

STUDIE COINN

MUDr. Ondřej Hrdý
KARIM FN Brno

CONFLICT OF INTEREST

OBSAH

- kritické onemocnění
- svalový metabolismus ve stresu
- studie srovnávající podávání EV
- guidelines
- KARIM FN Brno
- studie COINN

Czech Republic – heart of Europe



FÁZE KRITICKÉHO ONEMOCNĚNÍ

CLINICAL
NUTRITION

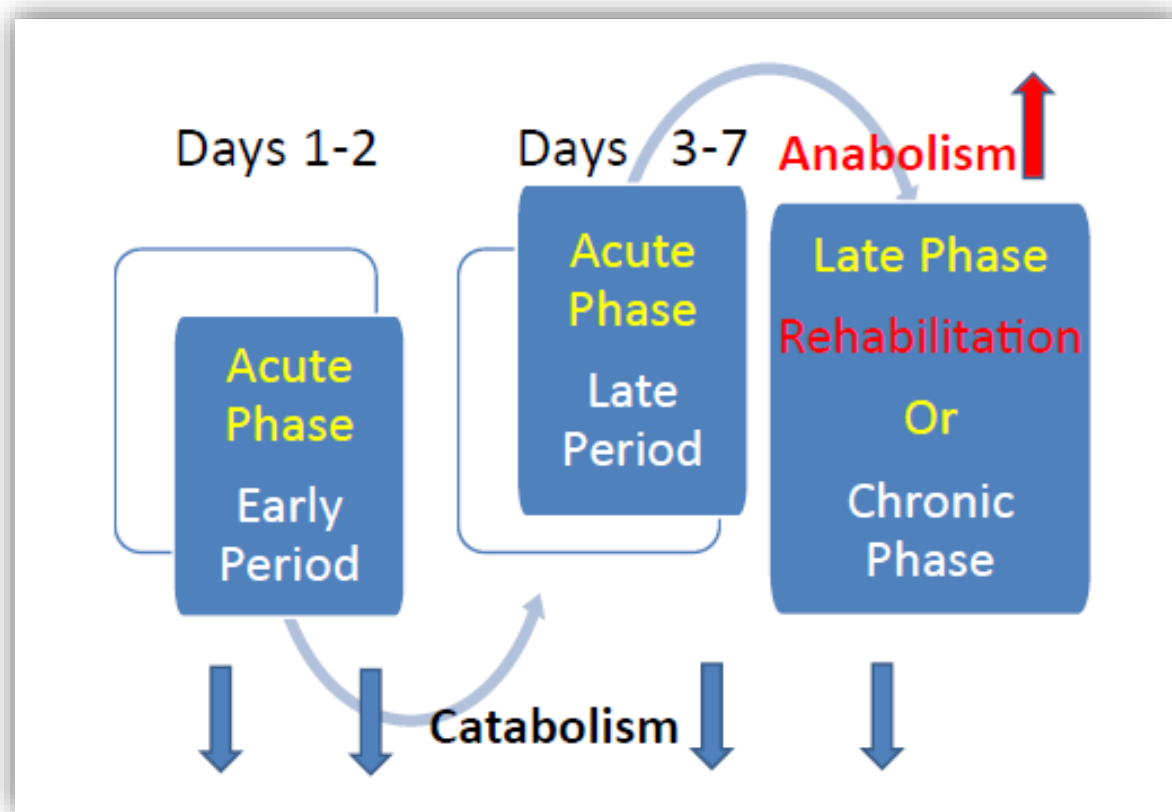
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February 2019 Volume 38, Issue 1, Pages 48–79

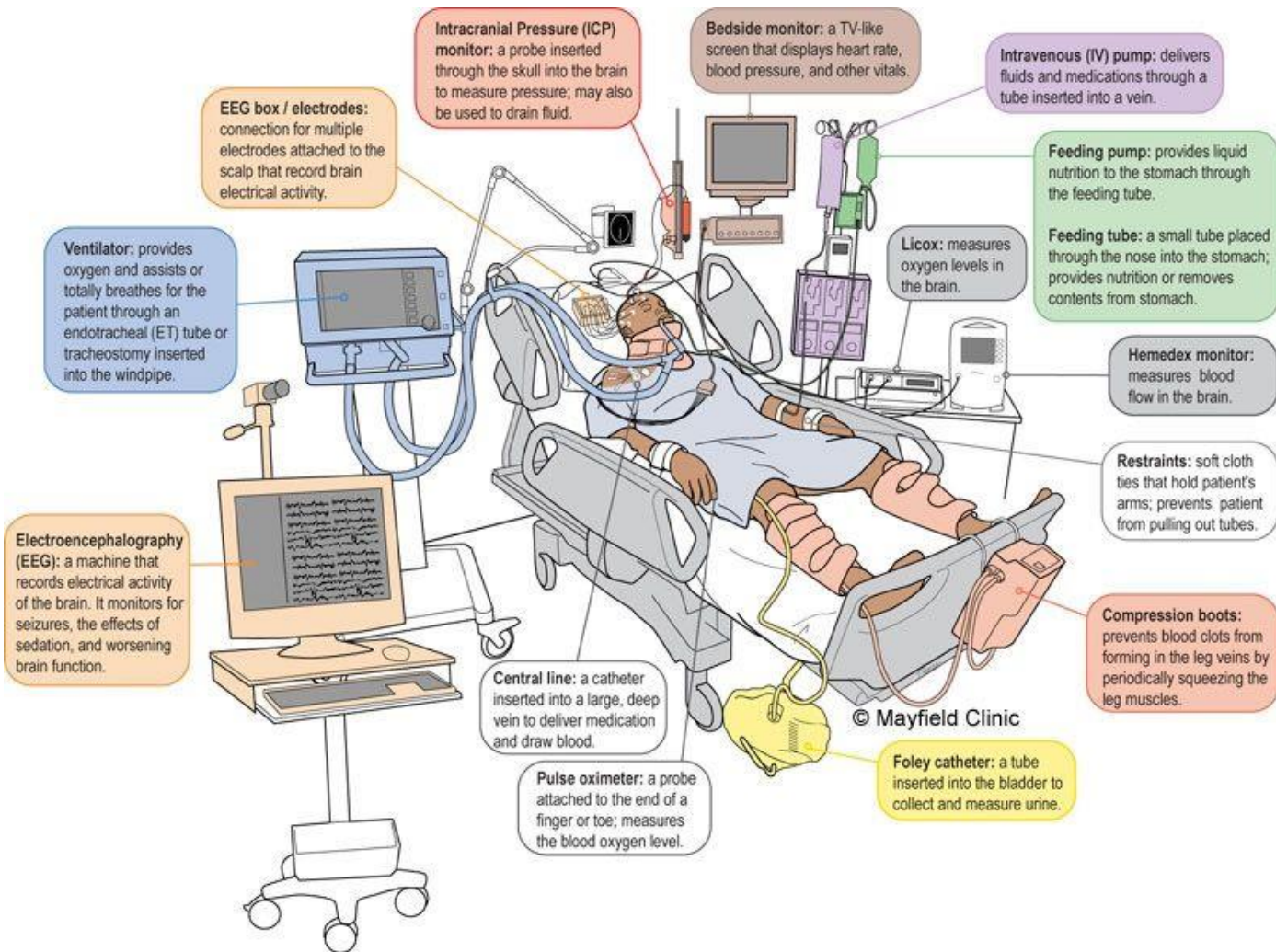
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ESPEN guideline on clinical nutrition in the intensive care unit

Pierre Singer^{a,*}, Annika Reintam Blaser^{a,c}, Mette M. Berger^a, Waleed Alhazzani^a, Philip C. Calder^a, Michael P. Casaer^a, Michael Hiesmayr^a, Konstantin Mayer^a, Juan Carlos Montejo^a, Claude Pichard^a, Jean-Charles Preiser^a, Arthur R.H. van Zanten^a, Simon Oczkowski^a, Wojciech Szczeklik^a, Stephan C. Bischoff^a



KRITICKÉ STAVY



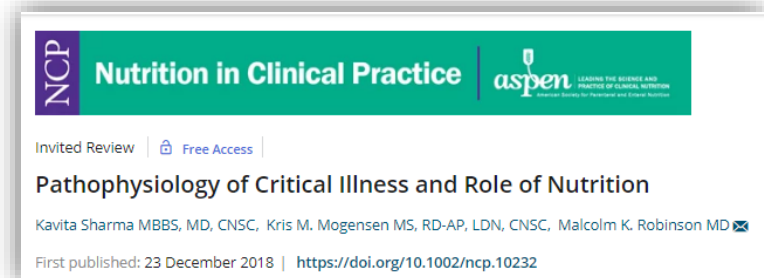
ROLE MALNUTIRCE



- 1/3 hospitalizovaných
- 1/3 bez MN získá za hospitalizace
- na JIP výskyt až $\frac{3}{4}$
- vyšší riziko infekčních komplikací
- vyšší četnost rehospitalizací
- vyšší mortalita

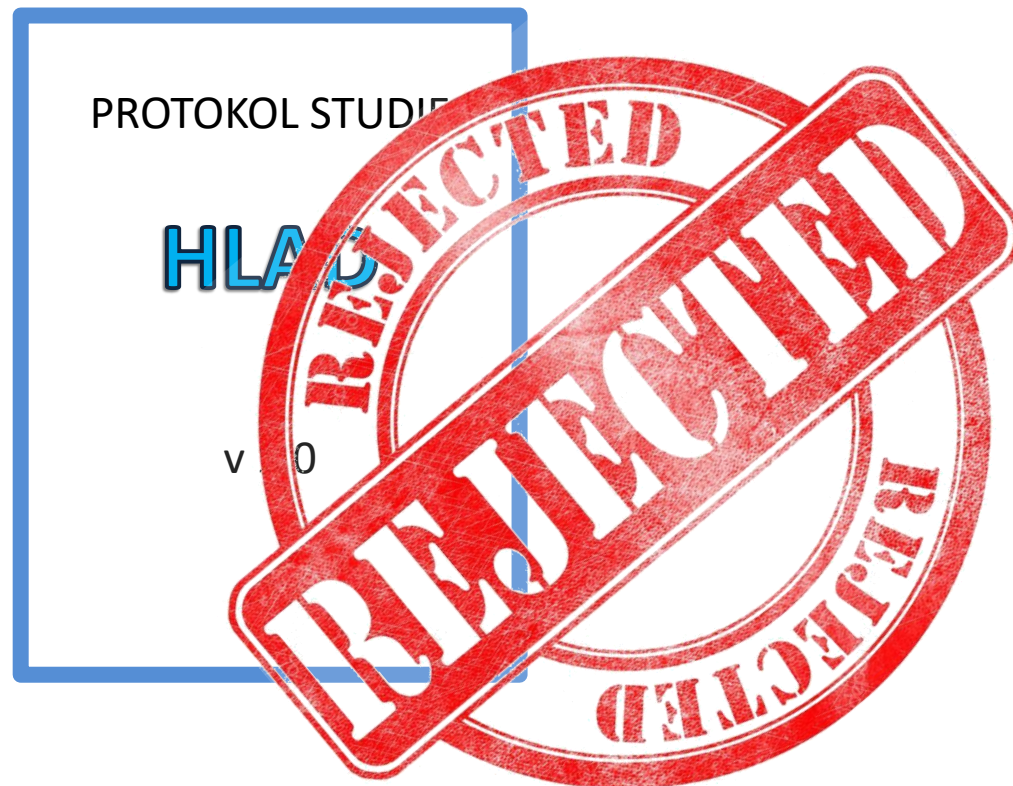
ROLE VÝŽIVY

- modulace inflamatorní odpovědi
- udržení imunitních funkcí
- zpomalení svalového katabolismu
- zlepšení hojení
- udržení integrity sliznice gastrointestinálního traktu
- korekce preexistující malnutrice



ZAHÁJIT NUTRIČNÍ INTERVENCI?

- nejsou studie zabývající se vlivem délky hladovění v kritickém stavu.....a nebudou



ČASNÁ vs. POZDNÍ EV

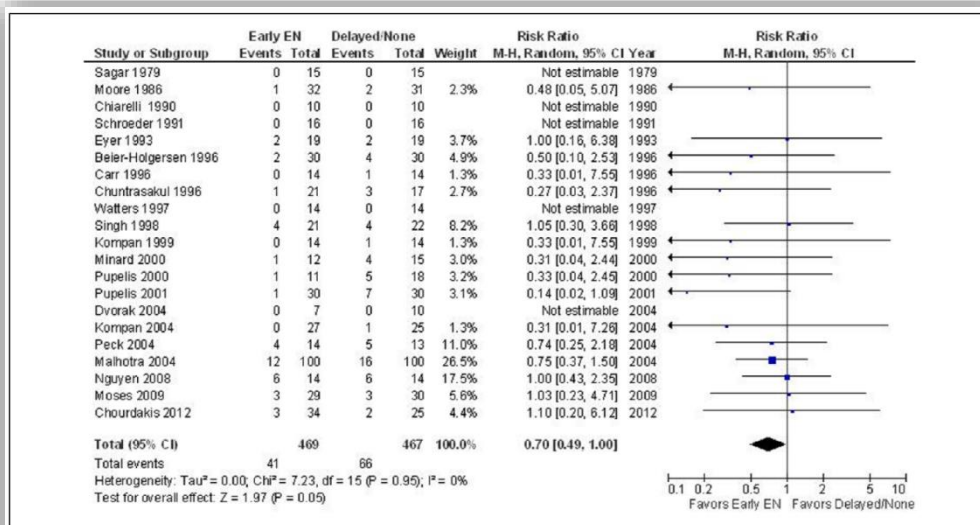


Figure 1. Early enteral nutrition (EN) vs delayed EN, mortality.

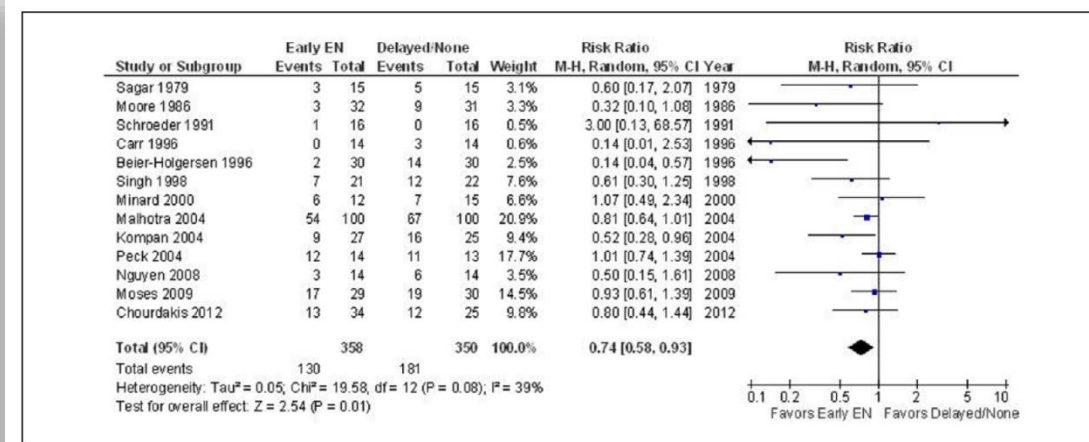
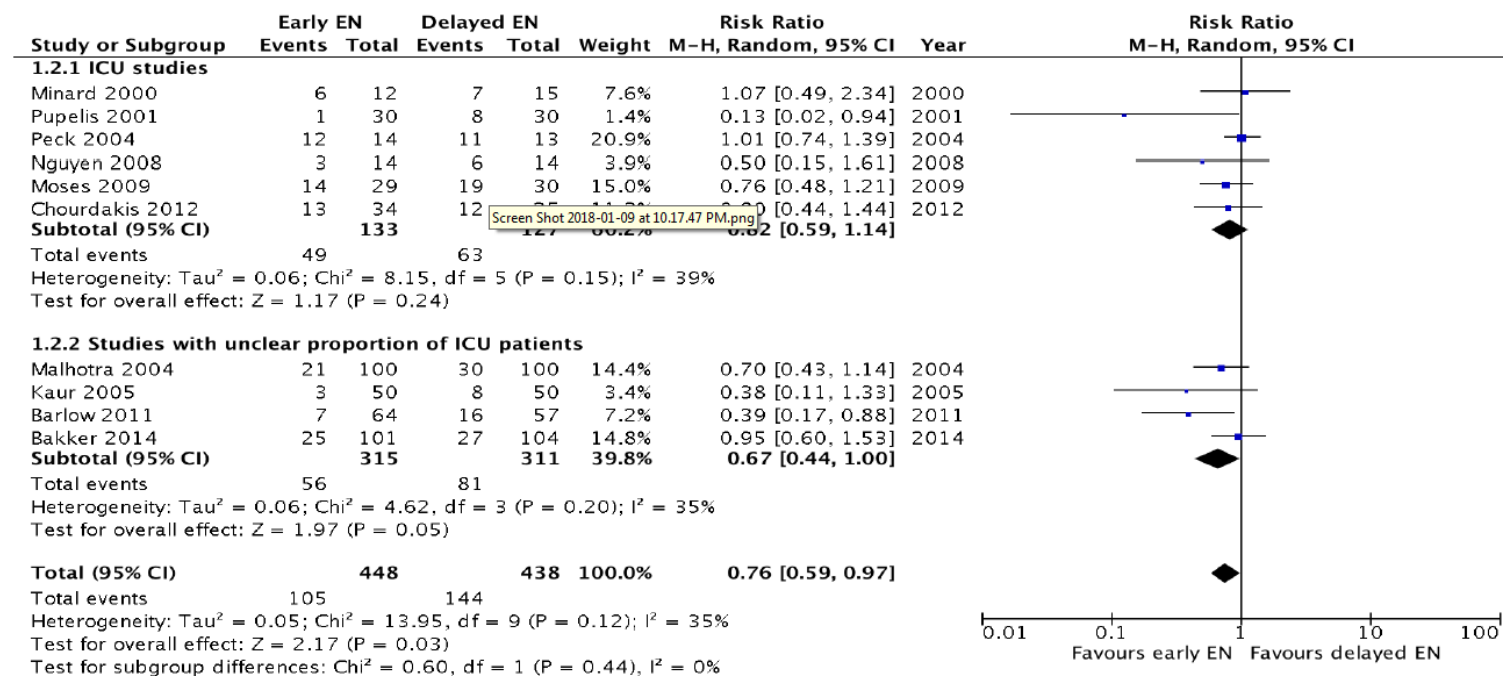


Figure 2. Early enteral nutrition (EN) vs delayed EN, infectious complications.

ČASNÁ vs. POZDNÍ EV

I., Figure 2: Infectious Complications (Includes Meta-analyses I A and I B)

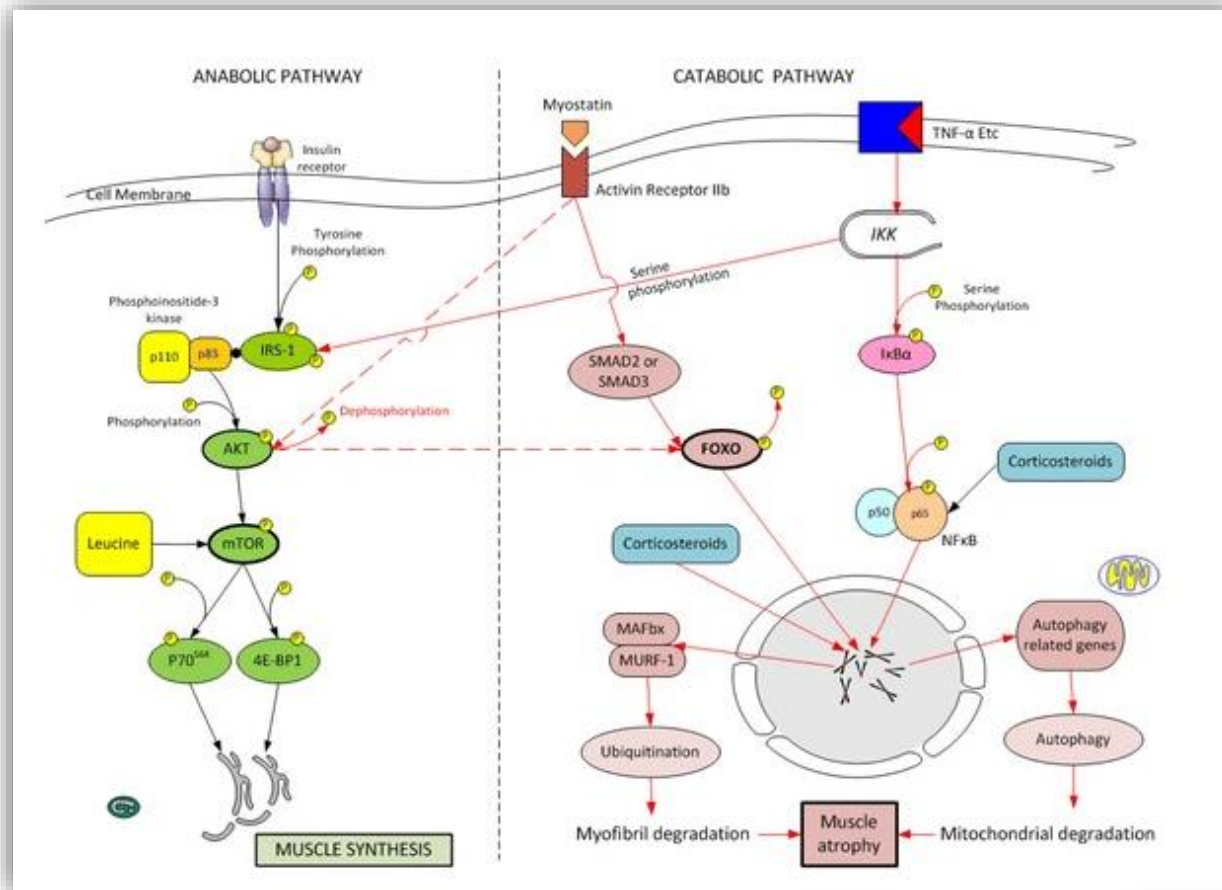


ZTRÁTA SVALOVÉ HMOTY

- ztráta svalové hmoty je běžná
- výsledná myopatie vede k funkčnímu postižení
- přetrvává dlouho po propuštění z ICU
- Rizikové faktory:
 - zánět
 - sepse
 - imobilizace
 - sedace
 - svalová relaxancia



Svalový anabolismus/katabolismus



Feeding critically ill patients the right 'whey': thinking outside of the box. A personal view

Paul E Marik

Annals of Intensive Care 2015 5:11

<https://doi.org/10.1186/s13613-015-0051-2> © Marik. 2015

Received: 3 March 2015 | Accepted: 15 May 2015 | Published: 28 May 2015

Efekt AMK na proteosyntézu

Suryawan et al. *Journal of Animal Science and Biotechnology* 2012, 3:3
http://www.jasbsci.com/content/3/1/3



JOURNAL OF ANIMAL SCIENCE
AND BIOTECHNOLOGY

RESEARCH

Open Access

Differential regulation of protein synthesis in skeletal muscle and liver of neonatal pigs by leucine through an mTORC1-dependent pathway

Agus Suryawan, Hanh V. Nguyen, Rosemarie D. Almonaci and Teresa A. Davis*



AMERICAN JOURNAL of PHYSIOLOGY

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ARTICLES

Insulin and amino acids independently stimulate skeletal muscle protein synthesis in neonatal pigs

Pamela M. J. O'Connor, Jill A. Bush, Agus Suryawan, Hanh V. Nguyen, and Teresa A. Davis
01 JAN 2003 // <https://doi.org/10.1152/ajpendo.00326.2002>

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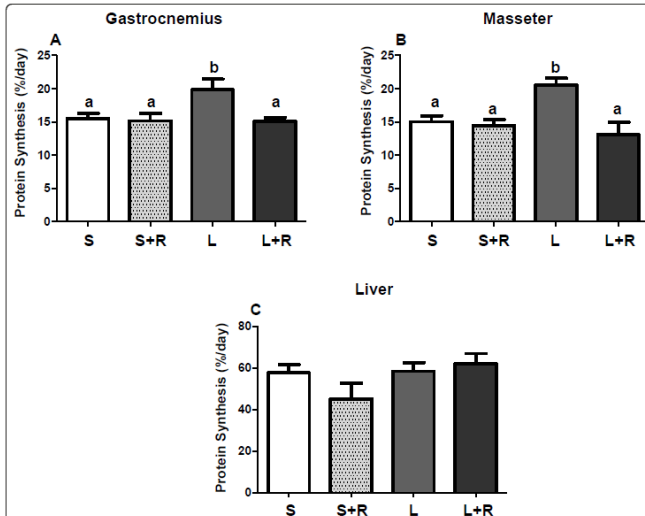
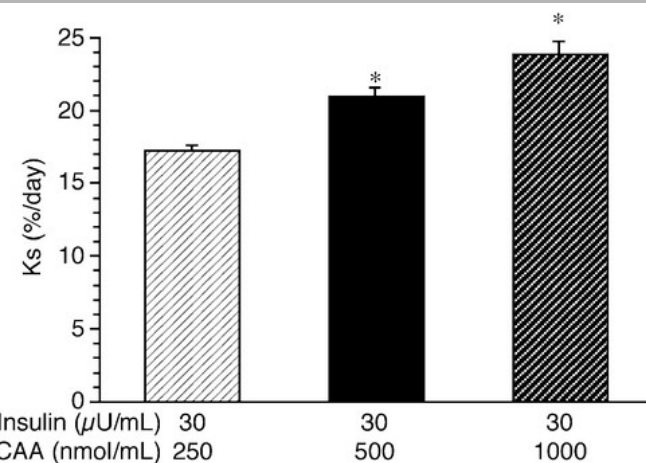
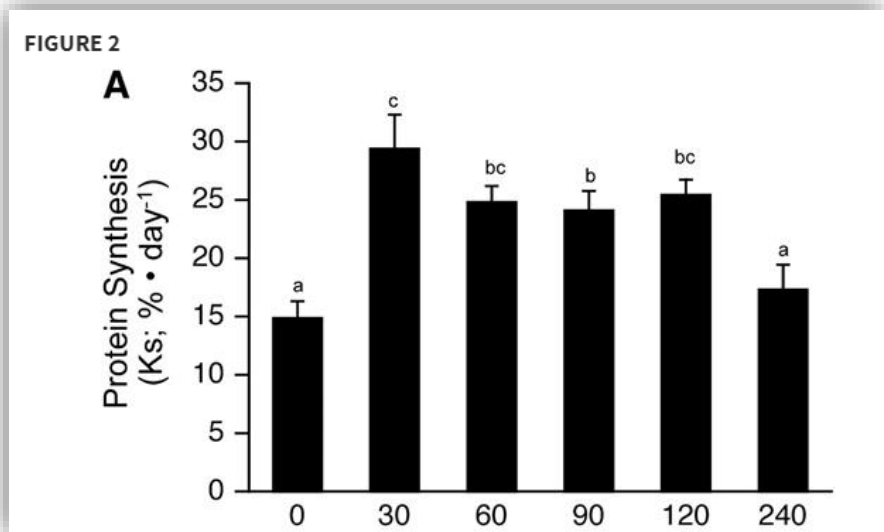
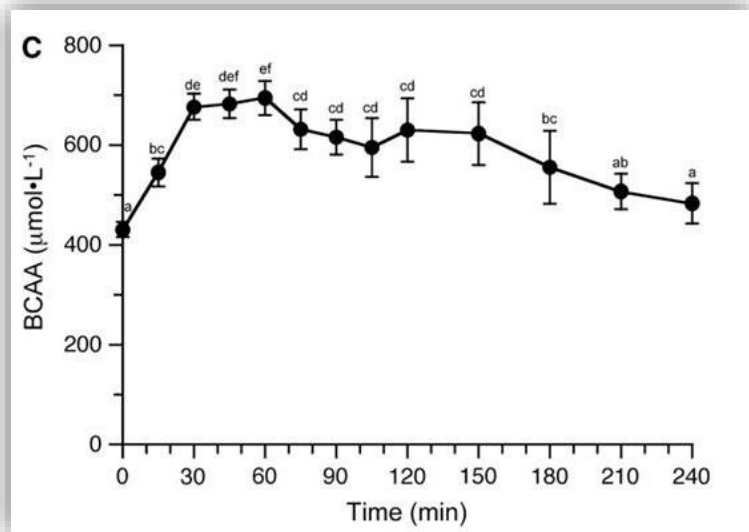


Figure 1 Fractional rates of protein synthesis in gastrocnemius muscle (A), masseter muscle (B) and liver (C) of 7-day-old pigs after 60 minutes of infusion of saline (Sal), saline with rapamycin (Sal+Rap), 400 $\mu\text{mol}\cdot\text{kg}^{-1}\cdot\text{h}^{-1}$ leucine without rapamycin (Leu), or 400 $\mu\text{mol}\cdot\text{kg}^{-1}\cdot\text{h}^{-1}$ leucine with rapamycin (Leu+Rap). Values are means $\pm$ pooled SE; $n = 5-7$ per treatment. Values with different superscripts differ significantly ($P < 0.05$).



Postprandiální proteosyntéza



Bolus vs. kont. a proteosyntéza

JN THE JOURNAL OF NUTRITION

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J Nutr. 2011 Dec; 141(12): 2152–2158.

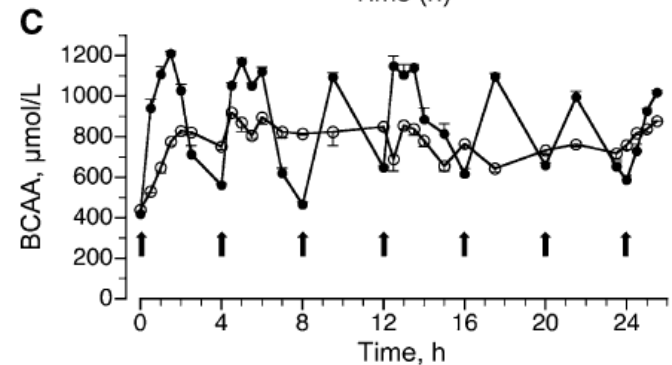
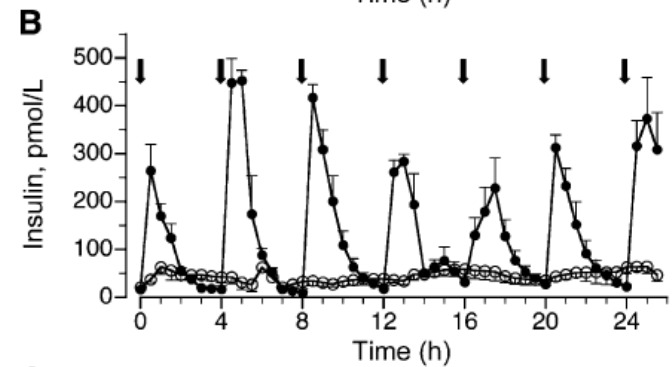
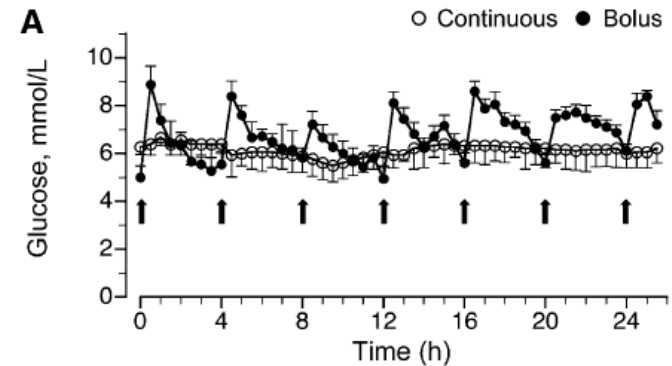
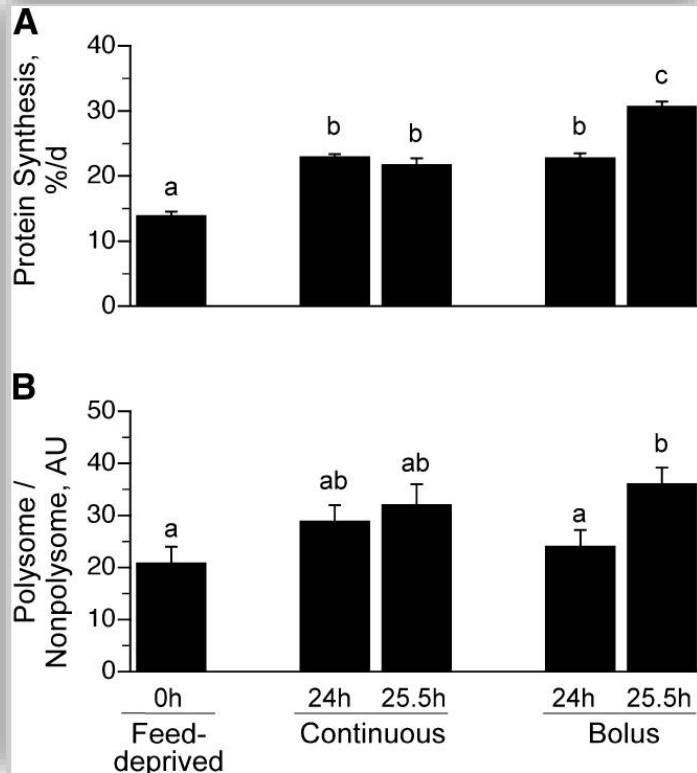
PMCID: PMC3223872

Published online 2011 Oct 19. doi: [10.3945/jn.111.147520](https://doi.org/10.3945/jn.111.147520)

PMID: [22013195](https://pubmed.ncbi.nlm.nih.gov/22013195/)

Intermittent Bolus Feeding Has a Greater Stimulatory Effect on Protein Synthesis in Skeletal Muscle Than Continuous Feeding in Neonatal Pigs^{1,2}

[Maria C. Gazzaneo](#)³, [Agus Suryawan](#)³, [Renán A. Orellana](#)³, [Roberto Murgas Torrazza](#)^{3,5}, [Samer W. El-Kadi](#)³, [Fiona A. Wilson](#)^{3,6}, [Scot R. Kimball](#)⁴, [Neeraj Srivastava](#)³, [Hanh V. Nguyen](#)³, [Marta L. Fiorotto](#)³ and [Teresa A. Davis](#)^{3,*}



Studie na lidech

Rapid Report

Latency and duration of stimulation of human muscle protein synthesis during continuous infusion of amino acids

Julien Bohé, J. F. Ailli Low, Robert R. Wolfe, Michael J. Rennie

First published: 05 August 2004 | <https://doi.org/10.1111/j.1469-7793.2001.0575f.x> | Cited by: 228

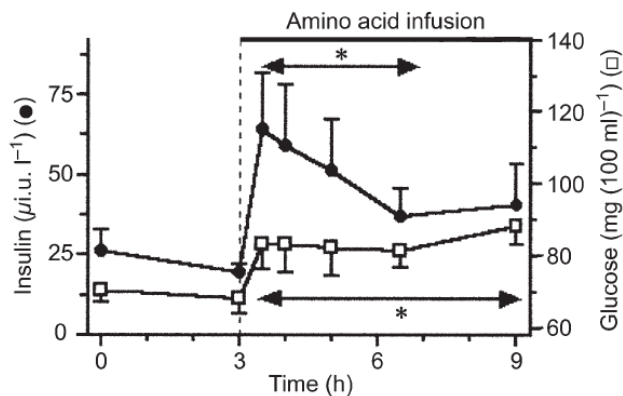


Figure 1. Time course of serum insulin and glucose

*Values for insulin and glucose significantly above basal values.

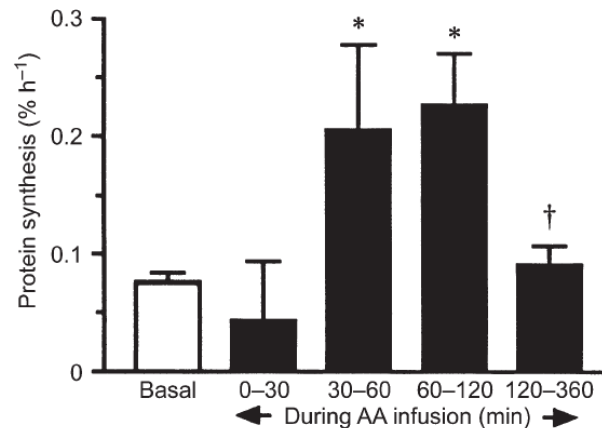
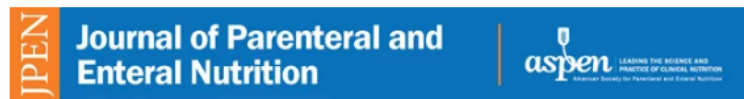


Figure 2. Time course of rate of synthesis of mixed muscle proteins

* $P < 0.05$ vs. basal; † $P < 0.05$ vs. peak value.

KONT vs. BOLUS APEN 2009



Clinical Guideline | [Free Access](#)

Guidelines for the Provision and Assessment of Nutrition Support Therapy in the Adult Critically Ill Patient:

Society of Critical Care Medicine (SCCM) and American Society for Parenteral and Enteral Nutrition (A.S.P.E.N.)

Stephen A. McClave MD, Robert G. Martindale MD, PhD, Vincent W. Vanek MD, Mary McCarthy RN, PhD, Pamela Roberts MD, Beth Taylor RD, Juan B. Ochoa MD, Lena Napolitano MD ... [See all authors](#)

First published: 27 April 2009 | <https://doi.org/10.1177/0148607109335234> | Cited by: 1034

The potential harm from aggressive bolus infusion of EN leading to increased risk of aspiration pneumonia was shown in 1 study.¹⁶⁰ Level II studies comparing bolus to continuous infusion have shown greater volume with fewer interruptions in delivery of EN with continuous feeding but no significant difference between techniques with regard to patient outcome.^{161,162} See [Table 10](#).¹⁶¹⁻¹⁶⁵

Table 10. Randomized Studies Evaluating Continuous vs Bolus Delivery of Enteral Nutrition (EN)

Study	Population	Study Groups	Infection	Difference in Feeding	ICU Mortality	Other
Hiebert et al, 1981 ¹⁶³ Level II	Burn (n = 76)		NR	Time to goal calories		Diarrhea (stool frequency)
		Continuous		3.1 ± 0.7 d ^a		1.8 ± 0.4 ^a
		Bolus		5.2 ± 0.8 d		3.3 ± 0.7
Kocan et al, 1986 ¹⁶⁴ Level II	Neuro ICU (n = 34)		NR	% Goal calories infused	NR	Aspiration (blue food coloring)
		Continuous		62.2%		1/17 (6%)
		Bolus		55.9%		3/17 (18%)
Ciocon et al, 1992 ¹⁶⁵ Level II	Hospitalized dysphagia (n = 60)			Daily caloric deficit	NR	Clogged tube
		Continuous	5/30 (17%) ^b	783 ± 29 kcal/d		15/30 (50%) ^a
		Bolus	10/30 (33%)	795 ± 25 kcal/d		5/30 (17%)
		Continuous				Diarrhea 20/30 (67%) ^a
		Bolus				29/30 (97%)
Bonten et al, 1996 ¹⁶¹ Level II	ICU (n = 60)			Interrupted EN		Mortality
		Continuous	5/30 (17%)	2/30 (7%)	6/30 (20%)	6/30 (20%)
		Bolus ^c	5/30 (17%)	5/30 (17%)	9/30 (30%)	9/30 (30%)
Steevens et al, 2002 ¹⁶² Level II	Trauma ICU (n = 18)			Interrupted EN	NR	
		Continuous	0/9 (0%) ^b	3/9 (33%)		
		Bolus	1/9 (11%)	5/9 (56%)		

KONT vs BOLUS ASPEN 2016

Guidelines for the Provision and Assessment of Nutrition Support Therapy in the Adult Critically Ill Patient: Society of Critical Care Medicine (SCCM) and American Society for Parenteral and Enteral Nutrition (A.S.P.E.N.)

Taylor, Beth E. RD, DCN¹; McClave, Stephen A. MD²; Martindale, Robert G. MD, PhD³; Warren, Malissa M. RD⁴; Johnson, Debbie R. RN, MS⁵; Braunschweig, Carol RD, PhD⁶; McCarthy, Mary S. RN, PhD⁷; Davanos, Evangelia PharmD⁸; Rice, Todd W. MD, MSc⁹; Cresci, Gail A. RD, PhD¹⁰; Gervasio, Jane M. PharmD¹¹; Sacks, Gordon S. PharmD¹²; Roberts, Pamela R. MD¹³; Compher, Charlene RD, PhD¹⁴

Critical Care Medicine: February 2016 - Volume 44 - Issue 2 - p 390-438

D4b. Based on expert consensus, we suggest that for high-risk patients or those shown to be intolerant to bolus gastric EN, delivery of EN should be switched to continuous infusion.

Rationale: The potential harm from aggressive bolus infusion of EN leading to increased risk of aspiration pneumonia was shown in one study (¹²³). An RCT showed a trend toward decreased mortality with continuous EN (13.9% intermittent vs 7.4% continuous, $p = 0.18$) (¹²⁴). Five small RCTs comparing bolus to continuous infusion have shown greater volume with fewer interruptions in delivery of EN with continuous EN, but no significant difference between techniques with regard to patient outcome (¹²⁵⁻¹²⁹).

125. Bonten MJ, Gaillard CA, van der Hulst R, et al. Intermittent enteral feeding: the influence on respiratory and digestive tract colonization in mechanically ventilated intensive-care-unit patients. *Am J Respir Crit Care Med.* 1996;154:394-399

[Cited Here...](#) | [View Full Text](#) | [PubMed](#) | [CrossRef](#)

126. Steevens EC, Lipscomb AF, Poole GV, et al. Comparison of continuous vs intermittent nasogastric enteral feeding in trauma patients: perceptions and practice. *Nutr Clin Pract.* 2002;17:118-122

[Cited Here...](#) | [View Full Text](#) | [PubMed](#) | [CrossRef](#)

127. Hiebert JM, Brown A, Anderson RG, et al. Comparison of continuous vs intermittent tube feedings in adult burn patients. *JPEN J Parenter Enteral Nutr.* 1981;5:73-75

[Cited Here...](#) | [PubMed](#) | [CrossRef](#)

128. Kocan MJ, Hickisch SM. A comparison of continuous and intermittent enteral nutrition in NICU patients. *J Neurosci Nurs.* 1986;18:333-337

[Cited Here...](#) | [View Full Text](#) | [PubMed](#) | [CrossRef](#)

129. Ciocon JO, Galindo-Ciocon DJ, Tiessen C, et al. Continuous compared with intermittent tube feeding in the elderly. *JPEN J Parenter Enteral Nutr.* 1992;16:525-528

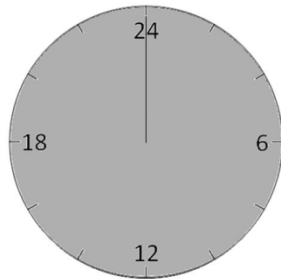
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KARIM FN BRNO

- 4 oddělení
- celkem 24 lůžek intenzivní péče
- 900 přijatých pacientů ročně
- enterální výživa podávána cca 57% hospitalizovaných pacientů

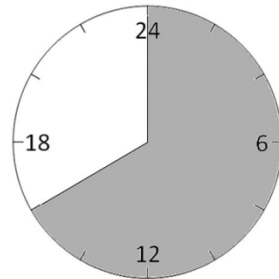


ZPŮSOBY PODÁVÁNÍ EV



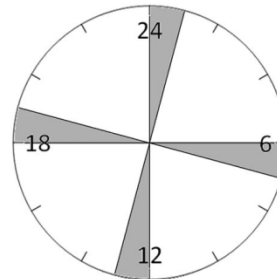
Continuous feeding

Providing EN by a feeding pump over 24 hours per day



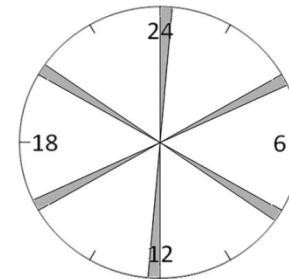
Cyclic feeding

Providing EN by a feeding pump in less than a 24-hour time period



Intermittent feeding

Providing EN over 20-60 minutes every 4-6 hours with or without a feeding pump



Bolus feeding

Providing EN over a very short period of time at specified time interval by gravity or with a syringe

■ Feeding time
□ Break time

EN, enteral nutrition.

[Home](#) > [Search Results](#) > Study Record Detail

Trial record 1 of 1 for: NCT03573453

[Previous Study](#) | [Return to List](#) | [Next Study](#)

Comparison of Continuous Versus Intermittent Enteral Nutrition in Critically Ill Patients. (COINN)

this study is the responsibility of the study sponsor and investigators. Listing a study does not constitute an endorsement by the U.S. Federal Government. [Know the risks and potential benefits](#) of clinical studies and before participating. Read our [disclaimer](#) for details.

ClinicalTrials.gov Identifier: NCT03573453

Recruitment Status ⓘ : Recruiting

First Posted ⓘ : June 29, 2018

Last Update Posted ⓘ : November 30, 2018

See [Contacts and Locations](#)

tvorba protokolu



COINN

- monocentrická prospektivní randomizovaná studie
- celkem 300 pacientů (150 v každém rameni)
- Výživa podávána ve zvyšujících se dávkách dle tolerance
- Sledování v průběhu 5 dní od zahájení EV
- Prim cíl: den dosažení energetického cíle
- Sek cíle:
 - den dosažení proteinového cíle
 - hodnocení tolerance (zvracení, průjmy, GRV)
 - výskyt komplikací (aspirace, VAP)
 - vliv na délku pobytu na JIP a v nemocnici
 - 28 denní mortalita

COINN

Vstupni kriteria

1. Vek 18 - 80 let

* must provide value

2. Indikována enteralní výživa gastricky nasogastrickou nebo orogastrickou sondou

* must provide value

3. NUTRIC score ≥ 5

* must provide value

4. BMI 18-50

* must provide value

5. Umělá plicní ventilace s předpokladanou délkou více než 72 hodin

* must provide value

6. Polohovatelnost

* must provide value

Vylučující kriteria

1. Operace na horním gastrointestinálním traktu (jícen, žaludek) jako důvod přijetí nebo v anamnéze

* must provide value

2. Ileus

* must provide value

3. Ischemie střeva

* must provide value

4. Akutní pankreatitida

* must provide value

5. Závažný průjem (nad 1 L/24 h)

* must provide value

6. Krvácení do GIT

* must provide value

7. Syndrom krátkého střeva

* must provide value

8. Malabsorbce v anamnéze

* must provide value

9. Probíhající EV 24 hodin před přijetím na JIP

* must provide value

COINN aktuálně

- běží 7. měsíc
- screenováno 415 pacientů
- randomizováno 71 pacientů
- cca 15% přijatých pacientů - cca 120/rok
- předpokládaný konec 5/2021
- analýza dat, publikace do konce roku 2021

POZOR

2019 publikovány nové ESPEN guidelines



KONT. vs. BOLUS ESPEN 2019

3.5. Clinical question 5: In adult critically ill patients, does intermittent EN have an advantage over continuously administered EN?

Recommendation 9

????????????????????

Commentary

Five studies [74, 75, 76, 77, 78] were identified and our Meta-analysis found a significant reduction in diarrhea with continuous versus bolus administration (RR 0.42, CI 0.19, 0.91, $p = 0.03$), whereas no difference was identified in other outcomes (see Fig. 4 and Meta-analysis III in Supplemental Materials). Despite the fact that bolus administration is significantly different from continuous feeding in normal volunteers, increasing significantly gastric volume and superior mesenteric artery blood volume, in critically ill patients [79] these differences are not always translated into clinical advantages. Four prospective small studies [75, 76, 77, 78] compared bolus (intermittent) to continuous administration of EN and did not find a difference in morbidity or mortality in small populations of ICU or trauma patients. Rhoney et al. [77] tested the tolerability of bolus gastric feeding in brain damaged patients and found large gastric residues. Tavares et al. [78] in an observational study found that continuous feeding reached the target faster, but no difference in gastrointestinal symptoms was observed between the groups. A systematic review [80] did not detect an advantage of one technique but bolus administration was associated with a lower aspiration rate and better calorie achievement. However, heterogeneity of the studies decreased the strength of the recommendation. In an ICU population fed through percutaneous endoscopic gastrostomy, bolus and continuous tube feeding achieved the same gastric volumes, insulin requirements, time to goal therapy or calorie intake [81]. This limited amount of data suggest that bolus and continuous enteral feeding can achieve the same target without an increase in side effects in any of these routes. Finally, bolus feeding could provide a greater stimulus for protein synthesis [82].

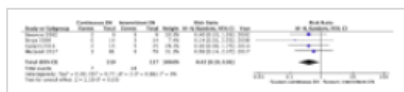


Fig. 4
Meta-analysis of occurrence of diarrhea in patients receiving continuous or intermittent enteral feeding (Meta-analysis III).

..mohou dosáhnout stejného cíle bez vzestupu nežádoucích účinků. Bolusové podávání může být větším stimulem pro proteosyntézu.

Raději bolusově

Raději kontinuálně

Je to jedno

CLINICAL
NUTRITION

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February 2019 Volume 38, Issue 1, Pages 48–79

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ESPEN guideline on clinical nutrition in the intensive care unit

Pierre Singer^{a,*}, Annika Reintam Blaser^{b,c}, Mette M. Berger^d, Waleed Alhazzani^e, Philip C. Calder^f, Michael P. Casaer^g, Michael Hiesmayr^h, Konstantin Mayerⁱ, Juan Carlos Montejo^j, Claude Pichard^k, Jean-Charles Preiser^l, Arthur R.H. van Zanten^m, Simon Oczkowskiⁿ, Wojciech Szczeklik^o, Stephan C. Bischoff^p

DĚKUJI ZA POZORNOST