures will be compared using mixed-effects models with a subject-specific random intercept.

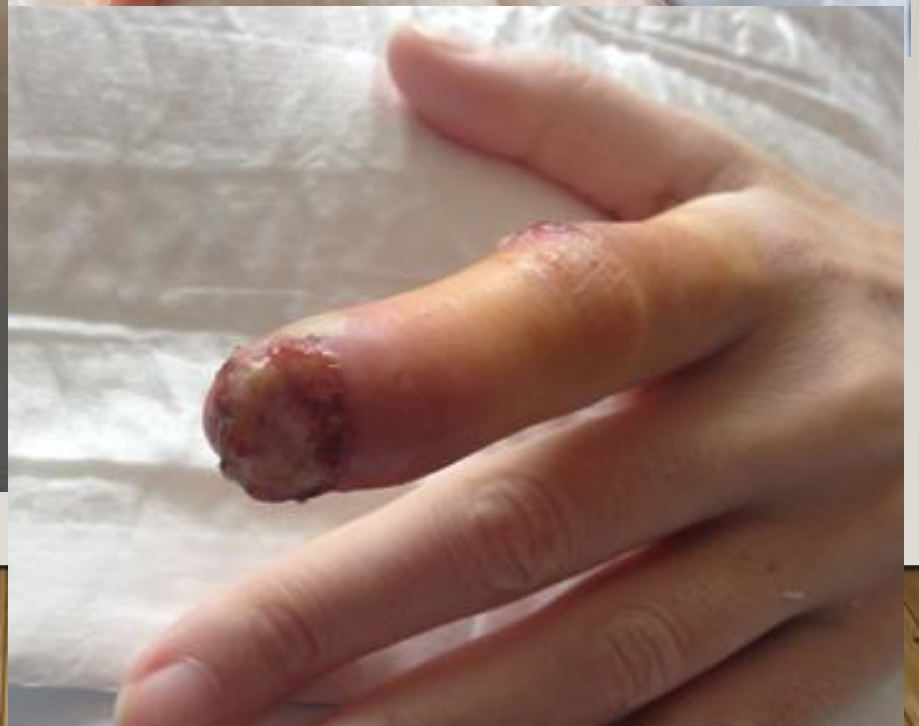
Ethics and dissemination: This trial will evaluate the protective effect of a single preoperative dose of methylprednisolone on the hazard of postoperative complications. A report releasing study results will be submitted for publication in an appropriate journal, approximately 3 months after finishing the data collection.

Trial registration number: NCT01997658; Pre-results.

PYODERMA GANGRENOSUM
– terapie kortikoidy







JAMA Dermatology | Consensus Statement

Diagnostic Criteria of Ulcerative Pyoderma Gangrenosum
A Delphi Consensus of International Experts

Emanual Maverakis, MD; Chelsea Ma, MD; Kanade Shinkai, MD, PhD; David Fiorentino, MD, PhD; Jeffrey P. Callen, MD; Uwe Wollina, MD; Angelo Valerio Marzano, MD; Daniel Wallach, MD; Kyoungmi Kim, PhD; Courtney Schadt, MD; Anthony Ormerod, MD; Maxwell A. Fung, MD; Andrea Steel, BA; Forum Patel, MD; Rosie Qin, MD; Fiona Craig, MRCP; Hywel C. Williams, DSc; Frank Powell, FRCPI; Alexander Merleev, PhD; Michelle Y. Cheng, MD

Často přehlédnutá diagnóza, nález se horší chirurgickou intervencí.

Hlavní kritérium:
Neutrofilní infiltrát v biopsii
+4 z 8 pomocných kritérií

stanovují diagnózu v 86%

IMPORTANCE Pyoderma gangrenosum is a rare inflammatory skin condition that is difficult to diagnose. Currently, it is a "diagnosis of exclusion," a definition not compatible with clinical decision making or inclusion for clinical trials.

OBJECTIVE To propose and validate diagnostic criteria for ulcerative pyoderma gangrenosum.

EVIDENCE REVIEW Diagnostic criteria were created following a Delphi consensus exercise using the RAND/UCLA Appropriateness Method. The criteria were validated against peer-reviewed established cases of pyoderma gangrenosum and mimickers using k-fold cross-validation with methods of multiple imputation.

FINDINGS Delphi exercise yielded 1 major criterion—biopsy of ulcer edge demonstrating neutrophilic infiltrate—and 8 minor criteria: (1) exclusion of infection; (2) pathergy; (3) history of inflammatory bowel disease or inflammatory arthritis; (4) history of papule, pustule, or vesicle ulcerating within 4 days of appearing; (5) peripheral erythema, undermining border, and tenderness at ulceration site; (6) multiple ulcerations, at least 1 on an anterior lower leg; (7) cribriform or "wrinkled paper" scar(s) at healed ulcer sites; and (8) decreased ulcer size within 1 month of initiating immunosuppressive medication(s). Receiver operating characteristic analysis revealed that 4 of 8 minor criteria maximized discrimination, yielding sensitivity and specificity of 86% and 90%, respectively.

CONCLUSIONS AND RELEVANCE This Delphi exercise produced 1 major criterion and 8 minor criteria for the diagnosis of ulcerative pyoderma gangrenosum. The criteria may serve as a guideline for clinicians, allowing for fewer misdiagnoses and improved patient selection for clinical trials.

JAMA Dermatol. doi:10.1001/jamadermatol.2017.5980
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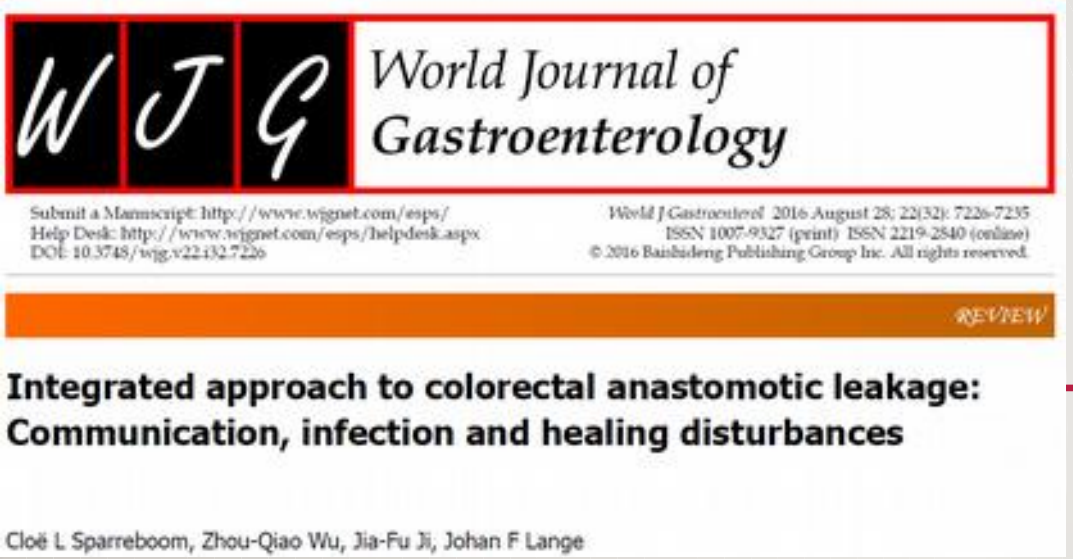

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REVIEW

Integrated approach to colorectal anastomotic leakage: Communication, infection and healing disturbances

Cloë L Sparreboom, Zhou-Qiao Wu, Jia-Fu Ji, Johan F Lange

Leak v colorektální anastomóze je v 4-33%

a jde o závažnou komplikaci:

- zvyšuje pooperační letalitu
- prodlužuje pooperační léčbu
- zvyšuje náklady
- zhoršuje kvalitu života
- znemožňuje protinádorovou léčbu

Etiologie dehiscence anastomózy:

1. Operační defekt – porucha sutury, ischemie, napětí v sutuře
2. Infekce – absces v anastomóze, peritonitida
3. Porucha hojení

Význam předoperačního vyšetření a přípravy.

DĚKUJI ZA POZORNOST