

The OUTCOMEREA - day

Faut-il nourrir précocement les malades en états de choc, avec quoi et comment ?



Nutrition en réanimation: le contexte

- **Voie orale souvent impossible** (ventilation mécanique, anorexie intense, troubles du comportement).
- **Dénutrition préalable fréquente**, dépendante de la typologie de la population admise (patients âgés, cancer, insuffisants respiratoires chroniques).
- **Catabolisme** protéique (+++) et lipidique, et constitution de carences en oligoéléments et vitamines proportionnelles à la gravité de la pathologie aiguë et des défaillances d'organes.

Nutrition du patient « défaillant »

Quand?

Combien?

Comment?

Par quelle voie?

ESPEN Guidelines on Enteral Nutrition: Intensive care ☆

K.G. Kreymann^{a,*}, M.M. Berger^b, N.E.P. Deutz^c, M. Hiesmayr^d, P. Jolliet^e,
G. Kazandjiev^f, G. Nitenberg^g, G. van den Berghe^h, J. Wernermanⁱ,
DGEM: ☆ ☆ C. Ebner, W. Hartl, C. Heymann, C. Spies

Clin Nutrition 2006

tolerance. During the acute and initial phase of critical illness an exogenous energy supply in excess of 20–25 kcal/kg BW/day may be associated with a less favourable outcome (C).

During recovery (anabolic flow phase), the aim should be to provide 25–30 total kcal/kg BW/day (C).

aspen
Clinical Guidelines

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

Journal of Parenteral and
Enteral Nutrition
Volume 33 Number 3
May/June 2009 277-316
© 2009 American Society for
Parenteral and Enteral Nutrition and
Society of Critical Care Medicine
10.1177/0148607109335234
http://jpen.sagepub.com
hosted at
http://online.sagepub.com

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;

JPEN 2009

→ 25-30 Kcal/kg/j (Protéines: 1,2-2g/kg/j)

C2. Efforts to provide >50%-65% of goal calories should be made in order to achieve the clinical benefit of EN over the first week of hospitalization. (Grade: C)

Réanimation (2014) 23:332-350
DOI 10.1007/s13546-014-0893-x

RÉFÉRENTIEL / GUIDELINES

Nutrition artificielle en réanimation

Guidelines for Nutrition Support in Critically Ill Patient

D. Hurel · J.-Y. Lefrant · N.J. Cano · C. Ichai · J.-C. Preiser · F. Tamion

Comité d'organisation

Société française d'anesthésie et de réanimation (Sfar)

Société de réanimation de langue française (SRLF)

Société francophone nutrition clinique et métabolique (SFNEP)

Encadré 10

En l'absence de calorimétrie indirecte, il faut probablement avoir un objectif calorique total de 20–25 kcal/kg par jour à la phase aiguë et de 25–30 kcal/kg par jour après stabilisation (**Accord faible**).

Hypocaloric feeding = increased risk of infections, delayed weaning of mechanical ventilation, increased mortality

Negative impact of hypocaloric feeding and energy balance on clinical outcome in ICU patients

Stéphane Villet^a, René L. Chiolero^b, Marc D. Bollmann^b, Jean-Pierre Revelly^b, Marie-Christine Cayeux RN^b, Jacques Delarue^c, Mette M. Berger^{b,*} Clinical Nutrition 2005

Table 4 Relationship between complications and cumulated energy deficit by regression analysis.

Variables	F	P
Length of stay	25.18	0.0001
Complications	15.15	0.0003
Infections	9.14	0.0042
Days on antibiotics	17.48	0.0003
Start of nutrition	17.17	0.0002
Days of mechanical ventilation	17.12	0.0002

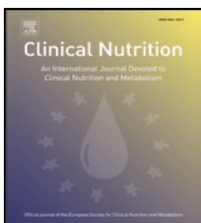
Early ICU Energy Deficit Is a Risk Factor for *Staphylococcus aureus* Ventilator-Associated Pneumonia

Christophe Faisy, MD, PhD; Maria Candela Llerena, MD; Magali Savalle, MD; Jean-Luc Mainardi, MD, PhD; and Jean-Yves Fagon, MD, PhD Chest 2011

Kenneth Ekpe
Ana Novara
Jean-Luc Mainardi
Jean-Yves Fagon
Christophe Faisy

Methicillin-resistant *Staphylococcus aureus* bloodstream infections are associated with a higher energy deficit than other ICU-acquired bacteremia

Int Care Med 2014



Inadequate energy delivery during early critical illness correlates with increased risk of mortality in patients who survive at least seven days: A retrospective study

Jong-Rung Tsai^{a,b}, Wen-Tsan Chang^c, Chau-Chyun Sheu^{a,b}, Yu-Ju Wu^d, Yu-Heng Sheu^d, Po-Len Liu^b, Chen-Guo Ker^{c,e}, Meng-Chuan Huang^{d,e,*}

Nutrition artificielle en réanimation

Guidelines for Nutrition Support in Critically Ill Patient

D. Hurel · J.-Y. Lefrant · N.J. Cano · C. Ichai · J.-C. Preiser · F. Tamion

Comité d'organisation

Société française d'anesthésie et de réanimation (Sfar)

Société de réanimation de langue française (SRLF)

Société francophone nutrition clinique et métabolique (SFNEP)

Les recommandations

Encadré 6

Il faut utiliser la nutrition entérale (NE) plutôt que la nutrition parentérale (NP), en l'absence de contre-indication formelle (**Accord fort**).

 **Canadian Clinical Practice Guidelines, (JPEN 2003)**

support for critically ill patients, we strongly recommend the use of EN over PN. »

 **ESPEN, (Clinical Nutrition 2006)**

« ... should receive EN. »

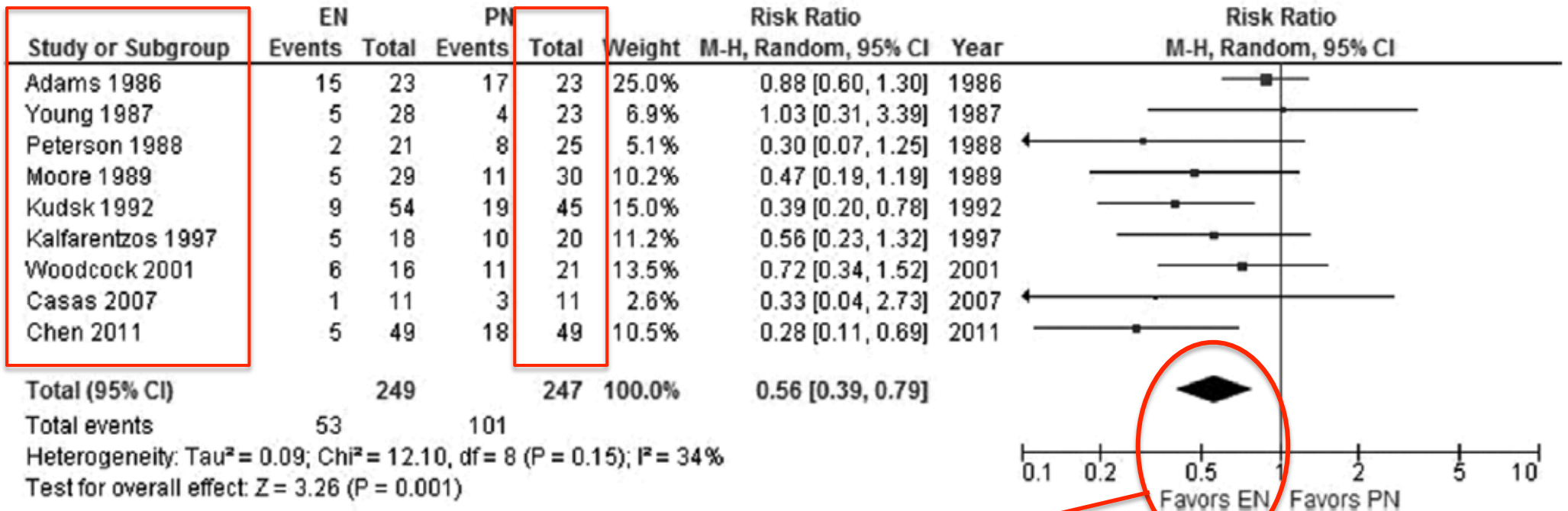
 **ASF**

[Quality of Evidence: Low to Very Low]

critically

Complications infectieuses

Limites méthodologiques+++



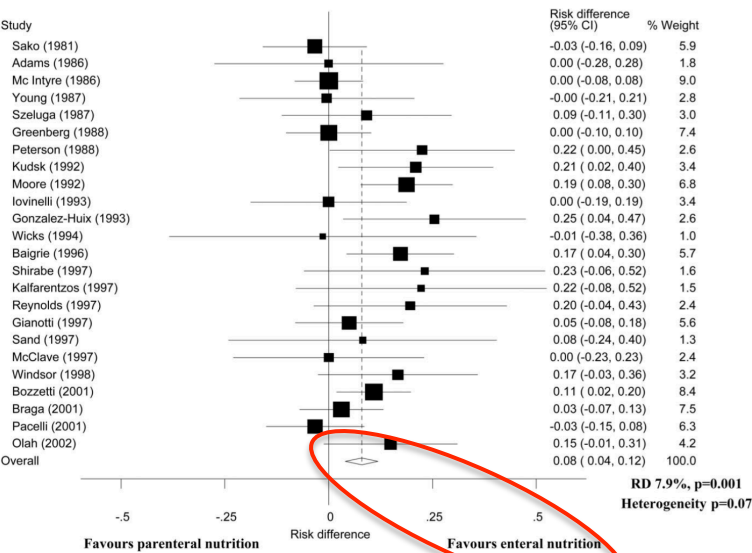
Entérale > parentérale ?

A metaanalysis of treatment outcomes of early enteral versus early parenteral nutrition in hospitalized patients*

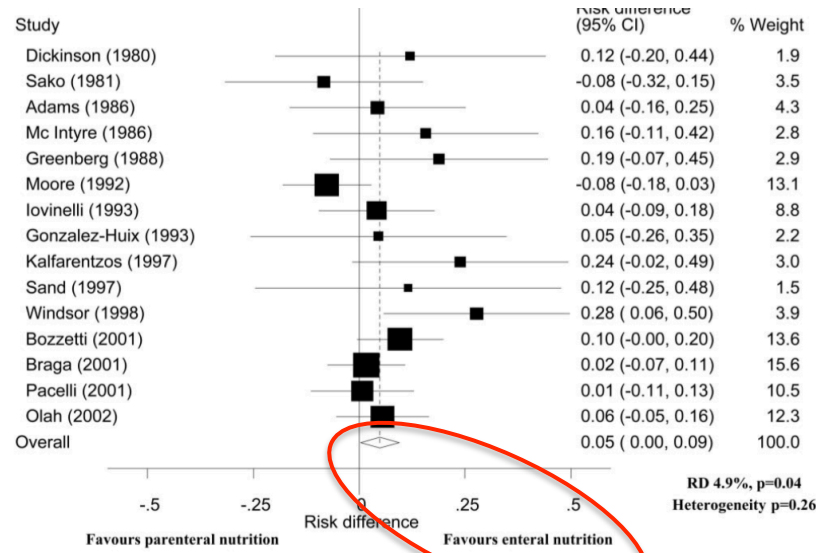
John Victor Peter, MBBS, MD, DNB (Med); John L. Moran, MBBS, FRACP, FANZCA;
Jennie Phillips-Hughes, RN

Crit Care Med 2005

Parenteral vs. Enteral feeding



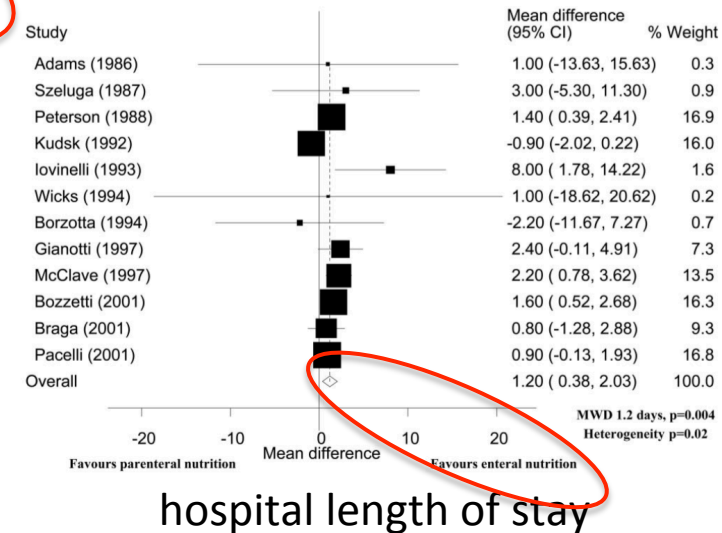
infections



Non infectious complications

Compared to parenteral nutrition, enteral was associated with reductions in:

- infectious complications
- non infectious complications
- length of stay



hospital length of stay

Entérale vs parentérale

Impact sur la mortalité?

Current practice in nutritional support and its association with mortality in septic patients—Results from a national, prospective, multicenter study*

Gunnar Elke, MD; Dirk Schädler, MD; Christoph Engel, MD; Holger Bogatsch; Inez Frerichs, MD; Maximilian Ragaller, MD; Jens Scholz, MD; Frank M. Brunkhorst, MD; Markus Löffler, MD; Konrad Reinhart, MD; Norbert Weiler, MD; for the German Competence Network Sepsis (SepNet)

- 399 septic patients from 454 ICU
- Prospective observational study

Crit Care Med 2008

Table 4. Independent predictors for mortality

Variable	Univariate		Multivariate ^a	
	OR	<i>p</i> Value	OR	95% CI
Enteral nutrition	0.68	.065	1.13	0.84–1.51
Parenteral nutrition	1.97	.003	2.09	1.29–3.37
APACHE II	1.07	<.0001	1.05	1.02–1.09
Renal dysfunction ^b	2.91	<.0001	2.07	1.30–3.31
Insulin dose (IU/24 hrs)	1.00	.338		
Serum glucose concentration (mg/dL)	1.00	.145		
Age	1.01	.051	1.01	0.99–1.02
Gender	0.90	.609		
Mechanical ventilation	2.88	.083		
Septic shock	1.85	.004	1.54	0.97–2.44

Surviving Sepsis Campaign: International Guidelines for Management of Sepsis and Septic Shock: 2016

We recommend **against the administration of parenteral nutrition** alone or in combination with enteral feeds (but rather to initiate IV glucose and advance enteral feeds as tolerated) **over the first 7 days in critically ill patients with sepsis or septic shock** for whom early **enteral feeding is not feasible** (strong recommendation, moderate quality of evidence).

Parenteral nutrition =

- lack of mortality benefit
- increased risk of infection
- extra cost

Nutrition artificielle en réanimation

Guidelines for Nutrition Support in Critically Ill Patient

D. Hurel · J.-Y. Lefrant · N.J. Cano · C. Ichai · J.-C. Preiser · F. Tamion

Comité d'organisation

Société française d'anesthésie et de réanimation (Sfar)

Société de réanimation de langue française (SRLF)

Société francophone nutrition clinique et métabolique (SFNEP)

Les recommandations

Encadré 5

Il faut administrer dans les 24 premières heures un support nutritionnel entéral aux patients dénutris ou jugés incapables de s'alimenter suffisamment dans les trois jours après l'admission (**Accord fort**).

 **ESPEN, (Clinical Nutrition 2006)**

critically ill patients who have a functioning gastrointestinal tract should be fed early (<24 h) »



« Haemodynamically stable

 **ASPEN – SCCM, (JPEN 2009)**

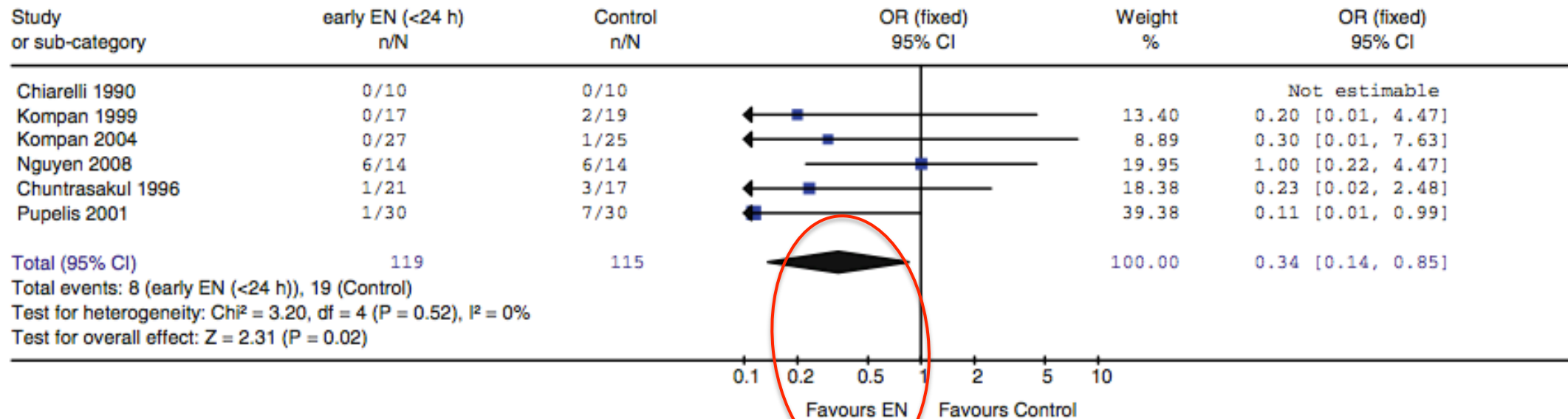
support therapy in the form of early EN be initiated within 24–48 hours in the critically ill patient. »



« We recommend that nutrition

Gordon S. Doig
 Philippa T. Heighes
 Fiona Simpson
 Elizabeth A. Sweetman
 Andrew R. Davies

Early enteral nutrition, provided within 24 h of injury or intensive care unit admission, significantly reduces mortality in critically ill patients: a meta-analysis of randomised controlled trials



The provision of early EN was associated with a significant **reduction in mortality** [OR = 0.34, 95% confidence interval (CI) 0.14–0.85] **and pneumonia** (OR = 0.31, 95% CI 0.12–0.78).

Surviving Sepsis Campaign: International Guidelines for Management of Sepsis and Septic Shock: 2016

We suggest the **early initiation of enteral feeding** rather than a complete fast or only IV glucose in critically ill patients with sepsis or septic shock who can be fed enterally (weak recommendation, low quality of evidence).

- evidence does not suggest harm with early versus delayed institution of enteral feeding,
- possible benefit from physiologic evidence suggesting reduced gut permeability, inflammation, and infection risk
- **Review: pas de différence sur mortalité et infections.**

**Review Article: Critical Care Medicine
Severe Sepsis and Septic Shock**

Angus DC, van der Poll T
2013

Table 2. Guidelines for the Treatment of Severe Sepsis and Septic Shock from the Surviving Sepsis Campaign.*

Element of Care	Grade†
Resuscitation	
Begin goal-directed resuscitation during first 6 hr after recognition	1C
Begin initial fluid resuscitation with crystalloid and consider the addition of albumin	1B
Consider the addition of albumin when substantial amounts of crystalloid are required to maintain adequate arterial pressure	2C
Avoid hetastarch formulations	1C
Begin initial fluid challenge in patients with tissue hypoperfusion and suspected hypovolemia, to achieve ≥30 ml of crystalloids per kilogram of body weight‡	1C
Continue fluid-challenge technique as long as there is hemodynamic improvement	UG
Use norepinephrine as the first-choice vasopressor to maintain a mean arterial pressure of ≥65 mm Hg	1B
Use epinephrine when an additional agent is needed to maintain adequate blood pressure	2B
Add vasopressin (at a dose of 0.03 units/min) with weaning of norepinephrine, if tolerated	UG
Avoid the use of dopamine except in carefully selected patients (e.g., patients with a low risk of arrhythmias and either known marked left ventricular systolic dysfunction or low heart rate)	2C
Infuse dobutamine or add it to vasopressor therapy in the presence of myocardial dysfunction (e.g., elevated cardiac filling pressures or low cardiac output) or ongoing hypoperfusion despite adequate intravascular volume and mean arterial pressure	1C
Avoid the use of intravenous hydrocortisone if adequate fluid resuscitation and vasopressor therapy restore hemodynamic stability; if hydrocortisone is used, administer at a dose of 200 mg/day	2C
Target a hemoglobin level of 7 to 9 g/dl in patients without hypoperfusion, critical coronary artery disease or myocardial ischemia, or acute hemorrhage	1B
Infection control	
Obtain blood cultures before antibiotic therapy is administered	1C
Perform imaging studies promptly to confirm source of infection	UG
Administer broad-spectrum antibiotic therapy within 1 hr after diagnosis of either severe sepsis or septic shock	1B/1C
Reassess antibiotic therapy daily for de-escalation when appropriate	1B
Perform source control with attention to risks and benefits of the chosen method within 12 hr after diagnosis	1C
Respiratory support	
Use a low tidal volume and limitation of inspiratory-plateau-pressure strategy for ARDS	1A/1B
Apply a minimal amount of positive end-expiratory pressure in ARDS	1B
Administer higher rather than lower positive end-expiratory pressure for patients with sepsis-induced ARDS	2C
Use recruitment maneuvers in patients with severe refractory hypoxemia due to ARDS	2C
Use prone positioning in patients with sepsis-induced ARDS and a ratio of the partial pressure of arterial oxygen (mm Hg) to the fraction of inspired oxygen of <100, in facilities that have experience with such practice	2C
Elevate the head of the bed in patients undergoing mechanical ventilation, unless contraindicated	1B
Use a conservative fluid strategy for established acute lung injury or ARDS with no evidence of tissue hypoperfusion	1C
Use weaning protocols	1A
Central nervous system support	
Use the equivalent of continuous venovenous hemofiltration or intermittent hemodialysis as needed for renal failure or fluid overload	2C
Administer prophylaxis for deep-vein thrombosis	1B
Administer stress-ulcer prophylaxis to prevent upper gastrointestinal bleeding	1B
Administer oral or enteral feedings, as tolerated, rather than either complete fasting or provision of only intravenous glucose within the first 48 hr after a diagnosis of severe sepsis or septic shock	2C
Address goals of care, including treatment plans and end-of-life planning as appropriate	1B

Administer oral or **enteral feedings** (...) within the first 48 hr after a diagnosis of severe sepsis or **septic shock**



Administer oral or enteral feedings, as tolerated, rather than either complete fasting or provision of only intravenous glucose within the first 48 hr after a diagnosis of severe sepsis or septic shock

2C

Intolerance to enteral nutrition

Upper digestive intolerance during enteral nutrition in critically ill patients: Frequency, risk factors, and complications

Hervé Mentec, MD; Hervé Dupont, MD; Maria Bocchetti, RN; Pascale Cani, RN; Frédérique Ponche, RN; Gérard Bleichner, MD

Crit Care Med 2001

46%

Definition, prevalence, and outcome of feeding intolerance in intensive care: a systematic review and meta-analysis

A. REINTAM BLASER¹, J. STARKOPF^{1,2}, Ü. KIRSIMÄGI³ and A. M. DEANE^{4,5}

¹Department of Anaesthesiology and Intensive Care, University of Tartu, Tartu, Estonia, Departments of ²Anaesthesiology and Intensive Care and ³Surgery, Tartu University Hospital, Tartu, Estonia, ⁴Discipline of Acute Care Medicine, University of Adelaide, Adelaide, SA, Australia and ⁵Department of Critical Care Services, Royal Adelaide Hospital, Adelaide, SA, Australia

Acta Anaesthesiol Scand 2014

38%

Effect of Not Monitoring Residual Gastric Volume on Risk of Ventilator-Associated Pneumonia in Adults Receiving Mechanical Ventilation and Early Enteral Feeding

A Randomized Controlled Trial

Reignier, JAMA 2013

Vomiting + RGV: 64%
Vomiting only: 40%

Les spécificités du choc

- Dysfonction marquée du tube digestif
- Hypercatabolisme accru à la phase aigue
- Etat de dénutrition plus marquée au décours avec séquelles fonctionnelles importantes

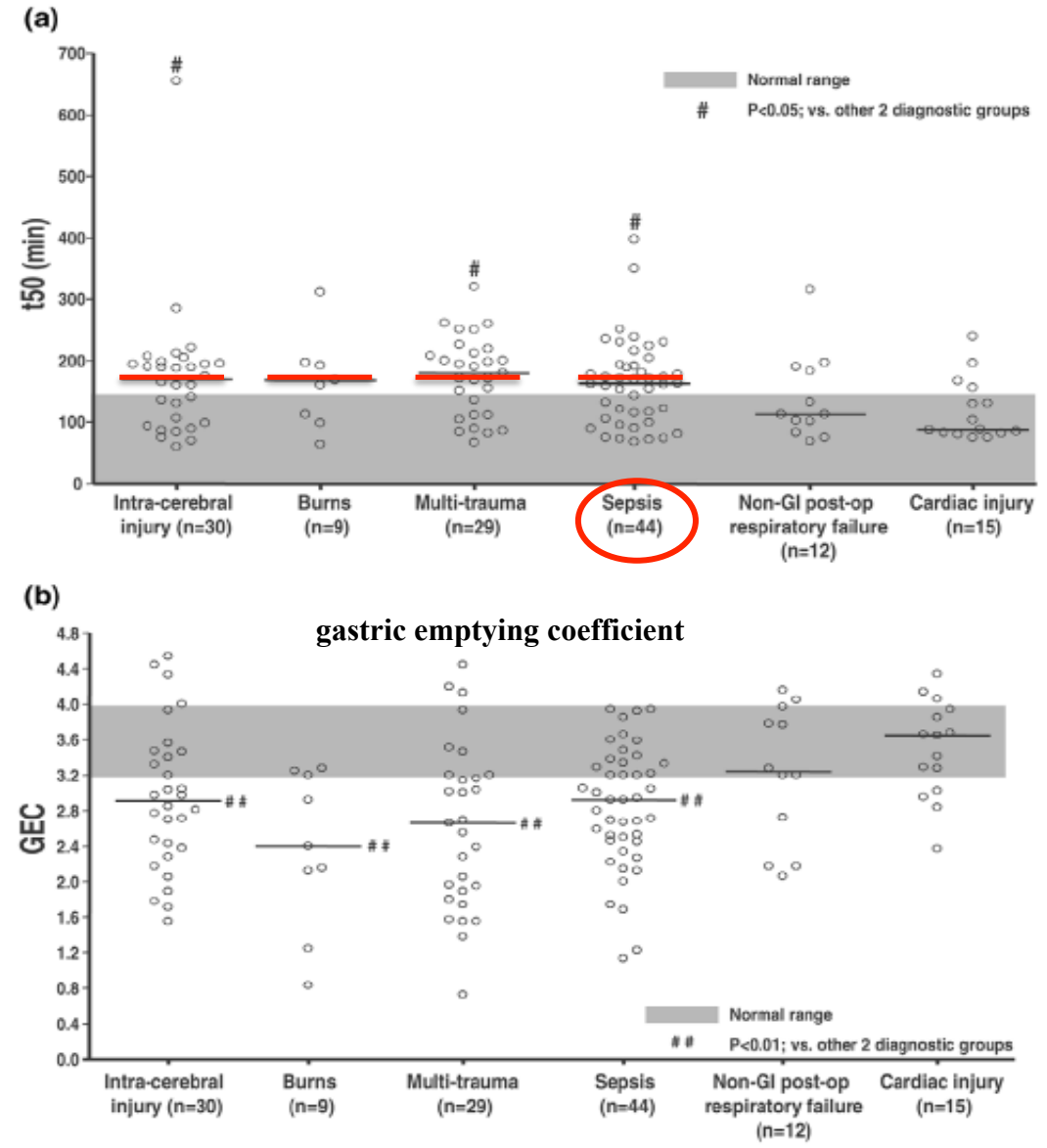
MAIS:

- Très peu d'études dédiées à cette population concernant la nutrition en réanimation
- Impact réel de la nutrition chez ces patients = inconnu
- Bénéfice peut-être important

The impact of admission diagnosis on gastric emptying in critically ill patients

Nam Q Nguyen^{1,2}, Mei P Ng¹, Marianne Chapman³, Robert J Fraser² and Richard H Holloway^{1,2}

Critical Care 2007,



Diagnostic Criteria for Sepsis, Severe Sepsis, and Septic Shock.

Table 1. Diagnostic Criteria for Sepsis, Severe Sepsis, and Septic Shock.*

Sepsis (documented or suspected infection plus ≥ 1 of the following)†

General variables

- Fever (core temperature, $>38.3^{\circ}\text{C}$)
- Hypothermia (core temperature, $<36^{\circ}\text{C}$)
- Elevated heart rate (>90 beats per min or >2 SD above the upper limit of the normal range for age)
- Tachypnea
- Altered mental status
- Substantial edema or positive fluid balance (>20 ml/kg of body weight over a 24-hr period)

Organ-dysfunction variables

Arterial hypoxemia (ratio of the partial pressure of arterial oxygen to the fraction of inspired oxygen, <300)

Acute oliguria (urine output, <0.5 ml/kg/hr or 45 ml/hr for at least 2 hr)

Increase in creatinine level of >0.5 mg/dl (>44 $\mu\text{mol/liter}$)

Coagulation abnormalities (international normalized ratio, >1.5 ; or activated partial-thromboplastin time, >60 sec)

Paralytic ileus (absence of bowel sounds)

Thrombocytopenia (platelet count, $<100,000/\text{mm}^3$)

Hyperbilirubinemia (plasma total bilirubin, >4 mg/dl [68 $\mu\text{mol/liter}$])

Coagulation abnormalities (international normalized ratio, >1.5 ; or activated partial-thromboplastin time, >60 sec)

Paralytic ileus (absence of bowel sounds)

Thrombocytopenia (platelet count, $<100,000/\text{mm}^3$)

Hyperbilirubinemia (plasma total bilirubin, >4 mg/dl [68 $\mu\text{mol/liter}$])

Tissue-perfusion variables

Hyperlactatemia (lactate, >1 mmol/liter)

Decreased capillary refill or mottling

Severe sepsis (sepsis plus organ dysfunction)

Septic shock (sepsis plus either hypotension [refractory to intravenous fluids] or hyperlactatemia)¶

Plus les patients sont graves, moins ils sont nourris

A prospective survey of nutritional support practices in intensive care unit patients:
What is prescribed? What is delivered?

De Jonghe. Crit Care Med 2001

Etude prospective observationnelle

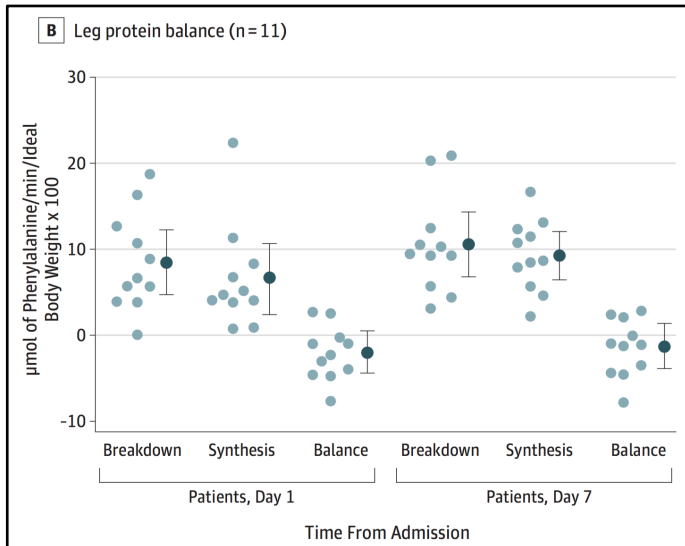
51 patients

Table 4. Variables associated with the ratio of calories prescribed/required, in univariate and multivariate linear regression analysis

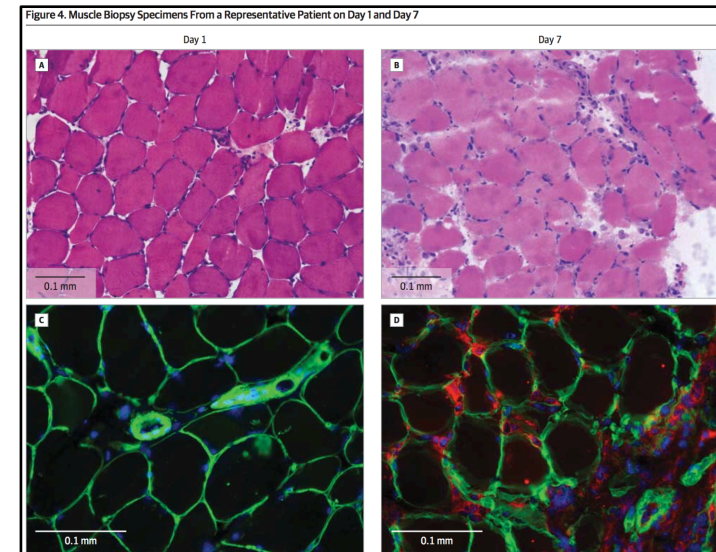
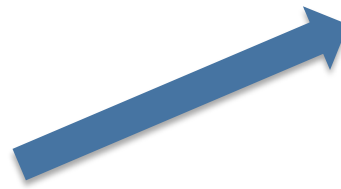
Variables Tested	Univariate Analysis, <i>p</i> Value	Multivariate Analysis, <i>p</i> Value
SAPS II	.31	
Vasoactive drugs	.03	.03
Extrarenal replacement	.04	.10
Central venous access	.05	.23
Geographic location in the ICU	.72	

Acute Skeletal Muscle Wasting in Critical Illness

Puthuchery, JAMA, 2013



Balance protéique négative...



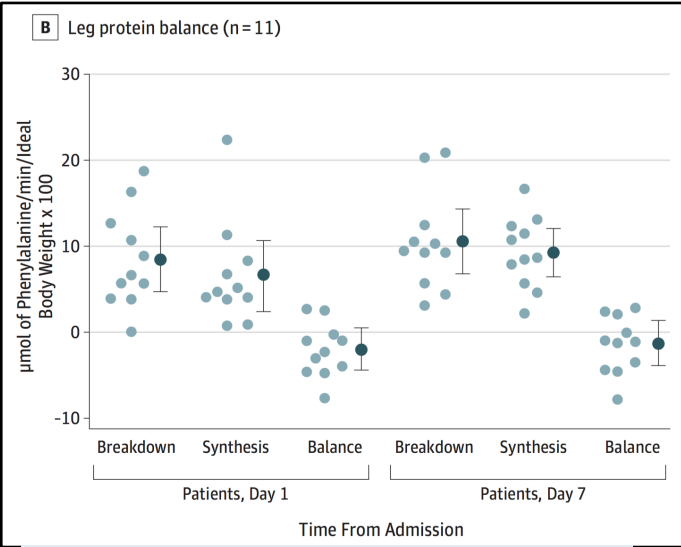
Destruction musculaire précoce

Atrophie musculaire

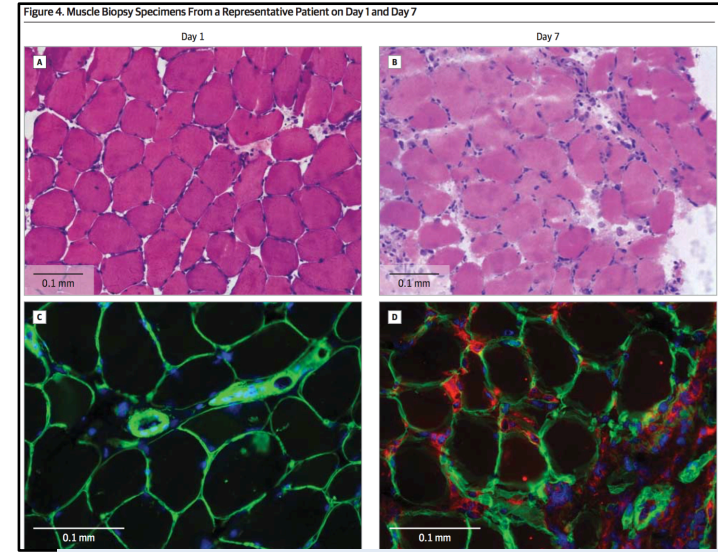
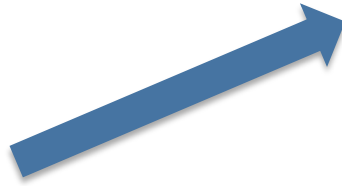
- *Cicatrisation retardée (sutures, parois, escarres)*
- *Sevrage de la ventilation mécanique retardée (faiblesse musculaire)*
- *Perte d'autonomie à long terme*

Acute Skeletal Muscle Wasting in Critical Illness

Puthuchery, JAMA, 2013

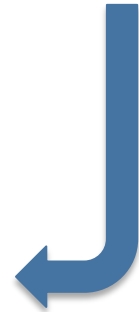
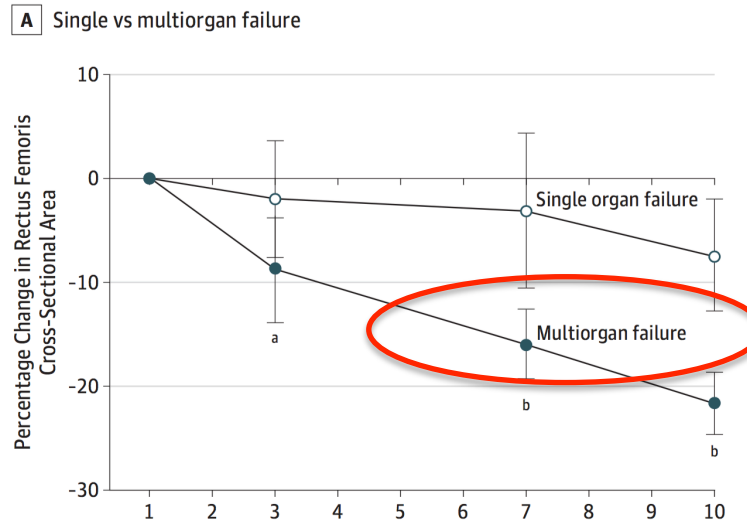


Balance protéique négative...



Destruction musculaire précoce

Figure 5. Measurements of Muscle Wasting During Critical Illness by Organ Failure



Les spécificités du choc (septique...)

- Dysfonction marquée du tube digestif
- Hypercatabolisme accru à la phase aigue
- Etat de dénutrition plus marquée au décours avec séquelles fonctionnelles importantes

MAIS:

- Très peu d'études dédiées à cette population concernant la nutrition en réanimation
- Impact réel de la nutrition chez ces patients = inconnu
- Impact peut-être important

Ronan Thibault
Claude Pichard
Jan Wernerman
Karim Bendjelid

Cardiogenic shock and nutrition: safe?

- Revelly JP, (2001) Early metabolic and splanchnic responses to enteral nutrition in postoperative cardiac surgery patients with circulatory compromise. Intensive Care Med
- Purcell PN (1993) Continuous duodenal feeding restores gut blood flow and increases gut oxygen utilization during PEEP ventilation for lung injury. Am J Surg

→NE précoce = augmentation du débit sanguin local et apport d'O₂

- Jorba R, (2000) Small bowel necrosis in association with early postoperative enteral feeding after pancreatic resection. Surgery.
- Melis M, (2006) Bowel necrosis associated with early jejunal tube feeding: a complication of postoperative enteral nutrition. Arch Surg.
- Berger MM (2000) Intestinal absorption in patients after cardiac surgery. Crit Care Med

→NE précoce = Altération de la circulation splanchnique et RISQUE ACCRU D'ICHÉMIE DIGESTIVE?

Ronan Thibault
Claude Pichard
Jan Wernerman
Karim Bendjelid

Cardiogenic shock and nutrition: safe?

- Jorba R, (2000) Small bowel necrosis in association with early postoperative enteral feeding after pancreatic resection. Surgery.
 - Melis M, (2006) Bowel necrosis associated with early jejunal tube feeding: a complication of postoperative enteral nutrition. Arch Surg.
 - Berger MM (2000) Intestinal absorption in patients after cardiac surgery. Crit Care Med
- NE précoce = Altération de la circulation splanchnique et RISQUE ACCRU D'ICHÉMIE DIGESTIVE?

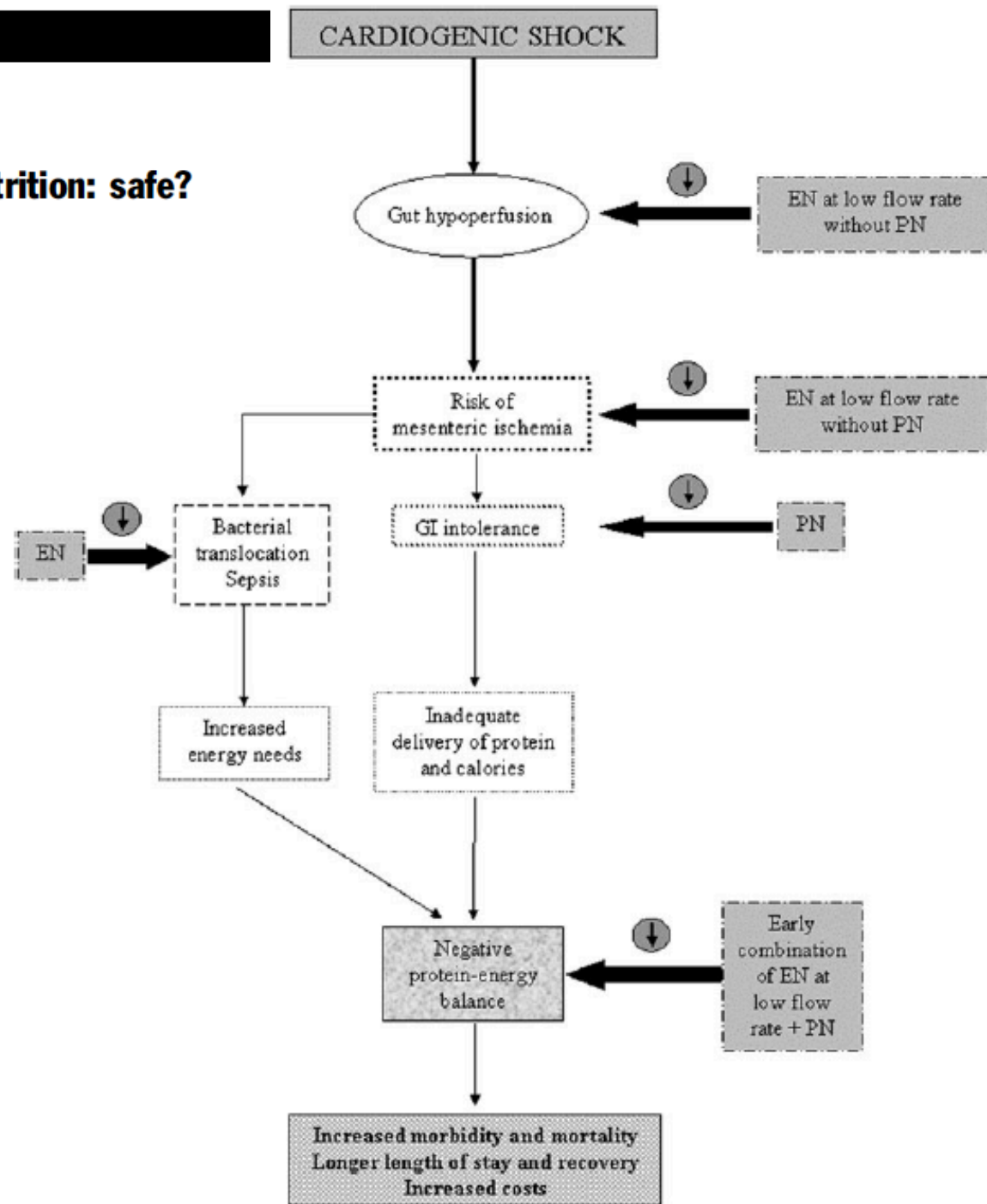
Ronan Thibault
Claude Pichard
Jan Wernerman
Karim Bendjelid

Cardiogenic shock and nutrition: safe?

In summary, nutritional support affects SMA blood flow in haemodynamically stable ICU patients. However, it is not possible to draw any conclusions about the clinical impact of these changes on ICU patients with CS.

Ronan Thibault
Claude Pichard
Jan Wernerman
Karim Bendjelid

Cardiogenic shock and nutrition: safe?



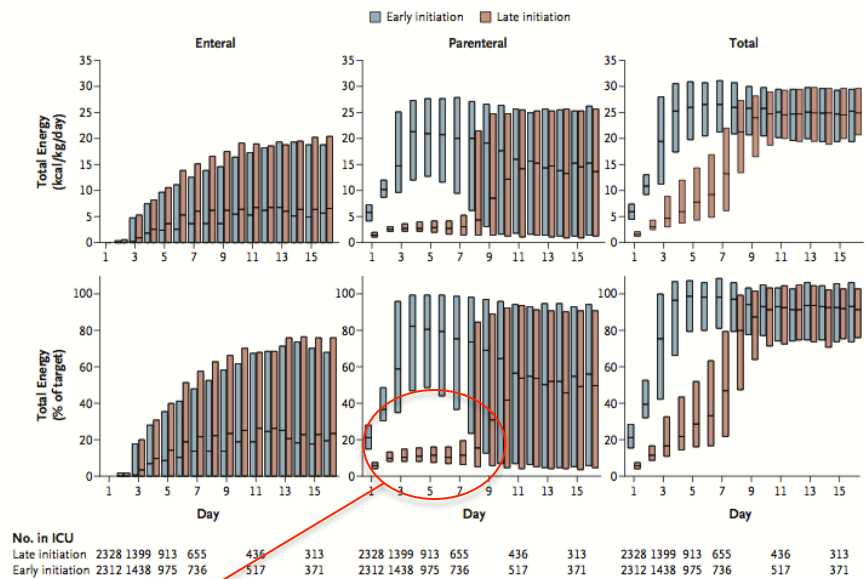
EN (faible dose) +
PN?

ORIGINAL ARTICLE

Early versus Late Parenteral Nutrition in Critically Ill Adults

Michael P. Casaer, M.D., Dieter Mesotten, M.D., Ph.D.,
 Greet Hermans, M.D., Ph.D., Pieter J. Wouters, R.N., M.Sc.,
 Miet Schetz, M.D., Ph.D., Geert Meyfroidt, M.D., Ph.D.,
 Sophie Van Cromphaut, M.D., Ph.D., Catherine Ingels, M.D.,
 Philippe Meersseman, M.D., Jan Muller, M.D., Dirk Vlasselaers, M.D., Ph.D.,
 Yves Debaveye, M.D., Ph.D., Lars Desmet, M.D., Jasperina Dubois, M.D.,
 Aime Van Assche, M.D., Simon Vanderheyden, B.Sc.,
 Alexander Wilmer, M.D., Ph.D., and Greet Van den Berghe, M.D., Ph.D.*

N Engl J Med 2011



Primary outcome

Duration of stay in ICU§

Median (interquartile range) — days

Duration >3 days — no. (%)

Hazard ratio (95% CI) for time to discharge alive from ICU

Secondary outcome

New infection — no. (%)

Any

Airway or lung

Bloodstream

Wound

Urinary tract

No. in ICU
 Late initiation 2328 1399 913 655 436 313 2328 1399 913 655 436 313 2328 1399 913 655 436 313
 Early initiation 2312 1438 975 736 517 371 2312 1438 975 736 517 371 2312 1438 975 736 517 371

Late PN

Early PN

	Late PN	Early PN	
Median (interquartile range) — days	3 (2–7)	4 (2–9)	0.02
Duration >3 days — no. (%)	1117 (48.0)	1185 (51.3)	0.02
Hazard ratio (95% CI) for time to discharge alive from ICU	1.06 (1.00–1.13)		0.04
Secondary outcome			
New infection — no. (%)			
Any	531 (22.8)	605 (26.2)	0.008
Airway or lung	381 (16.4)	447 (19.3)	0.009
Bloodstream	142 (6.1)	174 (7.5)	0.05
Wound	64 (2.7)	98 (4.2)	0.006
Urinary tract	60 (2.6)	72 (3.1)	0.28

Tolerability and Safety of Enteral Nutrition in Critically Ill Patients Receiving Intravenous Vasopressor Therapy

Erin E. Mancl, PharmD, BCPS¹; and Katie M. Muzevich, PharmD, BCPS¹

Journal of Parenteral and Enteral
Nutrition
Volume 37 Number 5
September 2013 641-651
© 2013 American Society
for Parenteral and Enteral Nutrition
DOI: 10.1177/0148607112470460
jpen.sagepub.com
hosted at
online.sagepub.com



Rétrospectif
Monocentrique
346 patients

Table 3. Adverse Events.

Adverse Event	Occurrence
≥1 Emesis, No. (%)	31/346 (9.0)
≥1 EN residual ≥300 mL, No. (%)	50/346 (14.5)
Rising serum lactate, No. (%)	106/346 (30.6)
Rising lactate >2 mmol/L, No. (%)	52/106 (50.0)
Max lactate, mmol/L, median (IQR), ^a	1.7 (1.1–2.6)
Abdominal KUB ordered, No. (%)	41/346 (11.9)
Positive findings	15/41 (36.6)
Abdominal CT ordered, No. (%)	14/346 (4.0)
Positive findings	3/346 (0.9)
Bowel ischemia/perforation, No. (%)	3/346 (0.9)

CT, computed tomography; EN, enteral nutrition; Max, maximum; IQR, interquartile range; KUB, kidney/ureter/bladder radiograph.

^an = 198.

Tolerability and Safety of Enteral Nutrition in Critically Ill Patients Receiving Intravenous Vasopressor Therapy

Erin E. Mancl, PharmD, BCPS¹; and Katie M. Muzevich, PharmD, BCPS¹

Journal of Parenteral and Enteral
Nutrition
Volume 37 Number 5
September 2013 641-651
© 2013 American Society
for Parenteral and Enteral Nutrition
DOI: 10.1177/0148607112470460
jpen.sagepub.com
hosted at
online.sagepub.com



Based on our findings, EN is relatively well tolerated in patients receiving IV vasopressor support equivalent to 12.5 mcg/min of norepinephrine or less. Tolerability was less likely in patients receiving higher doses of IV vasopressors and in those receiving dopamine or vasopressin. These patients should be monitored more closely for signs of intolerance. In summary, critically ill patients receiving IV vasopressor support generally tolerate EN.

Feeding the Hypotensive Patient: Does Enteral Feeding Precipitate or Protect Against Ischemic Bowel?

Stephen A. McClave, MD* and Wei-Kuo Chang, MD, PhD†

**From the Department of Medicine, University of Louisville School of Medicine, Louisville, Kentucky, and the*

†Division of Gastroenterology, Department of Internal Medicine, Tri-Service General Hospital, National Defense Medical Center, Taipei, Taiwan, Republic of China

Nutrition in Clinical Practice 2003

Changes in superior mesenteric artery blood flow after oral, enteral, and parenteral feeding in humans*

Marcel Gatt, MD, MRCS(Ed), MRCS (Eng); John MacFie, MBChB, MD, FRCS;
Alexander D.G. Anderson, MBChB, MRCS, MD, MRCGP; Gareth Howell, MRCS;
Bala S. Reddy, MBBS, MS, MRCS; Aravind Suppiah, MRCS; Ian Renwick, MBBS;
Charles J. Mitchell, BSc, MBChB, FRCP, FRCPE

Crit Care Med 2009

Postpyloric enteral nutrition in the critically ill child with shock: a prospective observational study

Jesús López-Herce*¹, Santiago Mencía¹, César Sánchez¹, Maria J Santiago¹,
Amaya Bustinza¹ and Dolores Vigil²

Nutrition Journal 2008

Question: Is EN safe during periods of hemodynamic instability in adult critically ill patients?

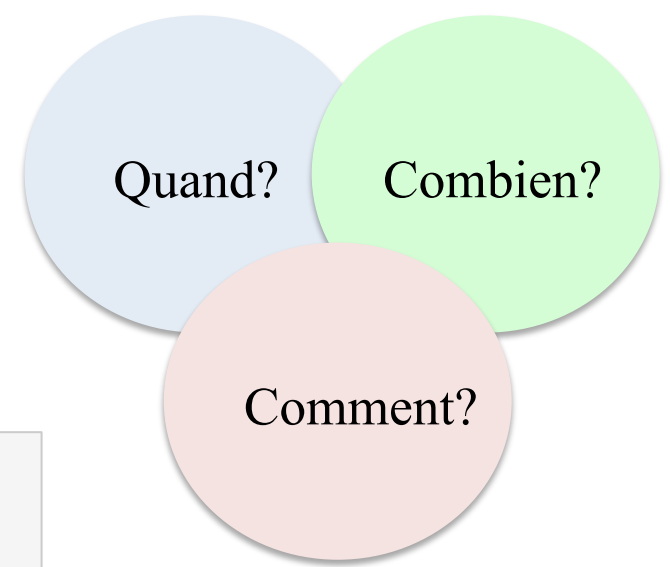
B5. Based on expert consensus, we suggest that in the setting of hemodynamic compromise or instability, EN should be withheld until the patient is fully resuscitated and/or stable. Initiation/re-initiation of EN may be considered with caution in patients undergoing withdrawal of vasopressor support.

→ **0 Kcal/kg/d ??**

Jusqu'à quand?

Impact of early nutrition and feeding route on outcomes of mechanically ventilated patients with shock: a post hoc marginal structural model study

Reignier, Intensive Care Med 2015



- 3032 patients with mechanical ventilation and shock (OutcomeRea)
- To assess associations linking early nutrition (EN and/or PN started within 48 h after intubation), feeding route and calorie intake to patients outcome.

- Early nutrition → reduced mortality

(HR, 0.89; 95% confidence interval [CI], 0.81-0.98; $P=0.01$)

- Feeding route → no impact

- Calorie intake → no impact

Nutrition du patient ventilé: comment?

Parentérale

- Facile à administrer
- Pas de problème d'intolérance
- Meilleur contrôle des apports
- Ne sollicite pas un tube digestif potentiellement ischémique et/ou peu fonctionnel

MAIS

- Nécessite un cathéter central
- Tube digestif au repos = atrophie villositaire
 - **Risque infectieux accru ?**
- Durée de séjour accrue?
- Surmortalité ?
- Complications hépatiques ?



Entérale

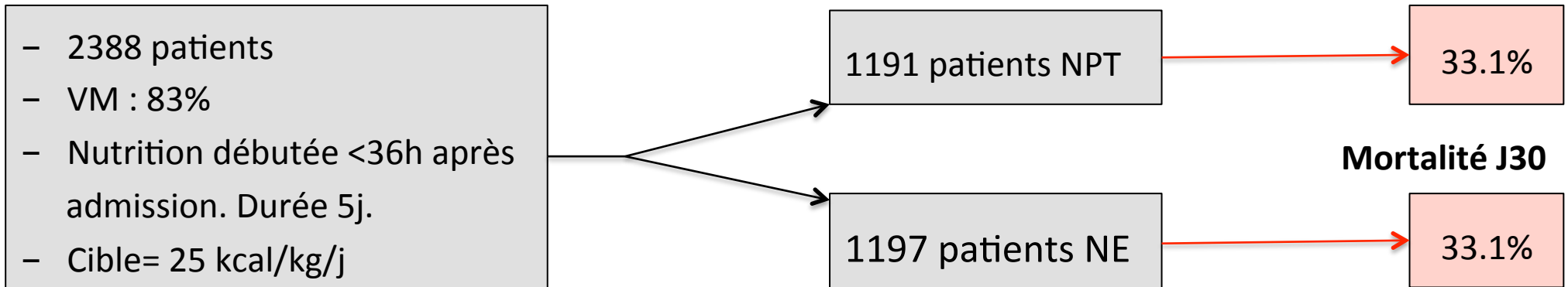
- Plus « physiologique »
 - Pas de cathéter central
 - Voie « naturelle »
- **Préserverait le tube digestif**

MAIS

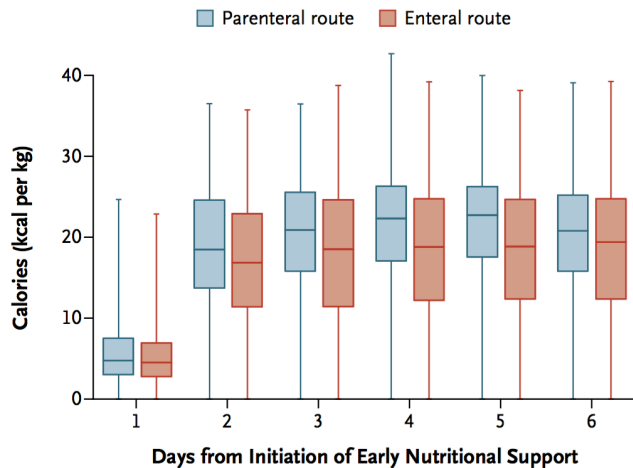
- Intolérance digestive
- Nécessite souvent l'association de prokinétique
- Objectifs rarement atteints
- Protège ou favorise ischémie digestive ?

Trial of the Route of Early Nutritional Support in Critically Ill Adults

Harvey, N Engl J Med 2015



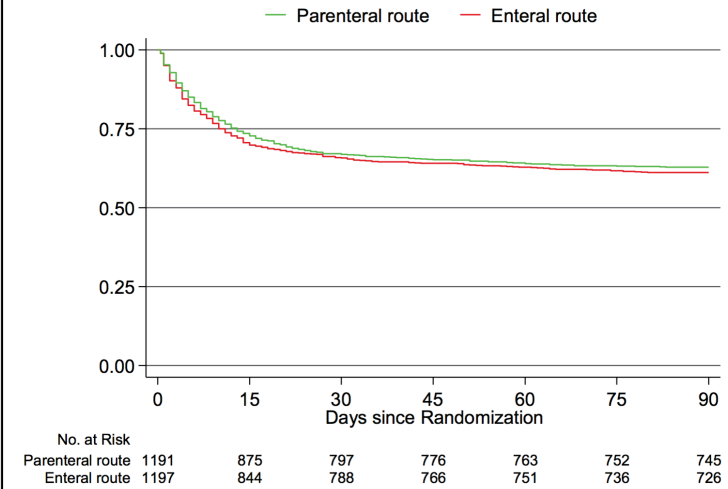
C Caloric Intake



Moins d'hypoglycémie et de vomissements avec NPT

Aucune différence sur:

- Infections (tous types)
- Ischémies digestives
- Durées de séjour
- Mortalités (réa, hospital...)



The LANCET 2017

Enteral versus parenteral early nutrition in ventilated adults with shock: a randomised, controlled, multicentre, open-label, parallel-group study (NUTRIREA-2)

Jean Reignier, Julie Boisramé-Helms, Laurent Brisard, Jean-Baptiste Lascarrou, Ali Ait Hssain, Nadia Anguel, Laurent Argaud, Karim Asehnoune, Pierre Asfar, Frédéric Bellec, Vlad Botoc, Anne Bretagnol, Hoang-Nam Bui, Emmanuel Canet, Daniel Da Silva, Michael Darmon, Vincent Das, Jérôme Devaquet, Michel Djibre, Frédérique Ganster, Maité Garrouste-Orgeas, Stéphane Gaudry, Olivier Gontier, Claude Guérin, Bertrand Guidet, Christophe Guitton, Jean-Etienne Herbrecht, Jean-Claude Lacherade, Philippe Letocart, Frédéric Martino, Virginie Maxime, Emmanuelle Mercier, Jean-Paul Mira, Saad Nseir, Gael Piton, Jean-Pierre Quenot, Jack Richecoeur, Jean-Philippe Rigaud, René Robert, Nathalie Rolin, Carole Schwebel, Michel Sirodot, François Tinturier, Didier Thévenin, Bruno Giraudeau, Amélie Le Gouge, for the NUTRIREA-2 Trial Investigators and the Clinical Research in Intensive Care and Sepsis (CRICS) group

Enteral versus parenteral early nutrition in ventilated adults with shock: a randomised, controlled, multicentre, open-label, parallel-group study (NUTRIREA-2)

Jean Reignier, Julie Boisramé-Helms, Laurent Brisard, Jean-Baptiste Lascarrou, Ali Ait Hssain, Nadia Anguel, Laurent Argaud, Karim Asehnoune, Pierre Asfar, Frédéric Bellec, Vlad Botoc, Anne Bretagnol, Hoang-Nam Bui, Emmanuel Canet, Daniel Da Silva, Michael Darmon, Vincent Das, Jérôme Devaquet, Michel Djibre, Frédérique Ganster, Maité Garrouste-Orgeas, Stéphane Gaudry, Olivier Gontier, Claude Guérin, Bertrand Guidet, Christophe Guitton, Jean-Etienne Herbrecht, Jean-Claude Lacherade, Philippe Letocart, Frédéric Martino, Virginie Maxime, Emmanuelle Mercier, Jean-Paul Mira, Saad Nseir, Gael Piton, Jean-Pierre Quenot, Jack Richecoeur, Jean-Philippe Rigaud, René Robert, Nathalie Rolin, Carole Schwebel, Michel Sirodot, François Tinturier, Didier Thévenin, Bruno Girardeau, Amélie Le Gouge, for the NUTRIREA-2 Trial Investigators and the Clinical Research in Intensive Care and Sepsis (CRICS) group

Essai de supériorité contrôlé randomisé multicentrique réalisé en ouvert

Objectif

Démontrer qu'une stratégie prévoyant une **nutrition entérale précoce en première intention** diminue la mortalité à J28 toutes causes confondues par rapport à une stratégie prévoyant une nutrition parentérale précoce en première intention.

Enteral versus parenteral early nutrition in ventilated adults with shock: a randomised, controlled, multicentre, open-label, parallel-group study (NUTRIREA-2)

Jean Reignier, Julie Boisramé-Helms, Laurent Brisard, Jean-Baptiste Lascarrou, Ali Ait Hssain, Nadia Anguel, Laurent Argaud, Karim Asehnoune, Pierre Asfar, Frédéric Bellec, Vlad Botoc, Anne Bretagnol, Hoang-Nam Bui, Emmanuel Canet, Daniel Da Silva, Michael Darmon, Vincent Das, Jérôme Devaquet, Michel Djibre, Frédérique Ganster, Maité Garrouste-Orgeas, Stéphane Gaudry, Olivier Gontier, Claude Guérin, Bertrand Guidet, Christophe Guitton, Jean-Etienne Herbrecht, Jean-Claude Lacherade, Philippe Letocart, Frédéric Martino, Virginie Maxime, Emmanuelle Mercier, Jean-Paul Mira, Saad Nseir, Gael Piton, Jean-Pierre Quenot, Jack Richecoeur, Jean-Philippe Rigaud, René Robert, Nathalie Rolin, Carole Schwebel, Michel Sirodot, François Tinturier, Didier Thévenin, Bruno Giraudeau, Amélie Le Gouge, for the NUTRIREA-2 Trial Investigators and the Clinical Research in Intensive Care and Sepsis (CRICS) group

Critères d'inclusion

- Patients sous **ventilation mécanique invasive** pour une durée prévisible d'au moins 48 heures
- **Traitement par amine(s) vasoactive(s)** (adrénaline, dobutamine ou noradrénaline) administré par un cathéter veineux central
- Nutrition artificielle pouvant être débutée dans les 24 heures suivant l'intubation (ou l'admission en réanimation si patient intubé avant entrée en réanimation)

Enteral versus parenteral early nutrition in ventilated adults with shock: a randomised, controlled, multicentre, open-label, parallel-group study (NUTRIREA-2)

Jean Reignier, Julie Boisramé-Helms, Laurent Brisard, Jean-Baptiste Lascarrou, Ali Ait Hssain, Nadia Anguel, Laurent Argaud, Karim Asehnoune, Pierre Asfar, Frédéric Bellec, Vlad Botoc, Anne Bretagnol, Hoang-Nam Bui, Emmanuel Canet, Daniel Da Silva, Michael Darmon, Vincent Das, Jérôme Devaquet, Michel Djibre, Frédérique Ganster, Maité Garrouste-Orgeas, Stéphane Gaudry, Olivier Gontier, Claude Guérin, Bertrand Guidet, Christophe Guitton, Jean-Etienne Herbrecht, Jean-Claude Lacherade, Philippe Letocart, Frédéric Martino, Virginie Maxime, Emmanuelle Mercier, Jean-Paul Mira, Saad Nseir, Gael Piton, Jean-Pierre Quenot, Jack Richecoeur, Jean-Philippe Rigaud, René Robert, Nathalie Rolin, Carole Schwebel, Michel Sirodot, François Tinturier, Didier Thévenin, Bruno Giraudeau, Amélie Le Gouge, for the NUTRIREA-2 Trial Investigators and the Clinical Research in Intensive Care and Sepsis (CRICS) group

Critères de non-inclusion

- Ventilation mécanique invasive débutée depuis plus de 24 heures
- Chirurgie digestive récente (<1 mois)
- Antécédents de gastrectomie, oesophagectomie, duodéno-pancréatectomie, bypass ou anneaux gastriques, syndrome du grêle court
- Présence d'une gastrostomie ou jéjunostomie

Enteral versus parenteral early nutrition in ventilated adults with shock: a randomised, controlled, multicentre, open-label, parallel-group study (NUTRIREA-2)

Jean Reignier, Julie Boisramé-Helms, Laurent Brisard, Jean-Baptiste Lascarrou, Ali Ait Hssain, Nadia Anguel, Laurent Argaud, Karim Asehnoune, Pierre Asfar, Frédéric Bellec, Vlad Botoc, Anne Bretagnol, Hoang-Nam Bui, Emmanuel Canet, Daniel Da Silva, Michael Darmon, Vincent Das, Jérôme Devaquet, Michel Djibre, Frédérique Ganster, Maité Garrouste-Orgeas, Stéphane Gaudry, Olivier Gontier, Claude Guérin, Bertrand Guidet, Christophe Guitton, Jean-Etienne Herbrecht, Jean-Claude Lacherade, Philippe Letocart, Frédéric Martino, Virginie Maxime, Emmanuelle Mercier, Jean-Paul Mira, Saad Nseir, Gael Piton, Jean-Pierre Quenot, Jack Richecoeur, Jean-Philippe Rigaud, René Robert, Nathalie Rolin, Carole Schwebel, Michel Sirodot, François Tinturier, Didier Thévenin, Bruno Giraudeau, Amélie Le Gouge, for the NUTRIREA-2 Trial Investigators and the Clinical Research in Intensive Care and Sepsis (CRICS) group

2 bras parallèles :

➤ **Entéral : NE exclusive J0 - J7**

➤ **Parentéral : NPT exclusive J0 - J3 puis relais par NE si état de choc résolutif**

Phase contrôle = Phase aigüe de prise en charge en réanimation (J0 – J7)

A partir de J8 : NE pour chaque groupe +/- NPT complémentaire

Patient intubé et ventilé ou, si déjà intubé, admis en réanimation depuis moins de 24 heures, traité par amine vasoactive, sans critère d'exclusion

RANDOMISATION = J0

Groupe NPT (Mélange ternaire habituel du service)
Débuter d'emblée à 20-25 kcal/kg/j
+ Oligoéléments et vitamines
Pas de L-Glutamine

Groupe NE (soluté iso-calorique habituel du service)
Débuter d'emblée à 20-25 kcal/kg/j

J1

J2

J3

EVALUATION APRÈS 72 HEURES DE NPT

J4

Arrêt des amine(s) vasoactive(s) pendant 24h consécutives
ET taux de lactates artériels < 2 mmol/L
ET voie entérale utilisable

J5

NON

OUI

RÉÉVALUATION QUOTIDIENNE

J6

Poursuite de la NPT
(20 kcal/kg/j)

**Arrêt NPT et
instauration NE**
(20 kcal/kg/j)

J7

J8

Arrêt de la NPT

- Nutrition entérale : 25-30 Kcal/kg et par jour.
- NPT de complément autorisée si intolérance persistante à la NE

J8

Surveillance de la NE
(cf. protocole d'intolérance : Annexe 1)

J Extubation = Fin d'étude

Surveillance de la NE

(cf. protocole d'intolérance : Annexe 1)

Pas de NPT de complément

sauf apparition d'une pathologie digestive contre-indiquant de façon absolue et prolongée la nutrition entérale.

NUTRIREA2

Critères de jugement secondaires

Complications infectieuses

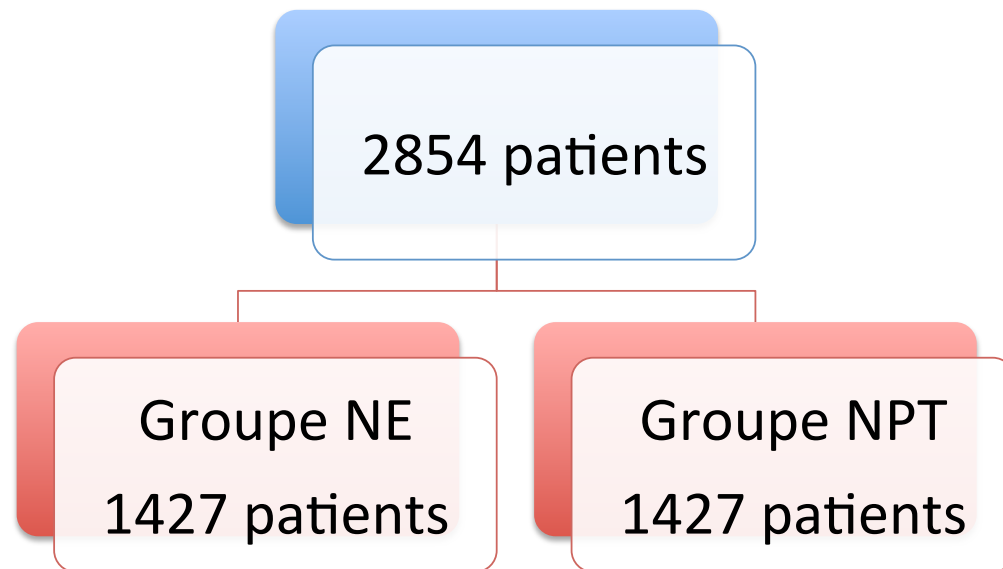
- PAVM (→ Comité d'adjudication)
- Bactériémies
- Infections sur cathéter veineux centraux
- Infections urinaires
- Infections des tissus mous
- Autre infection nosocomiale

Complications non infectieuses

- Ischémies digestives (critères diagnostiques préétablis)
- Pseudo-occlusions coliques
- Vomissements
- Diarrhées
- Hypoglycémies

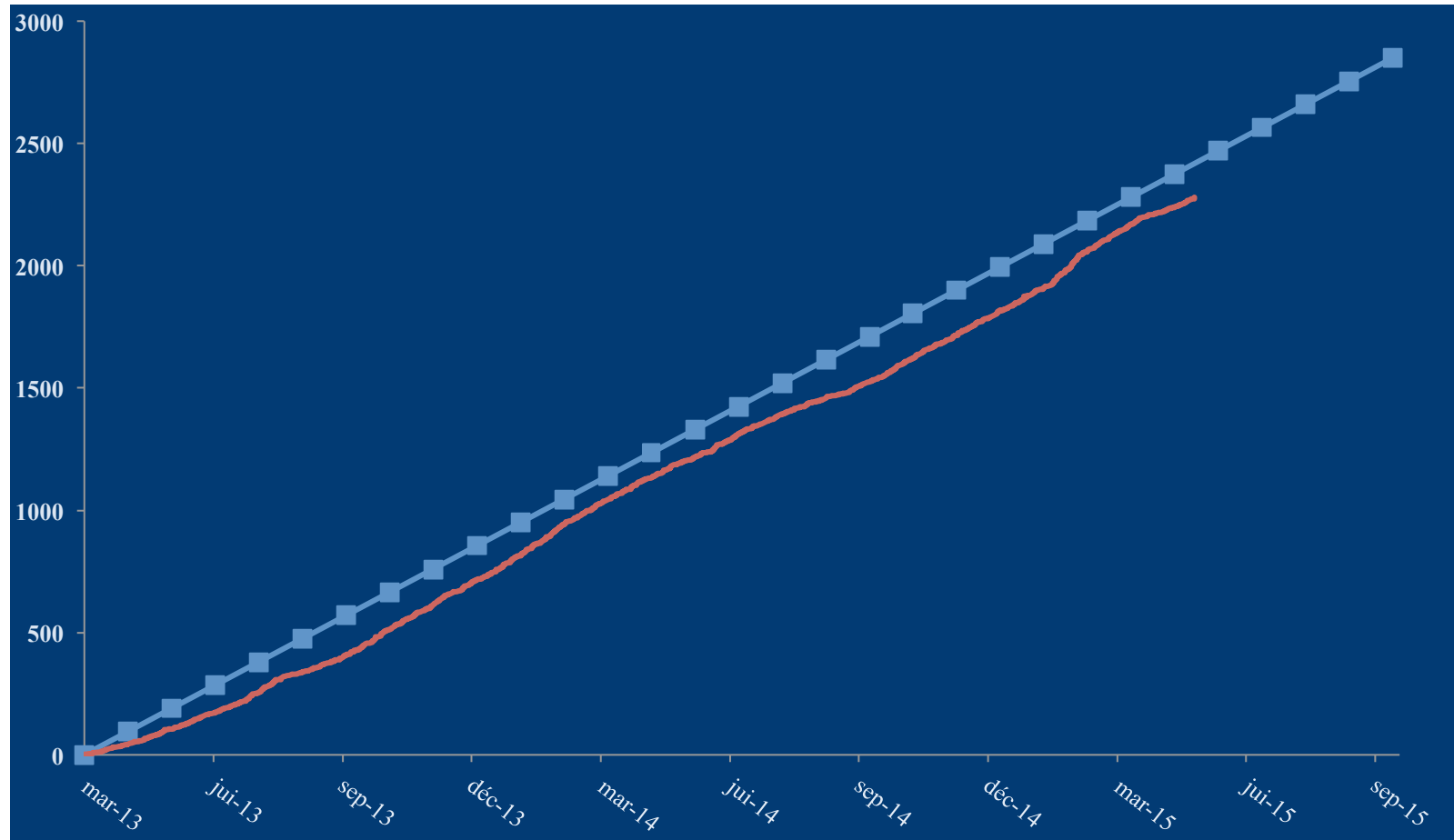
NUTRIREA2

- **Diminution de la mortalité à J28 de 5%**
 - Bras contrôle (NPT) : 37%
 - Bras interventionnel (NE précoce): 32 %
 - Risque $\alpha = 0,049$
 - Risque $\beta = 0,20$



- Deux analyses intermédiaires (n = 1000 et n = 2000)

- Inclusions du 22 mars 2013 au 30 juin 2015.



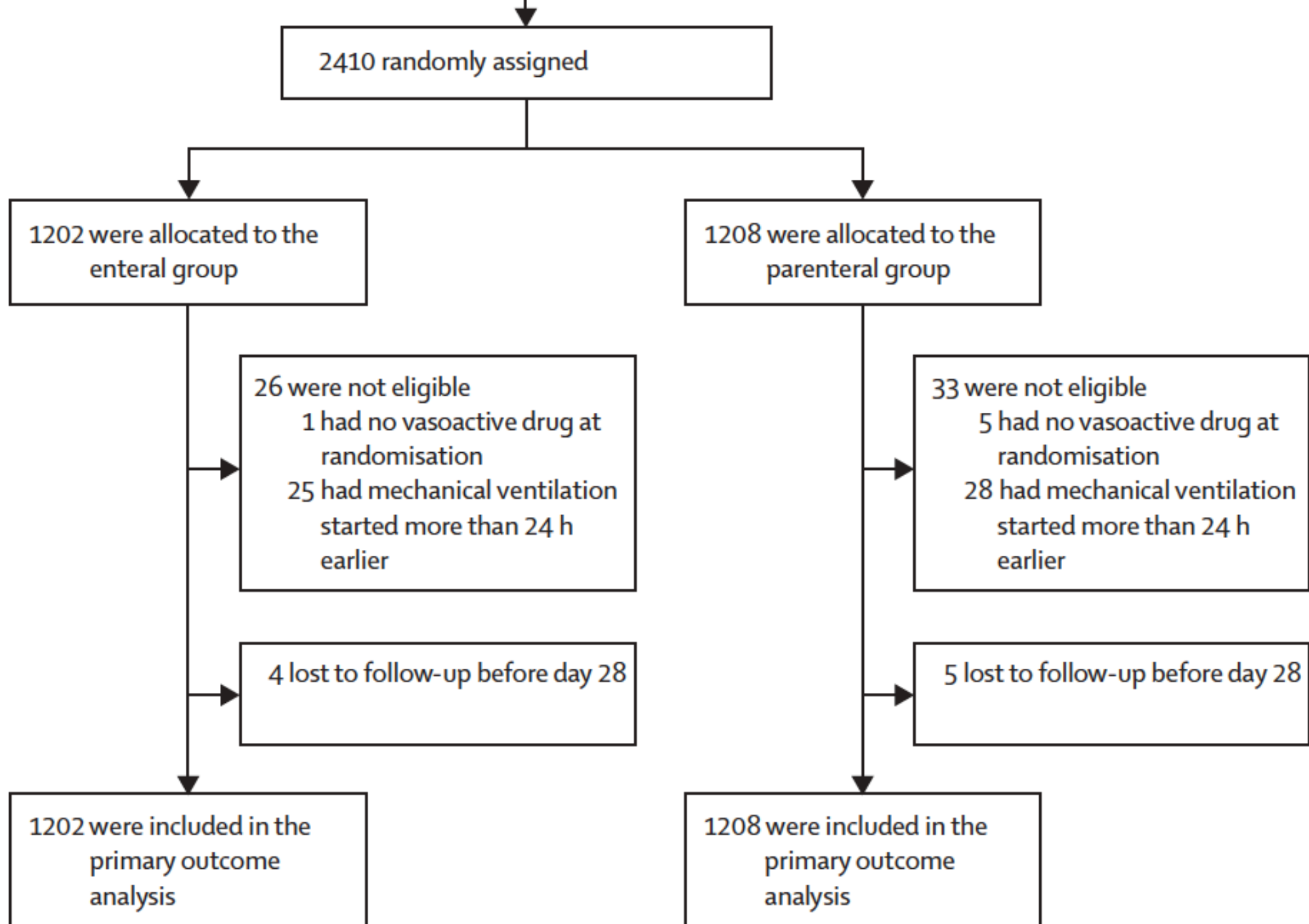
- Décision d'arrêt avec la 2^{ème} analyse intermédiaire sur préconisation du comité indépendant « pour futilité ».

10855 patients treated with mechanical ventilation and vasoactive drugs for shock within 24 h after ICU admission were assessed for eligibility

8445 were not eligible

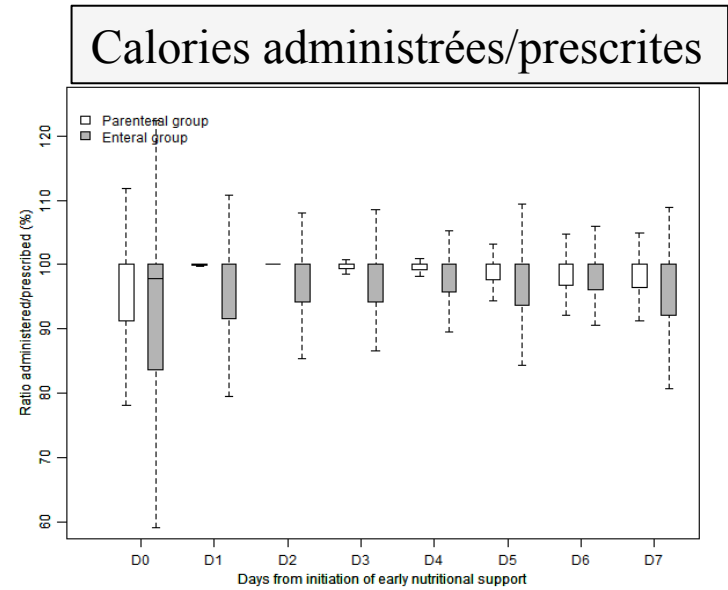
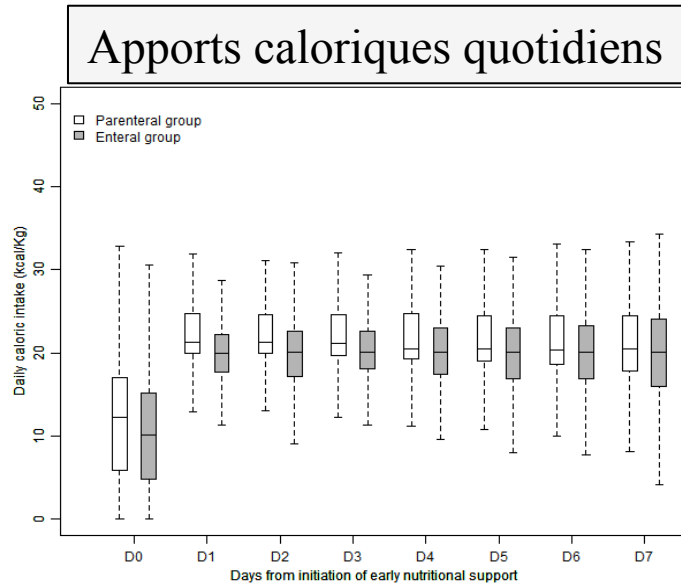
- 5995 had exclusion criteria
 - 747 had mechanical ventilation started more than 24 h earlier
 - 2828 had treatment-limitation decisions
 - 1472 had abdominal surgery within the past month
 - 395 had active gastrointestinal bleeding
 - 199 had previous digestive surgery*
 - 197 had pre-existing artificial nutrition
 - 113 had pre-existing gastrostomy or jejunostomy
 - 26 had previous intolerance to parenteral nutrition
 - 18 women were pregnant
- 2450 were eligible but not randomised
 - 1412 patients or relatives could not receive information about the study or refused to participate
 - 539 were inadvertently omitted from the study inclusion process
 - 243 did not have research staff available in time
 - 122 were excluded by the clinician
 - 93 were enrolled in another trial
 - 22 had study organisation problems
 - 19 had failed attempts to introduce the nasogastric tube

2410 randomly assigned

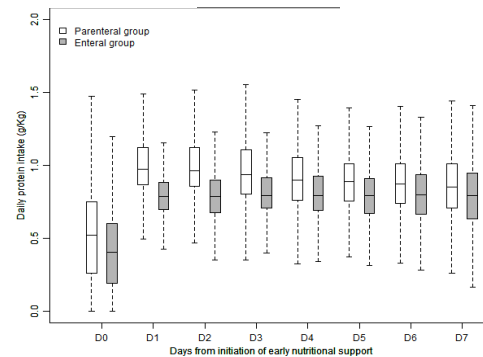


	Enteral group (n=1202)	Parenteral group (n=1208)
Age (y)	66 ± 14	66 ± 14
Male sex, n (%)	809 (67.3)	815 (67.5)
Preexisting illness at ICU admission, n (%)	869 (72.3)	880 (72.8)
Weight (Kg)	79.4 ± 20.5	79.2 ± 20.3
BMI (Kg/m ²)	28.0 ± 7.2	27.7 ± 6.8
SAPS II	59 ± 19	61 ± 20
SOFA at baseline	11±3	11±3
Medical diagnosis at admission, n (%)	1104 (92.0)	1127 (93.4)
Acute illness at ICU admission, n (%)		
Cardiac arrest	121 (10.1)	137 (11.4)
Acute heart failure	259 (21.6)	228 (18.9)
Acute central nervous failure	94 (7.8)	91 (7.5)
Acute respiratory failure	589 (49.1)	613 (50.8)
Trauma	27 (2.3)	25 (2.1)
Miscellaneous	110 (9.2)	112 (9.3)
Cause of choc		
Cardiac	229 (19.1)	227 (18.8)
Sepsis	728 (60.7)	776 (64.3)
Non septic SIRS	88 (7.3)	79 (6.6)
Other	155 (12.9)	124 (10.3)
Ongoing treatments, n (%)		
Prone position	44 (3.7)	59 (4.9)
Sedative agents	1038 (86.5)	1036 (86.0)
NMB agents	351 (29.3)	357 (29.6)
Insulin	469 (39.1)	482 (40.0)
Anti-ulcer medication	485 (40.4)	531 (44.1)
Prokinetic agents *	27 (2.3)	15 (1.2)
Anti-infectious treatment	1012 (84.3)	1000 (82.9)
Dialysis	189 (15.8)	183 (15.2)
FiO ₂	55 ± 23	55 ± 23
PEP (cmH ₂ O)	7±3	7±3
Serum creatinine (µmol/l)	189.4 ± 168.2	190.4 ± 156.9
Lactate (mEq/L)	3.8 ± 3.5	3.9 ± 3.5
Time from intubation to randomization (hrs), median [IQR]	15 [7 ; 20]	15 [7 ; 21]

	Enteral group (n=1202)	Parenteral group (n=1208)	Hazard Ratio (95% CI)	P value
Days with parenteral nutrition				
Median [IQR]	0.0 [0.0 ; 0.0]	4.0 [3.0 ; 6.0]		<.001
Days with enteral nutrition				
Median [IOR]	6.0 [3.0 ; 8.0]	1.0 [0.0 ; 3.0]		<.001
Daily amount of calories received (kcal/kg/24h)	17.8 ± 5.5	19.6 ± 5.3		<.001
Daily amount of proteins administered (g/kg24h)	0.7 ± 0.2	0.8 ± 0.2		<.001



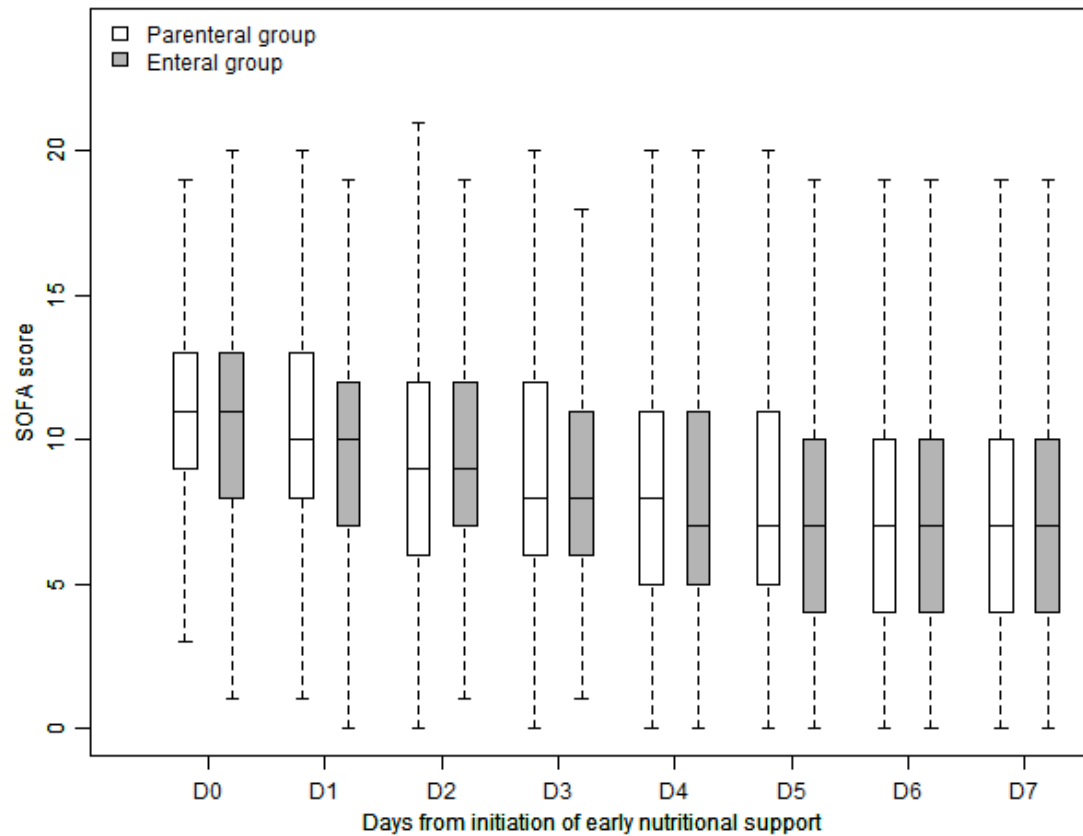
Apports
protéiques
quotidiens



	Enteral group (n=1202)	Parenteral group (n=1208)	Hazard Ratio (95% CI)	P value
Days with parenteral nutrition				
Median [IQR]	0.0 [0.0 ; 0.0]	4.0 [3.0 ; 6.0]		<.001
Days with enteral nutrition				
Median [IQR]	6.0 [3.0 ; 8.0]	1.0 [0.0 ; 3.0]		<.001
Daily amount of calories received (kcal/kg/24h)	17.8 ± 5.5	19.6 ± 5.3		<.001
Daily amount of proteins administered (g/kg24h)	0.7 ± 0.2	0.8 ± 0.2		<.001
Vomiting				
N of patients (%)	33/1202 (27.7)	158 /1208 (13.1)	2.37 [1.97; 2.84]	<.001
Absence of stool				
N patients/total (%)	154/1202 (12.8)	273/1208 (22.6)		<.001
Insulin				
N patients/total (%)	954/1202 (79.4)	995/1208 (82.4)	0.93 [0.87;0.98]	.009
Hypoglycemia				
N patients/total (%)	29/1202 (2.4)	13/1208 (1.1)	2.26 [1.18;4.33]	.01
Normalization of the blood lactate level				
N patients/total (%)	743/1202 (61.8)	797/1208 (65.9)		.03
Blood Bilirubinemia level, µmol/l				
Median daily highest [IQR]	16.0 [9.0 ; 31.0]	17.0 [9.0 ; 36.0]		.26
Blood alanine aminotransferase level, UI/L				
Median daily highest [IQR]	66 [33 ; 171]	71 [34 ; 185]		.39
Blood aspartate aminotransferase level, UI/L				
Median daily highest [IQR]	37 [23 ; 69]	38.0 [23 ; 69]		.94
Patients receiving antiulcer prophylaxis				
N patients/total (%)	809/1202 (67.3)	883/1208 (73.1)	0.90 [0.84; 0.97]	.005
Anti-infectious treatment				
N patients/total (%)	1147/1202 (95.4)	1132/1208 (93.7)	1.03 [0.99; 1.07]	.07
Prone position				
N patients/total (%)	161/1202 (13.4)	144/1208 (11.9)	1.12 [0.89; 0.90]	.30
Dialysis				
N patients/total (%)	407/1202 (33.9)	410/1208 (34.7)	0.97 [0.86; 1.10]	.67

	Enteral group (n=1202)	Parenteral group (n=1208)	Hazard Ratio (95% CI)	P value
Days with parenteral nutrition				
Median [IQR]	0.0 [0.0 ; 0.0]	4.0 [3.0 ; 6.0]		<.001
Days with enteral nutrition				
Median [IQR]	6.0 [3.0 ; 8.0]	1.0 [0.0 ; 3.0]		<.001
Daily amount of calories received (kcal/kg/24h)	17.8 ± 5.5	19.6 ± 5.3		<.001
Daily amount of proteins administered (g/kg/24h)	0.7 ± 0.2	0.8 ± 0.2		<.001
Vomiting				
N of patients (%)	33/1202 (27.7)	158 /1208 (13.1)	2.37 [1.97; 2.84]	<.001
Absence of stool				
N patients/total (%)	154/1202 (12.8)	273/1208 (22.6)		<.001
Insulin				
N patients/total (%)	954/1202 (79.4)	995/1208 (82.4)	0.93 [0.87; 0.98]	.009
Hypoglycemia				
N patients/total (%)	29/1202 (2.4)	13/1208 (1.1)	2.26 [1.18; 4.33]	.01
Normalization of the blood lactate level				
N patients/total (%)	743/1202 (61.8)	797/1208 (65.9)		.03
Blood Bilirubinemia level, µmol/l				
Median daily highest [IQR]	16.0 [9.0 ; 31.0]	17.0 [9.0 ; 36.0]		.26
Blood alanine aminotransferase level, UI/L				
Median daily highest [IQR]	66 [33 ; 171]	71 [34 ; 185]		.39
Blood aspartate aminotransferase level, UI/L				
Median daily highest [IQR]	37 [23 ; 69]	38.0 [23 ; 69]		.94
Patients receiving anti-tumor prophylaxis				
N patients/total (%)	809/1202 (67.3)	883/1208 (73.1)	0.90 [0.84; 0.97]	.005
Anti-infectious treatment				
N patients/total (%)	1147/1202 (95.4)	1132/1208 (93.7)	1.03 [0.99; 1.07]	.07
Prone position				
N patients/total (%)	161/1202 (13.4)	144/1208 (11.9)	1.12 [0.89; 0.90]	.30
Dialysis				
N patients/total (%)	407/1202 (33.9)	410/1208 (33.9)	0.97 [0.86; 1.10]	.67

SOFA J0-J7



	Enteral group (n=1202)	Parenteral group (n=1208)	Hazard Ratio (95% CI)	P value
Days with parenteral nutrition				
Median [IQR]	0.0 [0.0 ; 0.0]	4.0 [3.0 ; 6.0]		<.001
Days with enteral nutrition				
Median [IQR]	6.0 [3.0 ; 8.0]	1.0 [0.0 ; 3.0]		<.001
Daily amount of calories received (kcal/kg/24h)	17.8 ± 5.5	19.6 ± 5.3		<.001
Daily amount of proteins administered (g/kg24h)	0.7 ± 0.2	0.8 ± 0.2		<.001
Vomiting				
N of patients (%)	33/1202 (27.7)	158 /1208 (13.1)	2.37 [1.97; 2.84]	<.001
Absence of stool				
N patients/total (%)	154/1202 (12.8)	273/1208 (22.6)		<.001
Insulin				
N patients/total (%)	954/1202 (79.4)	995/1208 (82.4)	0.93 [0.87; 0.98]	.009
Hypoglycemia				
N patients/total (%)	29/1202 (2.4)	13/1208 (1.1)	2.26 [1.18; 4.33]	.01
Normalization of the blood lactate level				
N patients/total (%)	743/1202 (61.8)	797/1208 (65.9)		.03
Blood bilirubinemia level, µmol/l				
Median daily highest [IQR]	16.0 [9.0 ; 31.0]	17.0 [9.0 ; 36.0]		.26
Blood alanine aminotransferase level, UI/L				
Median daily highest [IQR]	66 [33 ; 171]	71 [34 ; 185]		.39
Blood aspartate aminotransferase level, UI/L				
Median daily highest [IQR]	37 [23 ; 69]	38.0 [23 ; 69]		.94
Patients receiving antiulcer prophylaxis				
N patients/total (%)	809/1202 (67.3)	883/1208 (73.1)	0.90 [0.84; 0.97]	.005
Anti-infectious treatment				
N patients/total (%)	1147/1202 (95.4)	1132/1208 (93.7)	1.03 [0.99; 1.07]	.07
Prone position				
N patients/total (%)	161/1202 (13.4)	144/1208 (11.9)	1.12 [0.89; 0.90]	.30
Dialysis				
N patients/total (%)	407/1202 (33.9)	419/1208 (34.7)	0.97 [0.86; 1.10]	.67

Critère de jugement principal: **Mortalité à J28**

Nutrition entérale

36.6% (439 / 1198 patients)

Nutrition parentérale

34.7% (417 / 1203 patients)

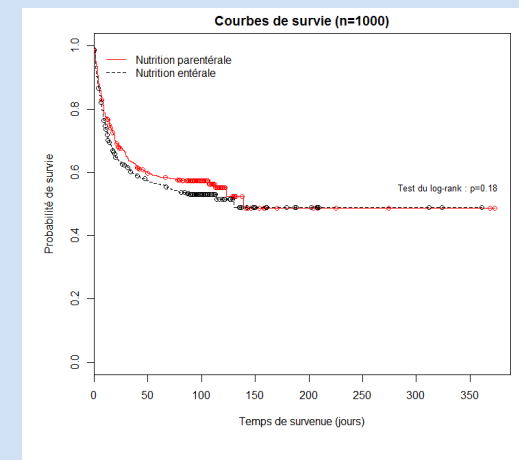
(difference, 2.1%; 95% [CI], -1.8% à 5.8%; **P=0.31**)

Analyses intermédiaires: mortalité à J28

À 1000 patients

Nutrition entérale (n=507)	Nutrition parentérale (n=493)	p
188/503 soit 37.4% [33.1% ; 41.6%]	164/492 soit 33.3% [29.2% ; 37.5%]	0.18

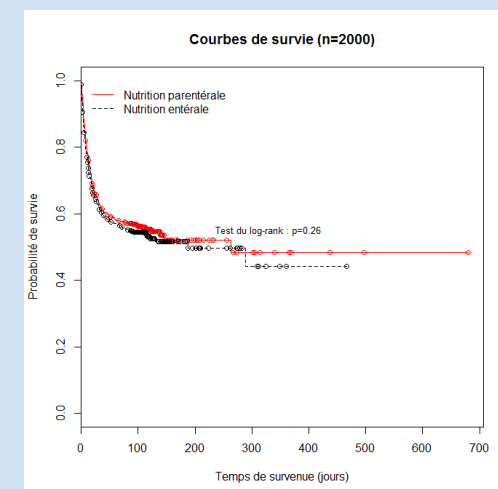
Différence (Entérale-Parentérale) = 4.1%, IC à 95% = [-1.9% ; 10.0%]



À 2000 patients

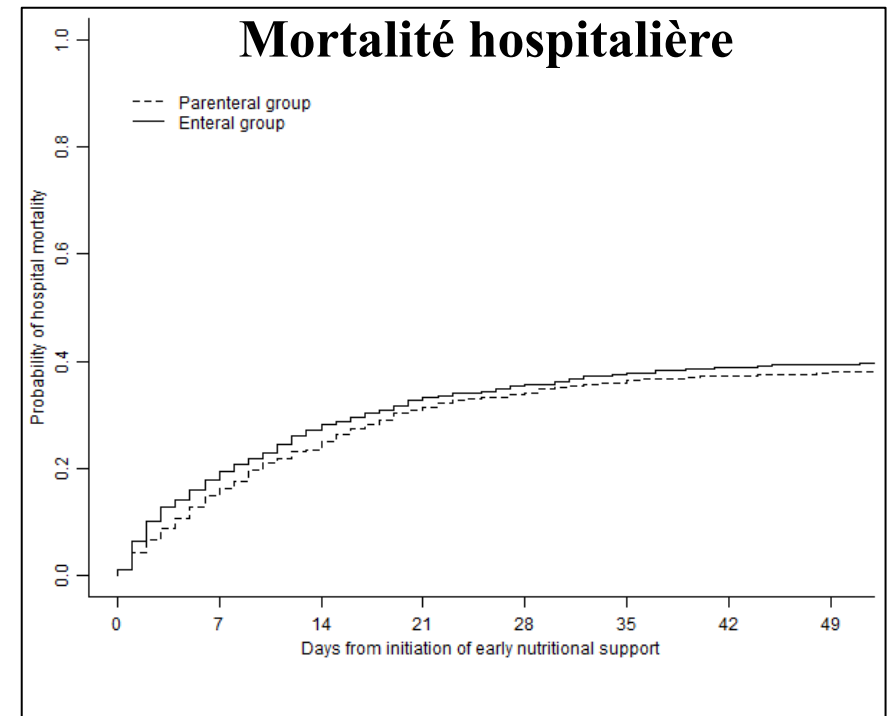
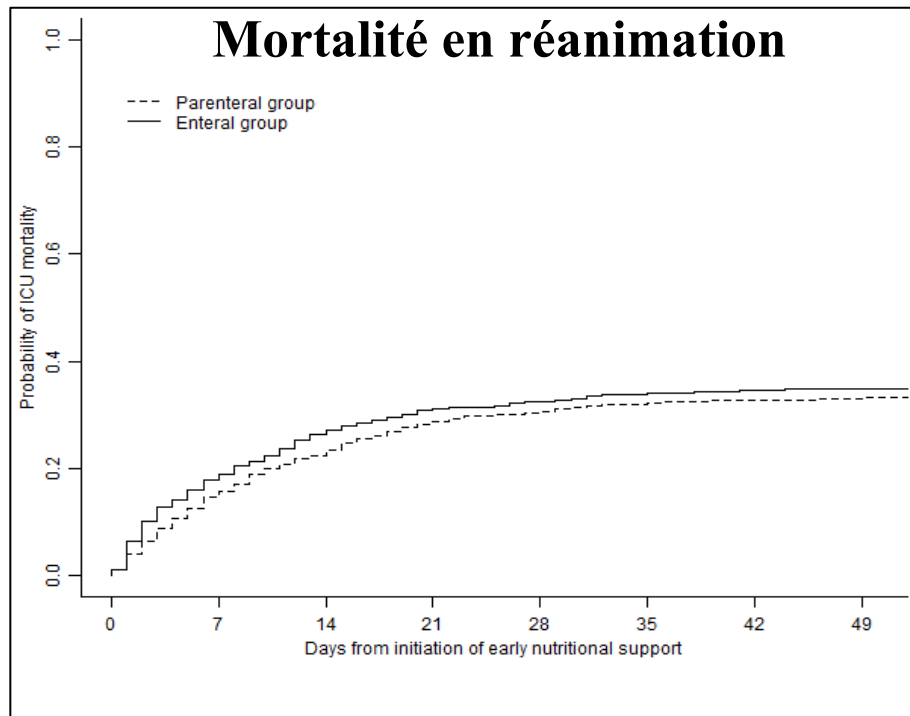
n=995	n=1005	p
365/985 soit 37.1% [34.0% ; 40.0%]	353/1001 soit 35.3% [32.3% ; 38.2%]	0.41

Différence (Entérale-Parentérale) = 1.8%, IC à 95% = [-2.4% ; 6.0%]

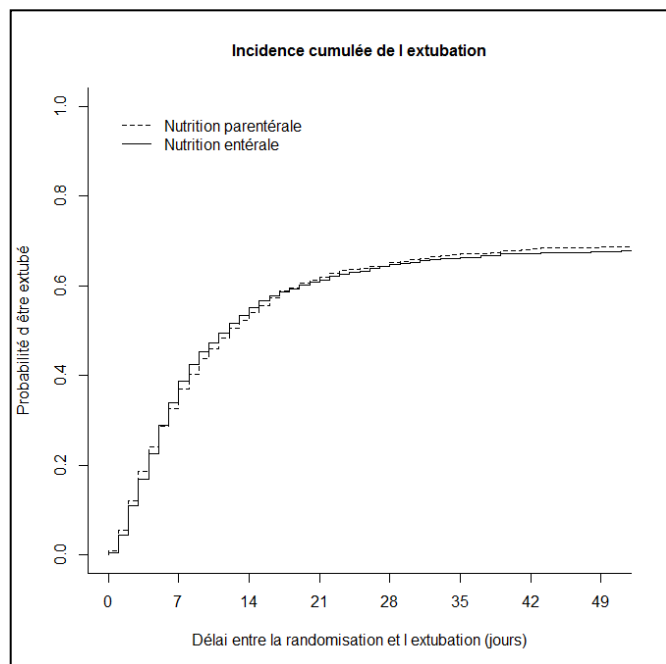


Critères secondaires : mortalité à J90

Nutrition entérale (n=1202)	Nutrition parentérale (n=1208)	Différence de proportion et IC à 95%	p
530/1185 44.7% [41.9% ; 47.6%]	507/1192 42.5% [39.7% ; 45.3%]	2.2% [-1.8% ; 6.2%]	0.28



Sevrage de la VM



Patients extubés vivants à J28:

- Entérale 64,8%
- Parentérale 65,2%

HR=0.99 ; IC à 95%=[0.90 ; 1.08], p=0.80

Durées de séjour	Nutrition entérale	Nutrition parentérale	p
en réanimation	9.0 [5.0 ; 16.0]	10.0 [5.0 ; 17.0]	0.08
à l'hôpital	17.0 [8.0 ; 32.0]	18.0 [9.0 ; 33.0]	0.11

Infections nosocomiales

	Nutrition entérale (n=1202)	Nutrition parentérale (n=1208)	HR (95% CI)	P value
ICU-acquired infection				
N patients/total (%)	173/1202 (14.4)	194/1208 (16.0)	0.89 [0.72; 1.09]	0.25
Ventilator-associated pneumonia				
N patients/total (%)	113/1202 (9.4)	118/1208 (9.8)	0.96 [0.74; 1.24]	0.75
Bacteriemia				
N patients/total (%)	38/1202 (3.2)	55/1208 (4.6)	0.69 [0.46; 1.04]	0.08
CVC-related infection				
N patients/total (%)	29/1202 (2.3)	27/1208 (2.3)	1.07 [0.64; 1.81]	0.79
Urinary infection				
N patients/total (%)	18/1202 (1.5)	16/1208 (1.3)	1.13 [0.58; 2.21]	0.73
Soft tissue infection				
N patients/total (%)	1/1202	6/1208		
Other infection				
N patients/total (%)	11/1202 (0.9)	21/1208 (1.7)	0.52 [0.25; 1.09]	0.08

Non infectious complications

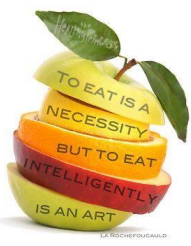
	Enteral group (n=1202)	Parenteral group (n=1208)	HR (95% CI)	P value
Vomiting (D28)				
N of patients (%)	406 (33.8)	246 (20.4)	1.89 [1.62; 2.20]	<0.001
Diarrhea (D28)				
N patients/total (%)	432/1202 (36.0)	393/1208 (32.6)	1.20 [1.05; 1.37]	0.009
Constipation (D6)				
N patients/total (%)	154/1202 (12.8)	273/1208 (22.6)		<0.001
Bowel ischemia (D28)				
N patients/total (%)	19/1202 (1.5)	5/1208 (0.3)	3.84 [1.43; 10.3]	0.007
Acute colonic pseudoobstruction (D28)				
N patients/total (%)	11/1202 (0.9)	3/1208 (0.2)	3.7 [1.03; 13.2]	0.04

Ischémies digestives

	Nutrition entérale (n=19)	Parentérale (n=5)
Délai entre la randomisation et la date de survenue de l'ischémie digestive, <i>jours</i>	4.0 [1.0 ; 12.0]	3.0 [1.0 ; 9.0]
Examen radiologique*	16 (84.2)	4 (80.0)
<i>Angio-TDM *</i>	14 (73.7)	4 (80.0)
<i>Artériographie*</i>	1 (5.3)	0 (0.0)
<i>Angio-RM *</i>	0 (0.0)	0 (0.0)
<i>Autre examen radiologique*</i>	1 (5.3)	0 (0.0)
Examen endoscopique*	7 (36.8)	2 (40.0)
<i>Rectosigmoidoscopie *</i>	2 (10.5)	0 (0.0)
<i>Colonoscopie *</i>	4 (21.1)	1 (20.0)
<i>Autre examen endoscopique *</i>	2 (10.5)	1 (20.0)
Traitement chirurgical	10 (52.6)	3 (60.0)

Médiane [Q1 ; Q3] pour les variables quantitatives et n (%) pour les variables qualitatives.

** Les patients ont pu avoir plusieurs examens (variables non exclusives).*



Conclusion

Pas de différence entre nutrition entérale et nutrition parentérale:

- Mortalité
- Complications infectieuses

Plus de complications digestives (Ischémie et pseudocclusion) avec la nutrition entérale

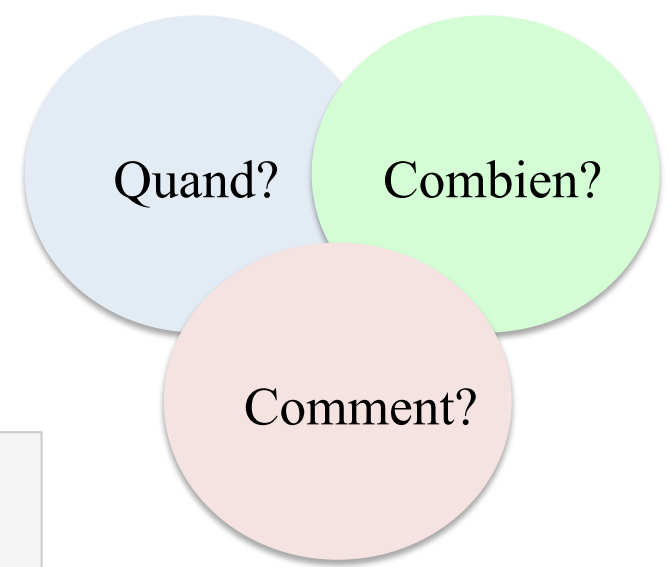
...chez le patient ventilé et traité par amine vasoactive pour état de choc

→ Contradiction avec les recommandations et études observationnelles antérieures

→ Pas de contradiction avec l'étude Calories

Impact of early nutrition and feeding route on outcomes of mechanically ventilated patients with shock: a post hoc marginal structural model study

Reignier, Intensive Care Med 2015



- 3032 patients with mechanical ventilation and shock (OutcomeRea)
- To assess associations linking early nutrition (EN and/or PN started within 48 h after intubation), feeding route and calorie intake to patients outcome.

- Early nutrition → reduced mortality

(HR, 0.89; 95% confidence interval [CI], 0.81-0.98; $P=0.01$)

- Feeding route → no impact

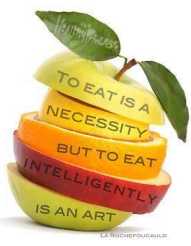
- Calorie intake → no impact

Question: Is EN safe during periods of hemodynamic instability in adult critically ill patients?

B5. Based on expert consensus, we suggest that in the setting of hemodynamic compromise or instability, EN should be withheld until the patient is fully resuscitated and/or stable. Initiation/re-initiation of EN may be considered with caution in patients undergoing withdrawal of vasopressor support.

→ **0 Kcal/kg/d ??**

Jusqu'à quand?



En pratique

Chez les patients ventilés et choqués:

→ préférer la nutrition parentérale à la phase aiguë (tant que la défaillance hémodynamique persiste pendant la 1^{ère} semaine)

Chez les patients ventilés non choqués:

→ pas de préférence.

Mais la nutrition parentérale n'est pas délétère+++ (et plus simple?)

→ En 1^{ère} intention chez le porteur d'un KT ?

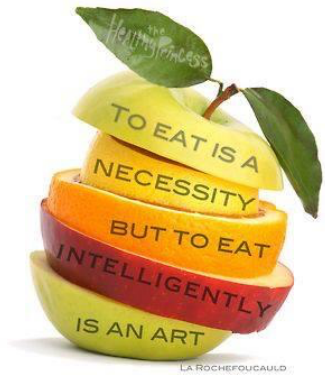
Pas de nutrition parentérale « de complément » si intolérance à la nutrition entérale choisie en 1^{ère} intention

Chez le patient non ventilé:

→ Nutrition orale

Chez le patient très grave?

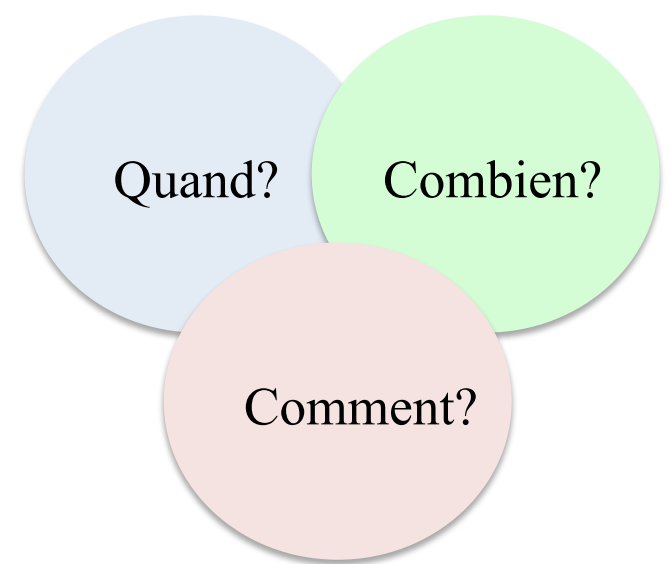
- Faut-il nourrir précocément les patients ou attendre que leur état soit stabilisé?
- Faut-il donner une nutrition « protectrice » pendant la phase aiguë?



Conclusions

- Il faut surement débiter la nutrition artificielle précocement après l'intubation (<24h)
- NUTRIREA2= seule étude à haut niveau preuve sur la nutrition du patient choqué
- Il faut peut-être privilégier la voie parentérale à la phase aigue chez les patients choqués.
- Le niveau des apports en macronutriments à la phase précoce reste à déterminer.

Le futur: NUTRIREA3



“Impact of Early Low-Calorie Low-Protein versus Standard-Calorie Standard-Protein Feeding on Outcomes of Patients Requiring Mechanical Ventilation and Catecholamines: A Multicentre, Randomised, Controlled Trial (NUTRIREA-3)”

The NUTRIREA-3 trial will focus on early calorie and protein targets in acute critical illness requiring MV and catecholamines for shock. Low-calorie low-protein feeding (6 kcal/kg/d; 0.4 g/kg/d) will be compared to normal-calorie normal-protein feeding (25 kcal/kg/d; 1.3g/kg/d) during the first ICU week.

Retenue au PHRCN 2017. Début des inclusions mai 2018.

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.)

Question: What are the protein and energy requirements for septic patients in the acute phase of management?

N4. Based on expert consensus, we suggest the provision of trophic feeding (defined as 10–20kcal/hr or up to 500 kcal/day) for the initial phase of sepsis, advancing as tolerated after 24–48 hours to > 80% of target energy goal over the first week. We suggest delivery of 1.2–2g protein/kg/day.

Surviving Sepsis Campaign: International Guidelines for Management of Sepsis and Septic Shock: 2016

We recommend **against the use of omega-3 fatty acids** as an immune supplement in critically ill patients with sepsis or septic shock (strong recommendation, low quality of evidence).

We recommend **against the use of IV selenium** to treat sepsis and septic shock (strong recommendation, moderate quality of evidence).

We suggest **against the use of arginine** to treat sepsis and septic shock (weak recommendation, low quality of evidence).

We recommend **against the use of glutamine** to treat sepsis and septic shock (strong recommendation, moderate quality of evidence).

We make **no recommendation about the use of carnitine** for sepsis and septic shock.