

**"NUTRIZIONE ARTIFICIALE IN OSPEDALE E SUL TERRITORIO:
ATTUALITA' CLINICHE E TECNICO-FARMACEUTICHE"**



**Milano, c/o AC HOTEL
Evento 313- 93078
21 maggio 2014**

Paziente Chirurgico: cos'è cambiato nell'era ERAS?



DOCT MARTA

UNIVERSITÀ MILANO
SCHOOL OF SPECIALIZATION

UNIVERSITÀ DEGLI STUDI
BICOCCA

DOCTORAL PROGRAM
GIA G



Eminence based practice



Scarsa comunicazione

Prolungato periodo di digiuno perioperatorio

Disidratazione o eccessivo carico di fluidi

Inadeguato controllo del dolore

Mobilizzazione tardiva

CV/SNG/drenaggi

Nil per os fino alla canalizzazione/TPN

Lunga degenza ospedaliera



Henrik Kehlet

- FAST-TRACK surgery
- Approccio multimodale
- *Evidence based practice*

ERAS study group

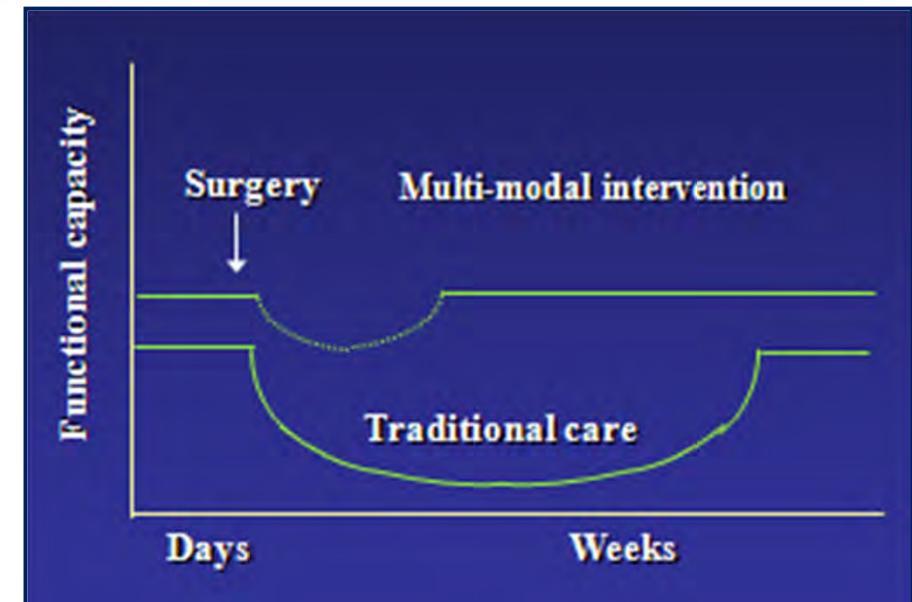


Cornelius deJong, Martin von Meyenfeldt, Arthur Revhaug



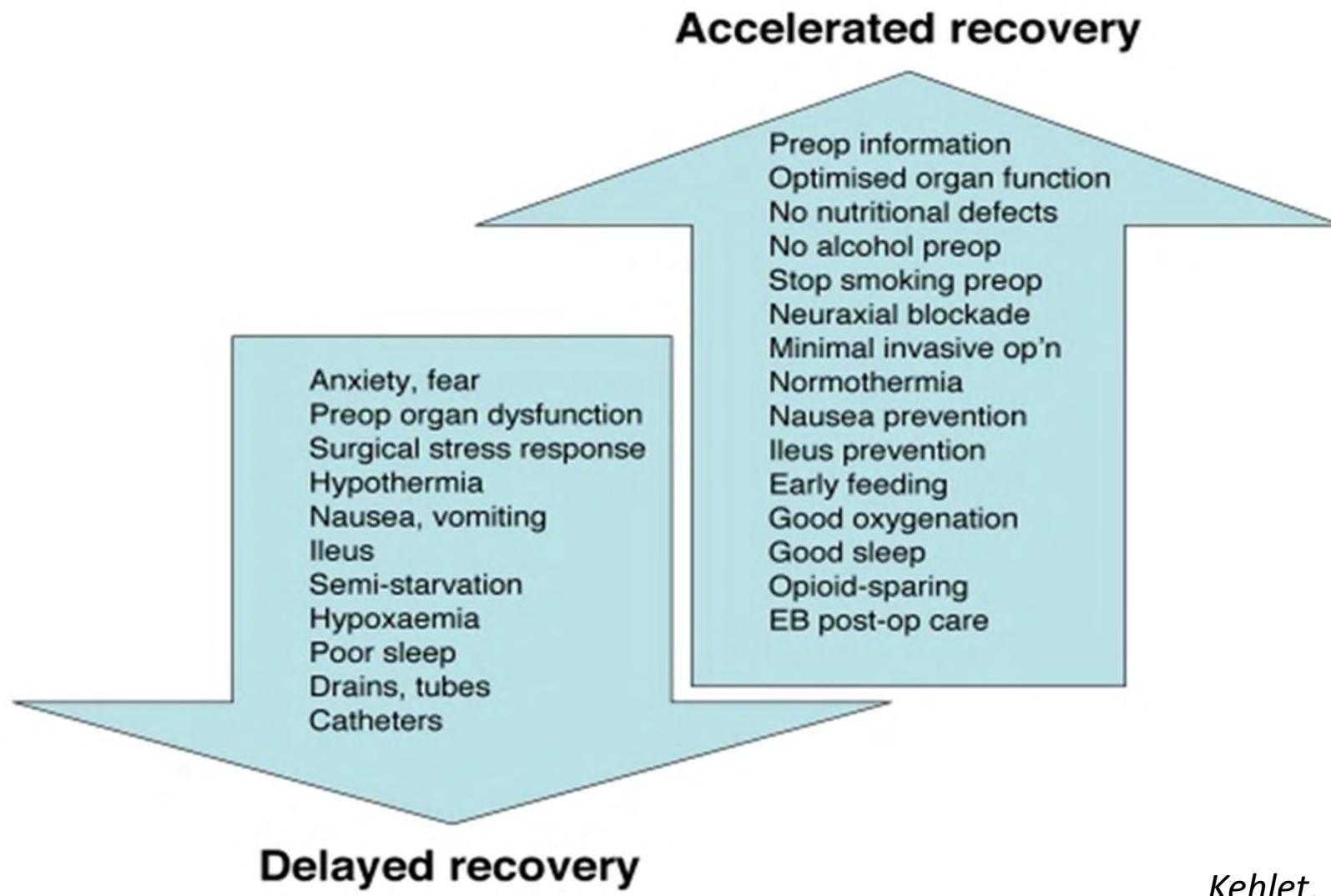
TARGET ERAS

- ↓ stress metabolico post-chirurgico
- ↓ degenza ospedaliera
- ...piu rapido recupero dell'autonomia
- ↓ disfunzione d'organo
- ↓ complicanze peri-op



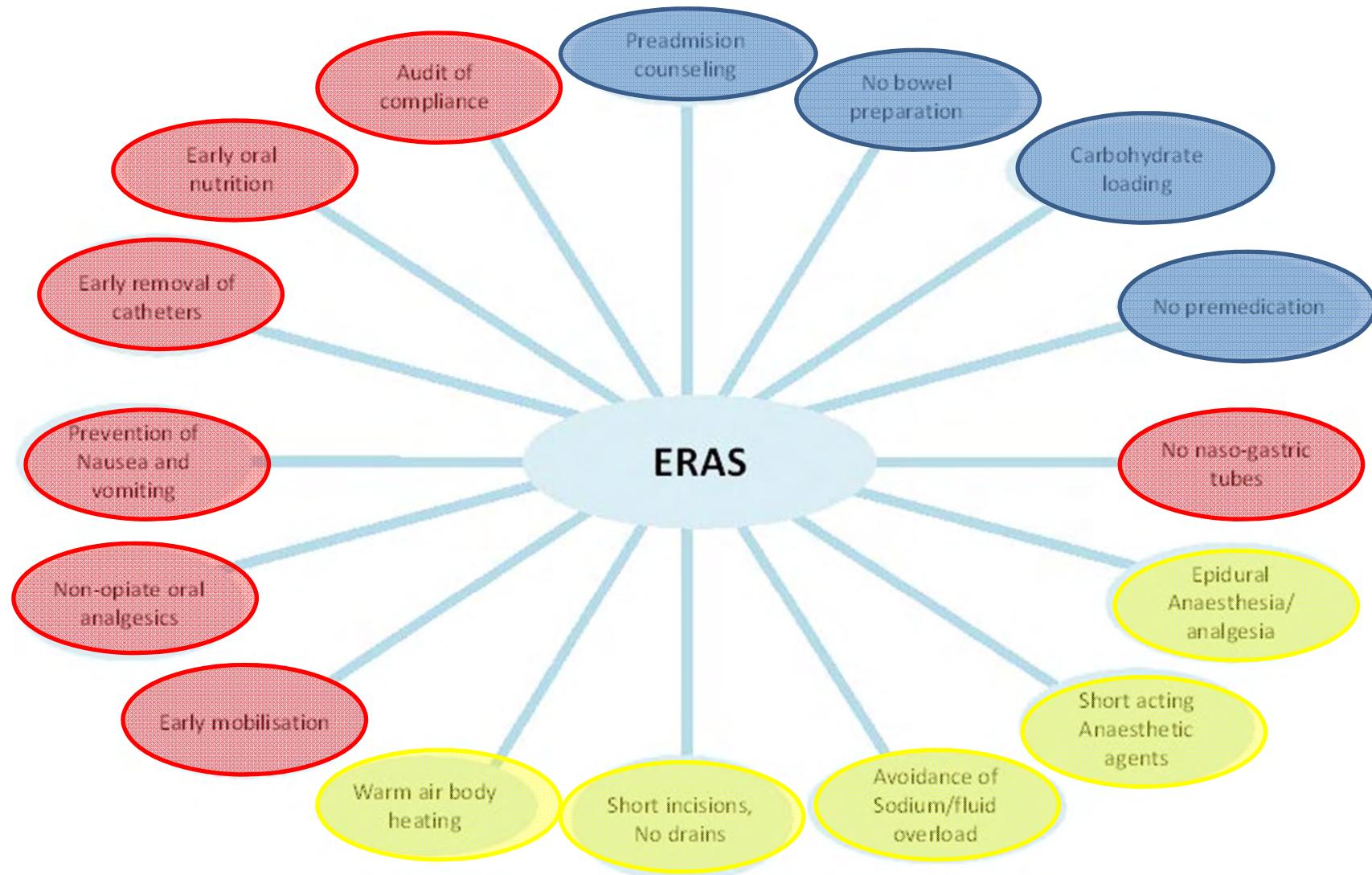


Quali fattori influenzano il recupero del paziente chirurgico?



Kehlet, 1980s

Enhanced Recovery Protocol



Gestione del preoperatorio

- Counselling
- Prehabilitation

The effectiveness of prehabilitation in general surgery.

Prehabilitation must be integrated into the overall patient medical management, and must be associated with preoperative refeeding and postoperative rehabilitation protocols.

By optimizing all stages of the surgical patient management, from diagnosis to recovery, prognosis of high-risk surgical patients could be improved.

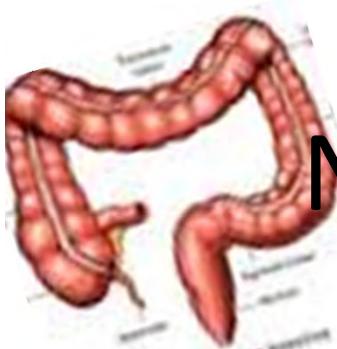
Debes et al., *Prehabilitation. Preparing patients for surgery to improve functional recovery and reduce postoperative morbidity*, 2013

Sorensen LT, Karlsmark T, Gottrup F, *Abstinence from smoking reduces incisional wound infection: a randomized controlled trial*. Ann Surg, 2002



Tonnesen H, Kehlet H, *Preoperative alcoholism and postoperative morbidity*. Br J Surg, 1999

- Medicina territoriale



Nessuna preparazione intestinale

- ↓ della disidratazione e delle conseguenze fisiopatologiche ad essa associate
 - Holte K et al., Physiologic effects of bowel preparation. *Dis Colon Rectum*, 2004
- ↓ del discomfort del paziente
 - Jung B, et al., Preoperative mechanical preparation of the colon: the patient's experience, 2007
- ↓ rischio di contaminazione addominale intraoperatoria nella chirurgia del colon
 - Mahajna A t al., Bowel preparation is associated with spillage of bowel contents in colorectal surgery, 2005

- ↓ rischio di complicanze rispetto ai pazienti che effettuano MBP

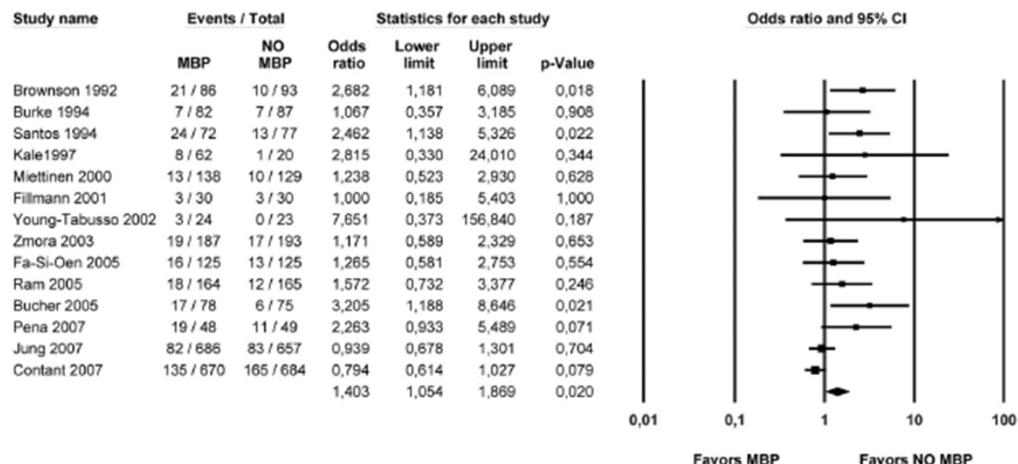
Updated Systematic Review and Meta-Analysis of Randomized Clinical Trials on the Role of Mechanical Bowel Preparation Before Colorectal Surgery

Karem Slim, MD, Eric Vicaut, MD, PhD,† Marie-Véronique Launay-Savary, MD,* Caroline Contant, MD,‡ and Jacques Chipponi, MD, PhD**

SSI →

MA...

- Trials su *open surgery*
 - Possibile maggior difficoltà tecnica senza MBP
 - Si è osservato un trend indicativo di un aumento dei leakage anastomotici nella chirurgia rettale senza MBP
 - Bretagnol F, et al., 2010, Rectal cancer surgery with or without bowel preparation: The French GRECCAR III multicenter single-blinded randomized trial.
- Non effettuare MBP nella chirurgia elettiva del colon; non sufficienti evidenze supportano l'omissione della preparazione intestinale nella chirurgia del retto



Liquidi e carboidrati nel preoperatorio

- Lasciare il paziente a digiuno dalla mezzanotte precedente l'intervento non incrementa il pH gastrico nè il rischio di complicanze anestesiologiche
- Cochrain review, 2003:

22 RCT, fasting from midnight VS free intake of clear fluids until -2h

Participants given a drink of water preoperatively were found to have a significantly lower volume of gastric contents than the groups that followed a standard fasting regimen. There was no indication that the volume of fluid permitted during the preoperative period (i.e. low or high) resulted in a difference in outcomes from those participants that followed a standard fast.

(Brady M et al., *Preoperative fasting for adults to prevent perioperative complications*)

Preoperative Management of Surgical Patients by “Shortened Fasting Time”: A Study on the Amount of Total Body Water by Multi-Frequency Impedance Method

Hideki Taniguchi^{1,2}✉, Toshio Sasaki², Hisae Fujita²

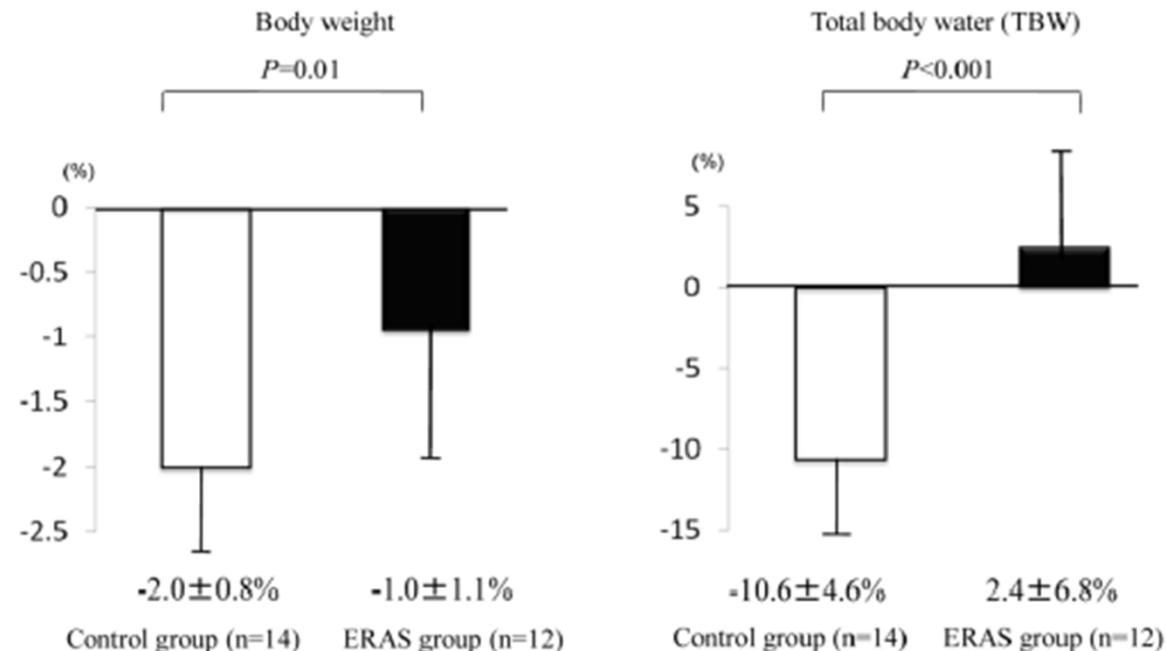
1. Department of Nutrition & Dietetics, Kanagawa University of Human Services, Yokosuka, Kanagawa 238-8522, Japan;

2. Department of Anesthesiology, Kanagawa Cancer Center, Yokohama 241-0815, Japan.

- 30 pts candidati a chirurgia gastrica per npl

- conventional care VS ERP

- BW e TBW POD -1 e 0



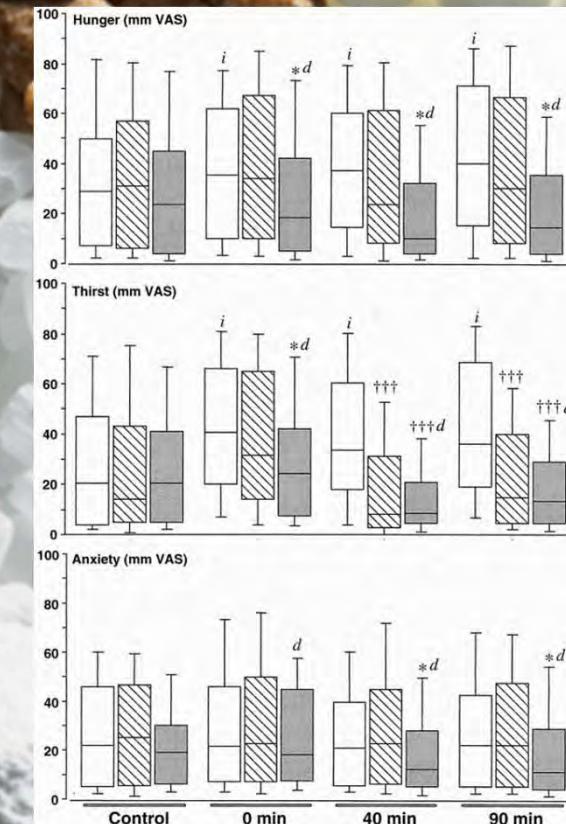
- L'utilizzo di liquidi chiari ad alta concentrazione di carboidrati complessi (maltodestrine) 2-3 ore prima dell'induzione porterebbe il paziente all'intervento in uno stato metabolicamente favorevole, con risvolti favorevoli su trofismo muscolare e controllo glicemico nel post-operatorio

Nygren J et al., *Preoperative gastric emptying. Effects of anxiety and oral carbohydrate administration*, 1995

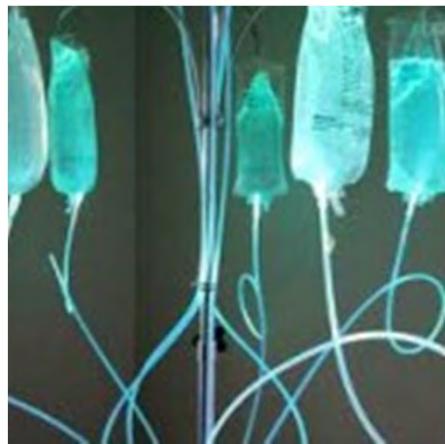
Nygren J et al., *Preoperative oral carbohydrate nutrition: an update*, 2001

Si raccomanda di acconsentire l'assunzione
di liquidi chiari fino a 2 h prima
dell'induzione e cibi solidi fino a 6 h prima.
Si consiglia la somministrazione routinaria
di carico orale di carboidrati preop.

European Society of
Anaesthesiology **ESA**

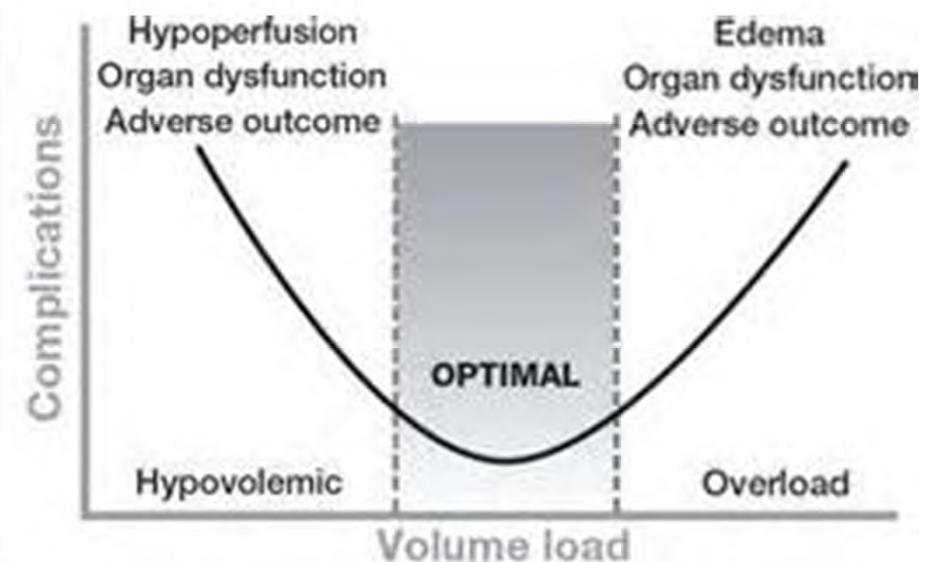
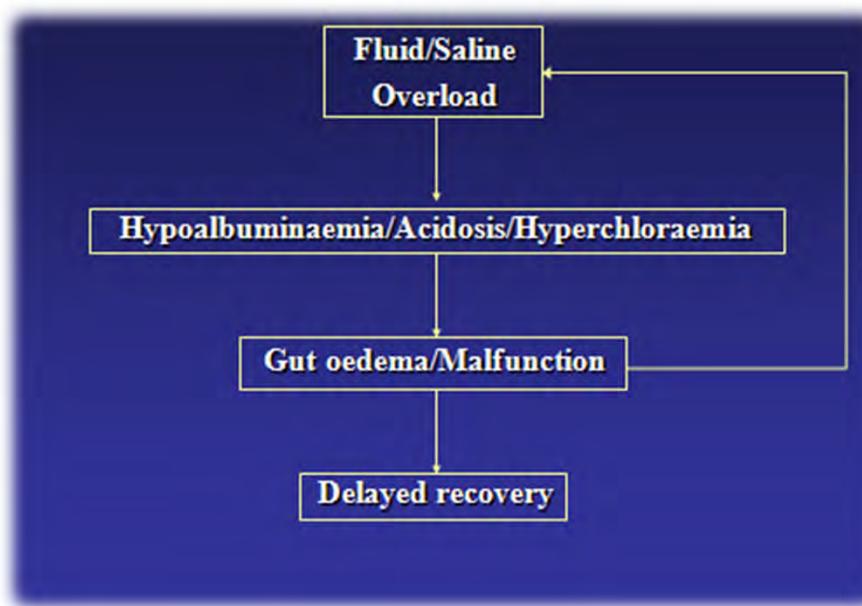


Hausel J et al., *A carbohydrate-rich drink reduces preoperative discomfort in elective surgery patients*. 2001



Goal-directed fluid therapy

L'approccio convenzionale raccomanda la sostituzione delle perdite idriche stimate, considerando anche il cosiddetto *terzo spazio*, con un incremento del peso corporeo nel post-operatorio di circa 3–6 kg!



Conference on ‘Malnutrition matters’

Symposium 3: Death by drowning A meta-analysis of randomised controlled trials of intravenous fluid therapy in major elective open abdominal surgery: getting the balance right

Krishna K. Varadhan and Dileep N. Lobo*

Division of Gastrointestinal Surgery, Nottingham Digestive Diseases Centre, NIHR Biomedical Research Unit,
Nottingham University Hospitals, Queen's Medical Centre, Nottingham NG7 2UH, UK

5 RCT
284 pts

↓ complicanze
↓ degenzza

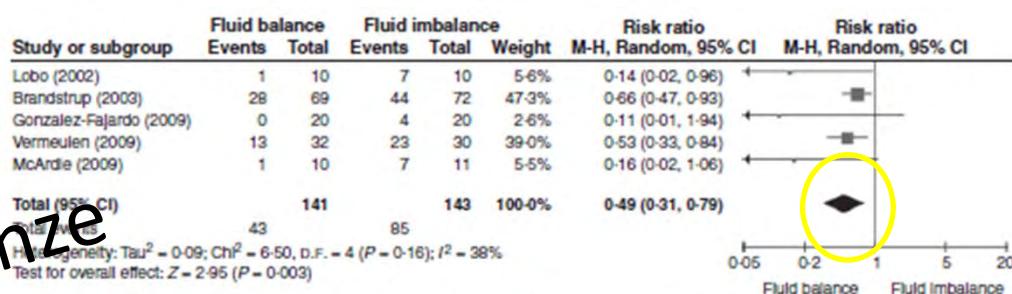


Fig. 7. Forest plot of comparison: complications using revised definitions of intervention groups (fluid balance v. fluid imbalance). Secondary analysis using five studies in which saline-based crystalloid therapy was used. (One study⁽³⁵⁾ in which both groups were in fluid balance was excluded.) M-H, Mantel-Haenszel test.

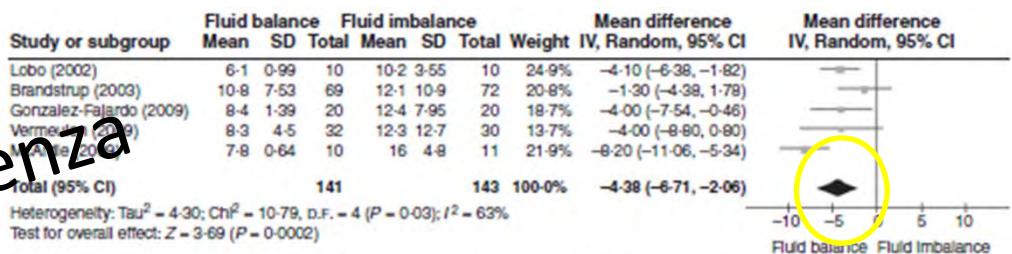


Fig. 8. Forest plot of comparison: length of hospital stay (d) using revised definitions of intervention groups (fluid balance v. fluid imbalance). Secondary analysis using five studies in which saline-based crystalloid therapy was used. (One study⁽³⁵⁾ in which both groups were in fluid balance was excluded.) IV, inverse variance.

Which goal for fluid therapy during colorectal surgery is followed by the best outcome: near-maximal stroke volume or zero fluid balance?

B. Brandstrup et al, Br J Anaesth., 2012

- double blind, ITT, 30 days of follow-up
- 150 pts undergoing elective colorectal surgery
- Near-maximal SV (esophageal doppler) **VS** zero balance

NO difference in
morbidity/LOS →

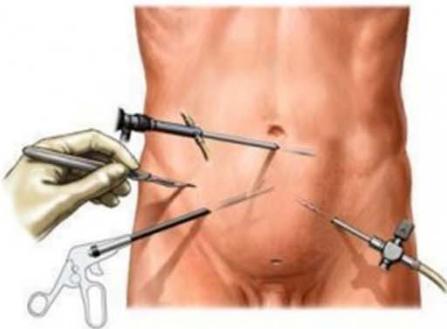
Goal-directed fluid therapy to near-maximal SV guided by ED adds no extra value to the fluid therapy using zero balance and normal BW in patients undergoing elective colorectal surgery.

Chirurgia laparoscopica/mini invasiva

- Nelle resezioni coliche laparoscopiche si osserva una riduzione del rischio di **complicanze** post-operatorie e della **degenza** media e un miglior controllo del **dolore**

Abraham NS, Young JM, Solomon MJ (2004) Meta-analysis of short-term outcomes after laparoscopic resection for colorectal cancer. Br J Surg 91(9):1111–1124

- E' stata inoltre osservata una minor prevalenza di **immunosoppressione** post-operatoria e conseguentemente miglior **outcome oncologico**



Veldkamp R, Kuhry E, Hop WC, Jeekel J, Kazemier G, Bonjer HJ et al (2005) Laparoscopic surgery versus open surgery for colon cancer: short-term outcomes of a randomised trial. Lancet Oncol 6(7):477–484

Vlug MS, Wind J, Hollmann MW, Ubbink DT, Cense HA, Engel AF et al (2011) Laparoscopy in combination with fast track multimodal management is the best perioperative strategy in patients undergoing colonic surgery: a randomized clinical trial (LAFA-study). Ann Surg 254(6):868–875

Laparoscopy in Combination with Fast Track Multimodal Management is the Best Perioperative Strategy in Patients Undergoing Colonic Surgery

A Randomized Clinical Trial (LAFA-study)

Malaika S. Vlug, MD, PhD,* Jan Wind, MD, PhD,* Markus W. Hollmann, MD, PhD, DEAA,†
Dirk T. Ubbink, MD, PhD,‡ Huib A. Cense, MD, PhD,§ Alexander F. Engel, MD, PhD,¶
Michael F. Gerhards, MD, PhD,** Bart A. van Wagensveld, MD, PhD,†† Edwin S. van der Zaag, MD,‡‡
Anna A.W. van Geloven, MD, PhD, §§ Mirjam A.G. Sprangers, PhD, ¶¶ Miguel A. Cuesta, MD, PhD,*** and
Willem A. Bemelman, MD, PhD,* on behalf of the collaborative LAFA study group

2011, Olanda, multicentrico

427 pts randomizzati.

	Laparoscopy and Fast Track (n = 100)	Open and Fast Track (n = 93)	Laparoscopy and Standard care (n = 109)	Open and Standard care (n = 98)	P
Total hospital stay, median (IQR), days	5 (4–8)	7 (5–11)	6 (4.5–9.5)	7 (6–13)	<0.001*†
Postoperative hospital stay, median (IQR), days	5 (4–7)	6 (4.5–10)	6 (4–8.5)	7 (6–10.5)	<0.001*‡
Overall morbidity < 30 days, No. (%)	34 (34.0)	43 (46.2)	37 (33.9)	41 (40.8)	0.20*

Degenza ospedaliera -2 gg

Nell'analisi di regressione, la laparoscopia rappresentava l'unico fattore predittivo di ridotta degenza e morbidità.

SNG

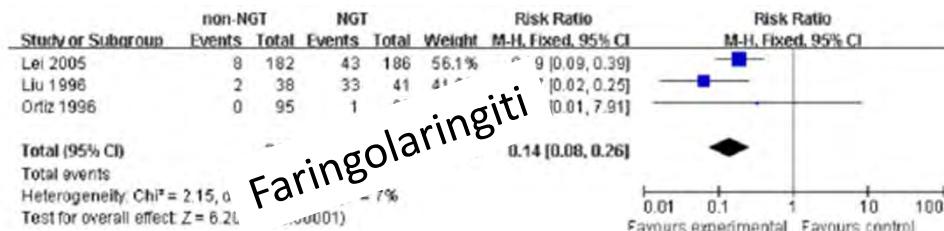
- Il posizionamento del SNG non modifica il rischio anestesiologico o di complicanze post-op

Bauer VP, *The Evidence against Prophylactic Nasogastric Intubation and Oral Restriction*, Clin Colon Rectal Surg, 2013

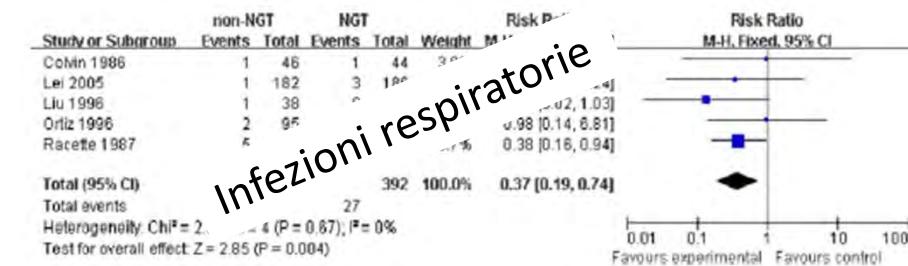


- E' stato osservato un incremento delle complicanze respiratorie conseguentemente al mantenimento del SNG nel periodo post-op

Wensheng R., *The role of nasogastric tube in decompression after elective colon and rectum surgery : a meta-analysis*, Int J Colorectal Dis, 2011



- La letteratura mostra una tendenza all'incremento della degenza e del discomfort nei pazienti con SNG



Rao W, Zhang X, Zhang J, Yan R, Hu Z, Wang Q (2011) *The role of nasogastric tube in decompression after elective colon and rectum surgery: a meta-analysis*. Int J Colorectal Dis 26(4):423-429

E' indicato l'utilizzo del SNG per prevenire il rischio di aspirazione conseguente alla ventilazione pre-IOT; si raccomanda di rimuovere il SNG prima del risveglio

CV



- L'utilizzo del CV ha lo scopo di monitorare l'output urinario nel perioperatorio:
 - La diuresi non sembra essere predittiva della funzionalità renale

Alpert RA et al., *Intraoperative urinary output[...]*, Surg, 1984

né di insufficienza renale acuta nel perioperatorio

Kheterpal S. et al., *Predictors of postoperative acute renal failure [...]*, Anesth, 2007

- ↑ IVU

Zaouter C, Kaneva P, Carli F (2009) Less urinary tract infection by earlier removal of bladder catheter in surgical patients receiving thoracic epidural analgesia. Reg Anesth Pain Med 34(6):542–548

- Analgesia peridurale e ritenzione urinaria

Basse L. et al, *Is urinary drainage necessary during continuous epidural analgesia after colonic resection?* Reg Anesth Pain Med. 2000

L'utilizzo routinario del CV e la sua rimozione tardiva sono sconsigliati in quanto non supportati dalle evidenze e associati a ridotta mobilizzazione del paziente.

Mobilizzazione

- La mobilizzazione forzata sembra associata a
 - ↓ tasso complicanze respiratore
 - Miglior compenso glicometabolico
 - Incremento della forza muscolare post-operatoria
- L'intolleranza alla mobilizzazione precoce correla con la scarsa compliance agli ERP e l'aumento della degenza ospedaliera.
- Smart NJ et al, Deviation and failure of enhanced recovery after surgery following laparoscopic colorectal surgery: early prediction model, Colorectal Disease, 2012
- *Early mobilisation* non incrementa il rischio di laparocele

Jargon D et al, *Risk factors and prevention of incisional hernia. What is evidence-based?*, 2008
Prevention of postoperative complications by adequate pain management, respiratory training and early mobilisation are procedures to **reduce the incidence of incisional hernias**.

Ripresa precoce dell'alimentazione per os



Il programma ERAS prevede di minimizzare il digiuno perioperatorio e favorire la normale alimentazione per bocca.

- ↓ rischio complicanze settiche
- ↓ degenza ospedaliera
- Non incremento delle deiscenze anastomotiche
- ↑ nausea e vomito post-op

Original Article

Fast-track improves post-operative nutrition and outcomes of colorectal surgery: a single-center prospective trial in China

Ka Li BSc¹, Ji-Ping Li BSc², Nan-hai Peng BSc³, Li-li Jiang BSc¹, Yan-Jie Hu MD², Ming-Jun Huang MD¹

¹Department of Gastrointestinal Surgery, West China Hospital, Sichuan University, Chengdu, Sichuan, China

²Nursing Faculty of West China, Sichuan University, Chengdu, Sichuan, China

³Research Institute of General Surgery, Nanjing General Hospital of Nanjing Military Command, PLA, Nanjing, Jiangsu, China

加速康复外科改善结直肠癌患者术后营养状态及临床效果：中国的一项单中心、前瞻性研究

研究证明加速康复外科能够促进手术患者康复。本研究的目的是比较加速康复外科流程与传统流程下的营养支持对患者术后康复的影响，同时探究加速康复外科流程在结直肠手术患者营养支持方案中的临床适用性。本研究前瞻性地纳入 464 例结直肠癌手术患者，随机分为加速康复外科流程组(FT 组)和传统流程组。终点指标为 NRS2002，术后康复指标，术后并发症。FT 组 NRS2002 评分低于传统流程组($p<0.05$)；FT 组血红蛋白，白蛋白，白球比及淋巴细胞比率、IgA、CD4+等指标在术后第 5 天均优于传统流程组($p<0.05$)；FT 组首次排气、排便、经口进食及下床活动时间短于传统流程组($p<0.05$)；FT 组的并发症发生率低于传统流程组($p<0.05$)；传统流程组的吻合口瘘发生率高于 FT 组(2.8% 比上 0.5%， $p<0.05$)。综上所述，本研究表明加速康复外科能够改善结直肠癌术后患者的营养状态及临床效果。

关键词：加速康复外科、营养、术后、结直肠癌、前瞻性

464 pts candidate to colorectal surgery
RCT

	Fast track group (n=208)		Tradition group (n=237)	
	Pre-operative day 1	Post-operative day 5	Pre-operative day 1	Post-operative day 5
Nutrition indicators				
HGB (g/L)	136±11.3	133±15.7*	135±13.6	125±14.9
TP (g/L)	65.4±5.03	66.2±5.29	64.9±4.38	62.0±5.31
ALB (g/L)	43.1±5.87	41.2±5.52*	42.7±5.09	36.1±4.41
PA (mg/L)	151±48.9	227±58.4*	153±50.3	155±50.2
A/G	1.65±0.32	1.55±0.27*	1.69±0.50	1.38±0.21
Immune function indicators				
Lymphocyte rate (LYMPH%)	32.4±6.87	31.5±7.70*	31.7±7.93	20.3±6.38
IgA	2.12±0.73	2.97±0.79*	2.27±0.88	2.03±0.98
IgM	1.54±0.48	1.81±0.68	1.61±0.55	1.51±0.58
CD4+ (%)	45.3±6.76	46.1±7.16*	44.9±7.22	39.2±5.38
CD8+ (%)	29.4±6.87	31.0±5.94	28.4±6.54	31.6±6.24

Note: HGB-Haemoglobin; TP-TotalProtein; ALB-Albumin; PA-pre-albumin; A/G: Albumin/ Globulin; IgA-Immunoglobulin A; IgM-Immunoglobulin M.

* p<0.05 compared to Tradition group.

	Fast track group (n=208)	Tradition group (n=237)	p
Complications post-operation			
Yes	18 (8.7)	47 (19.8)	0.001 ↙
No	190 (91.3)	190 (80.2)	
Anastomotic bleeding, n (%)	2 (1.0)	7 (3.0)	0.184
Anastomotic leakage, n (%)	1 (0.5)	9 (2.8)	0.023 ↙
Wound infection, n (%)	5 (2.4)	10 (4.2)	0.290
Pulmonary infection, n (%)	1 (0.5)	5 (2.1)	0.222
Intestinal obstruction, n (%)	1 (0.5)	7 (3.0)	0.072
Urinary retention, n (%)	8 (3.8)	9 (3.8)	0.979
Mortality, n (%)	0 (0)	0 (0)	/

- Non è giustificato prostrarre il digiuno post-operatorio per prevenire il rischio di deiscenze anastomotiche
- La supplementazione nutrizionale per bocca (ONS) introdotta il giorno prima dell'intervento e proseguita almeno fino alla 4° giornata post-operatoria ottimizza l'apporto calorico giornaliero

Smedley F, Bowling T, James M, Stokes E, Goodger C, O'Connor O et al (2004) Randomized clinical trial of the effects of preoperative and postoperative oral nutritional supplements on clinical course and cost of care. Br J Surg 91(8):983–990

Drenaggi

PROs

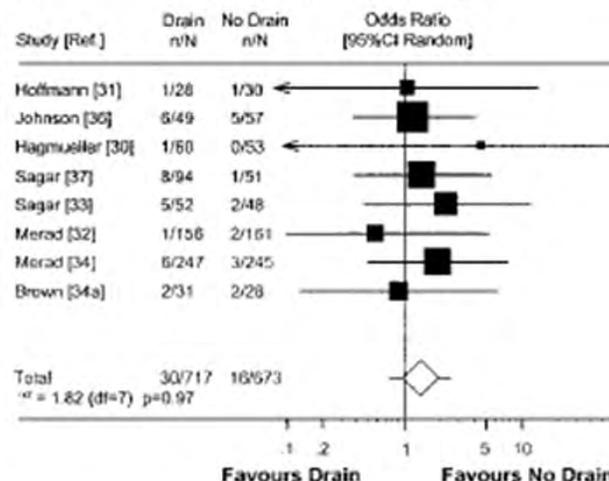
Liquido addominale → raccolto
→ deiscenza anastomotica

Identificazione precoce di leak

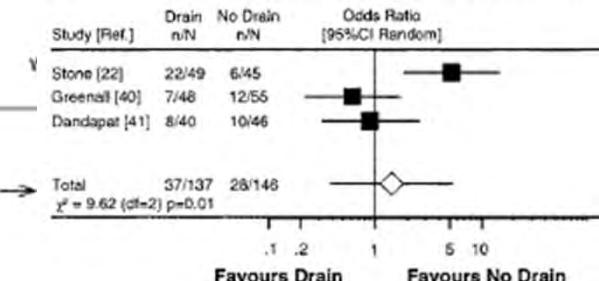
Terapia conservativa fistole po-

CONs

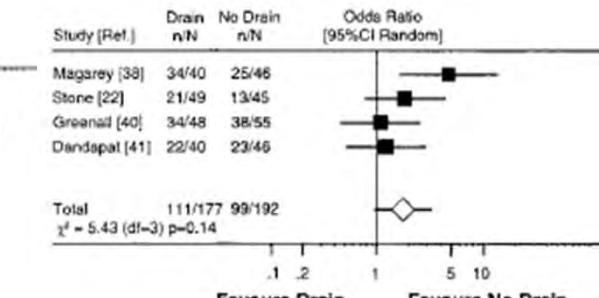
A Endpoint Clinical Leakage



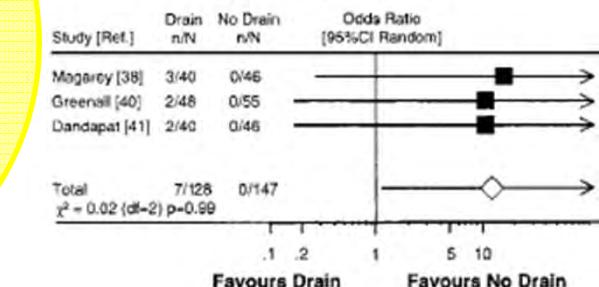
A Endpoint Intra-abdominal Infections



B Endpoint Wound Infections



C Endpoint Fecal Fistulas



Meta-analisi

Petrowsky H et al., *Evidence-based value of prophylactic drainage in gastrointestinal surgery: a systematic review and meta-analyses*, Ann. Surg, 2004

- Nessun impatto su
 - Deiscenze anastomotiche,
 - Infezione di ferita
 - Reintervento
 - Complicanze extra-addominali

La consuetudine a posizionare drenaggi addominali dovrebbe essere dismessa, in quanto non supportata dalla letteratura e associata a ridotta mobilizzazione.

A Randomized Prospective Multicenter Trial of Pancreaticoduodenectomy With and Without Routine Intraperitoneal Drainage

George Van Buren II, MD, Mark Bloomston, MD,† Steven J. Hughes, MD,‡ Jordan Winter, MD,§ Stephen W. Behrman, MD,¶ Nicholas J. Zyromski, MD,|| Charles Vollmer, MD,** Vic Velanovich, MD,†† Taylor Riall, MD,‡‡ Peter Muscarella, MD,† Jose Trevino, MD,‡ Attila Nakeeb, MD,|| C. Max Schmidt, MD,|| Kevin Behrns, MD,‡ E. Christopher Ellison, MD,† Omar Barakat, MD,* Kyle A. Perry, MD,† Jeffrey Dreibin, MD,† Michael House, MD,† Sherif Abdel-Misih, MD,† Eric J. Silberfein, MD,* Steven Goldin, MD,†† Kimberly Brown, MD,‡‡ Somalia Mohammed, MD,* Sally E. Hodges, BS,* Amy McElhany, MPH,* Mehdi Issazadeh, BS,* Eunji Jo, MS,* Qianxing Mo, PhD,* and William E. Fisher, MD**

Objective: To test by randomized prospective multicenter trial the hypothesis that pancreaticoduodenectomy (PD) without the use of intraperitoneal drainage does not increase the frequency or severity of complications.

Background: Some surgeons have abandoned the use of drains placed during pancreas resection.

Methods: We randomized 137 patients to PD with ($n = 68$, drain group) and without ($n = 69$, no-drain group) the use of intraperitoneal drainage and compared the safety of this approach and spectrum of complications between the 2 groups.

Results: There were no differences between drain and no-drain cohorts in demographics, comorbidities, pathology, pancreatic duct size, pancreas texture, baseline quality of life, or operative technique. PD without intraperitoneal drainage was associated with an increase in the number of complications per patient [1 (0-2) vs 2 (1-4), $P = 0.029$]; an increase in the number of patients who had at least 1 \geq grade 2 complication [35 (52%) vs 47 (68%), $P = 0.047$]; and a higher average complication severity [2 (0-2) vs 2 (1-3), $P = 0.027$]. PD without intraperitoneal drainage was associated with a higher incidence of gastroparesis, intra-abdominal fluid collection, intra-abdominal abscess (10% vs 25%, $P = 0.027$), severe (\geq grade 2) diarrhea, need for a postoperative percutaneous drain, and a prolonged length of stay. The Data Safety Monitoring Board stopped the study early because of an increase in mortality from 3% to 12% in the patients undergoing PD without intraperitoneal drainage.

Conclusions: This study provides level I data, suggesting that elimination of intraperitoneal drainage in all cases of PD increases the frequency and severity of complications.

Keywords: drain, multicenter, pancreaticoduodenectomy, randomized, Whipple

(*Ann Surg* 2014;259:605-612)

Advances in operative technique and perioperative management have reduced the mortality for pancreaticoduodenectomy (PD) to 3%. However, the morbidity of the procedure remains high and pancreatic fistula continues to be a common complication.¹ An unrecognized, and untreated, pancreatic fistula can lead to increased morbidity and mortality after PD. Routine placement of intraperitoneal drains after PD has traditionally been considered mandatory. The rationale behind placement of these drains is to evacuate blood, bile, pancreatic juice, or chyle that may accumulate after surgery and to serve as an early warning sign of anastomotic leak and associated hemorrhage. Pancreatic fistula is thought to contribute to the most morbid complications of the operation such as erosion of retroperitoneal vessels and hemorrhage, intra-abdominal abscess, sepsis, multisystem organ failure, and death.

Although the use of drains has proven to be unnecessary or even deleterious in other operations such as splenectomy, hepatectomy, gastrectomy, and colorectal resection, many surgeons fear that abandoning routine intraperitoneal drainage after PD may not be safe.² However, the majority of patients do not develop a postoperative pancreatic fistula; furthermore, the experience with drains in other operations suggests that drains may do more harm than good. Common concerns, which may be unfounded, are that drains can serve as portal of entry for bacteria; this may change a benign postoperative fluid collection into an abscess. Concerns also exist that drains may cause trauma from suction and can potentially erode into anastomoses and cause a fistula. Because most patients do not develop a pancreatic fistula, routine intraperitoneal drainage may subject many patients to the potential drain-related morbidities with potentially no benefit. With significant improvements in abdominal imaging and image-guided drain placement, a growing number of pancreatic surgeons have abandoned the routine use of drains arguing that a drain can be placed postoperatively in the minority of patients who require drainage.

The safety of this approach has been suggested recently in retrospective cohort studies and 1 single-institution randomized controlled trial.³⁻⁹ The objective of this multicenter randomized

From the *Baylor College of Medicine, The Elkins Pancreas Center, Michael E. DeBakey Department of Surgery, and The Dan L. Duncan Cancer Center, Houston, TX; †Department of Surgery, The Ohio State University, Columbus, OH; ‡Department of Surgery, University of Florida, Gainesville, FL; §Department of Surgery, Jefferson Medical College, Philadelphia, PA; ¶Department of Surgery, Baptist Memorial Hospital/The University of Tennessee Health Science Center, Memphis, TN; ||Department of Surgery, Indiana University, Indianapolis, IN; **Department of Surgery, University of Pennsylvania, Philadelphia, PA; ‡‡Department of Surgery, University of South Florida, Tampa, FL; and ††Department of Surgery, The University of Texas Medical Branch, Galveston, TX.

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Reprints: William E. Fisher, MD, The Elkins Pancreas Center, Michael E. DeBakey Department of Surgery, Baylor College of Medicine, 6620 Main St, Ste 1450, Houston, TX 77030. E-mail: wfisher@bcm.edu.

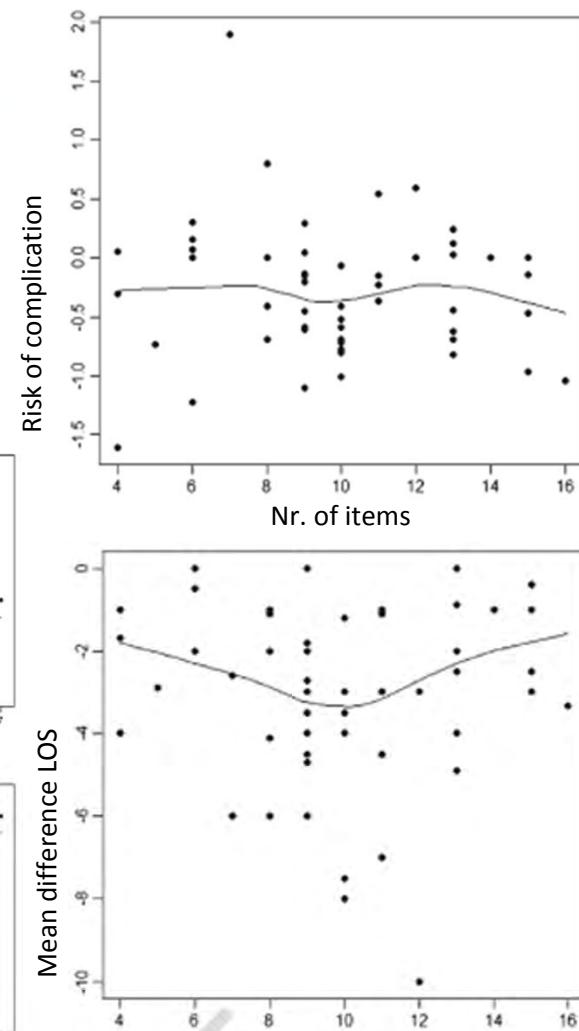
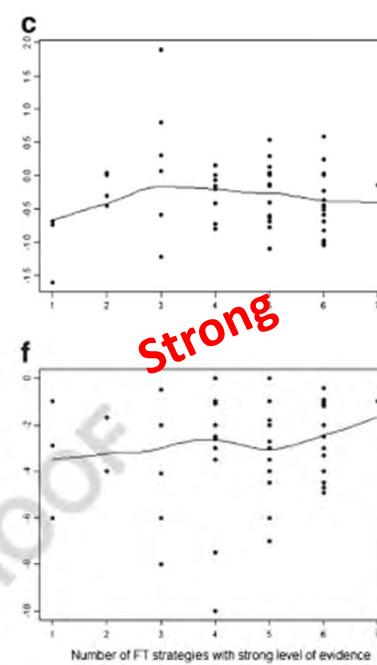
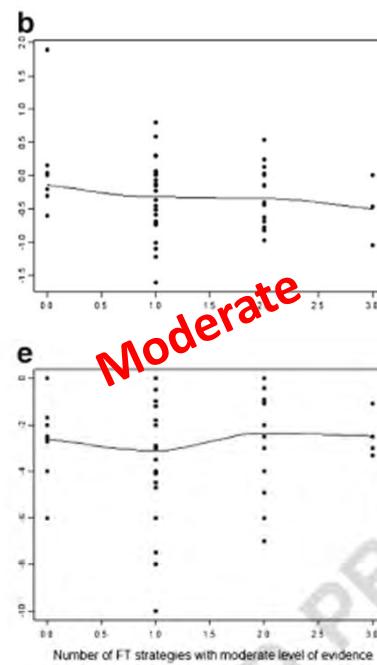
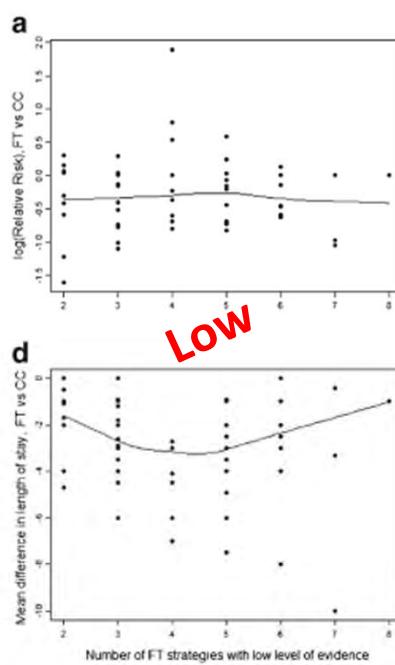
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ERAS...quali e quanti

**Enhanced recovery strategies in colorectal surgery:
is the compliance with the whole program required
to achieve the target?**

Luca Gianotti · Simone Beretta · Margherita Luperto ·
Davide Bernasconi · Maria Grazia Valsecchi ·
Marco Braga

Metanalisi, 53 RCT/nRCT



Low

Moderate

Strong

A Systematic Review of Economic Evaluations of Enhanced Recovery Pathways for Colorectal Surgery

Lawrence Lee, MD, MSc,* Chao Li, MD, MSc,* Tara Landry, MLIS,† Eric Latimer, PhD,‡§ Franco Carli, MD, Gerald M. Fried, MD,* and Liane S. Feldman, MD*

Annals of Surgery, aprile 2014

- 10 articoli
- CHEC (Consensus of Health Economic Criteria) per la valutazione dei costi

ERP nella chirurgia elettiva colorettale riduce la durata della degenza ospedaliera e conseguentemente la spesa sanitaria

For most patients, the costs directly attributable to the last day of a hospital stay are an economically insignificant component of total costs. Reducing LOS by as much as 1 full day reduces the total cost of care on average by 3% or less. Going forward, physicians and administrators must deemphasize LOS and focus instead on process changes that better use capacity and alter care delivery during the early stages of admission, when resource consumption is most intense.

ERAS PROGRAMMES REDUCE HOSPITAL COSTS BUT DO NOT INCREASE COMMUNITY COSTS

C. Jones, L. Kelliher, E. Mathers, T. Husain, M. Dickinson, M. Scott, N. Quiney
Anaesthesia, ROYAL SURREY COUNTY HOSPITAL NHS FOUNDATION TRUST, Guildford, United Kingdom

Length of stay has minimal impact on the cost of hospital admission.

Taheri PA et al, J Am Coll. Surg., 2000

RCT, single blind
91 pts EE versus CC
Follow-up to POD 28

- ↓ hospital costs
- No ↑ primary health care services
- No ↑ readmission rate

Pittfalls...

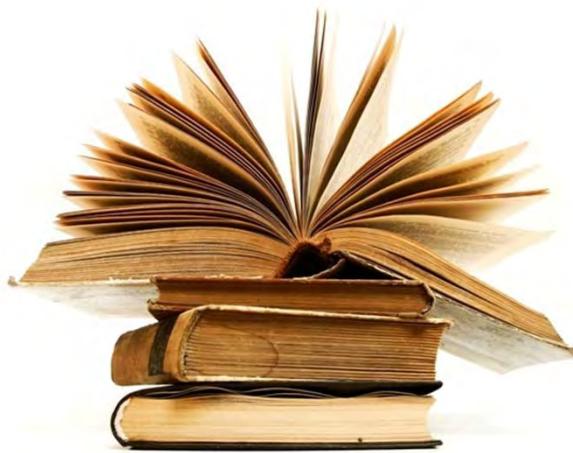
- Molti items



- Team



- Risorse



- Cultura