



Imunonutrição no Paciente Crítico: Evidências Atuais

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Imunonutrição

DEFINIÇÃO:

- Utilização clínica de nutrientes imunomoduladores

Nutrientes Imunomoduladores:

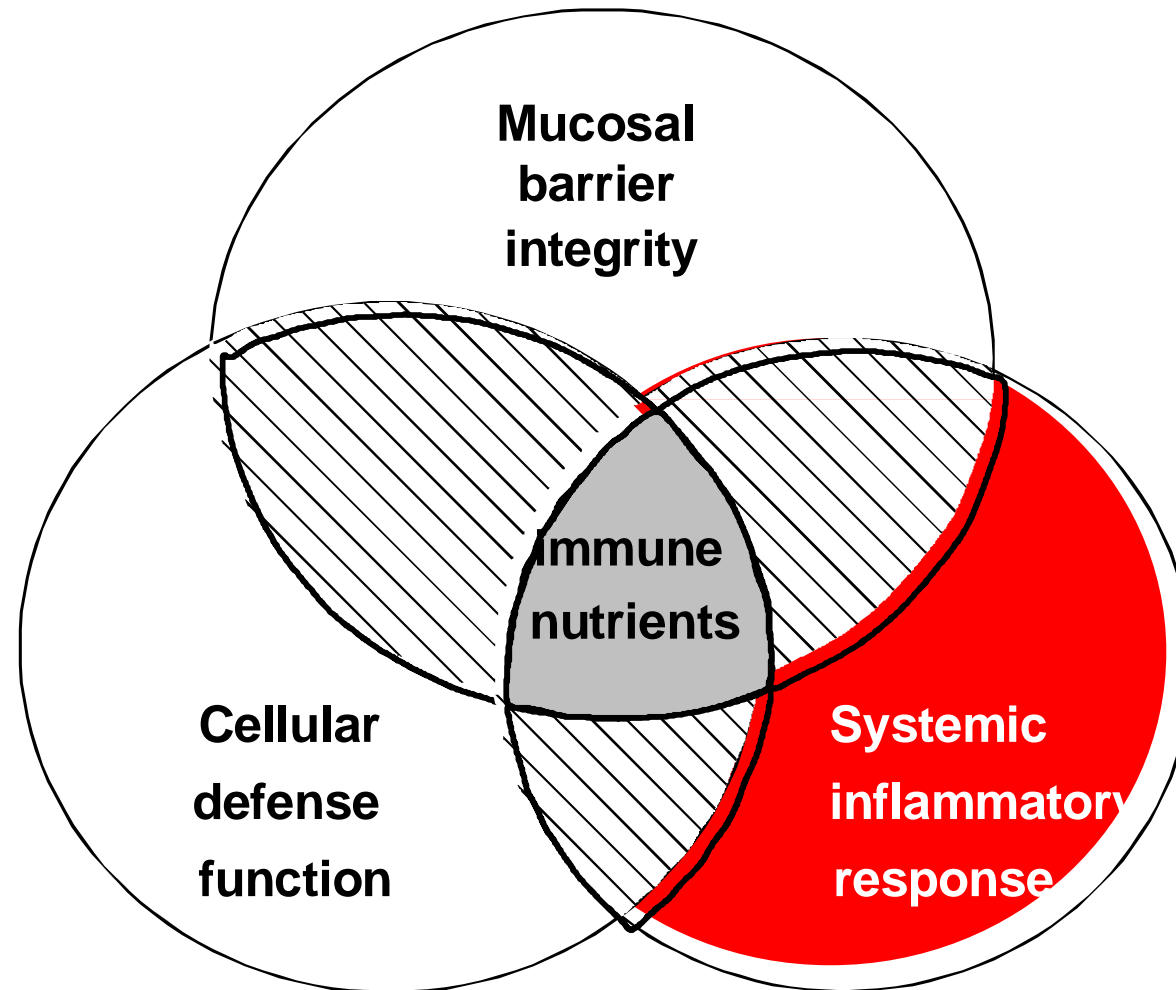
- São nutrientes que atuam na resposta imunológica , estimulando-a ou suprimindo-a dependendo da quantidade ingerida ou administrada.

Causas da Imunossupressão

- Desnutrição
- Cirurgias de grande porte
- Transfusão de sangue
- Transplantes
- Sepse
- Infecções pós-cirúrgicas
- Presença de Tumor

Áreas Integradas da Defesa Imune

Pontos de trabalho dos imunonutrientes



Nutrientes Immunomoduladores

3 Glutamina

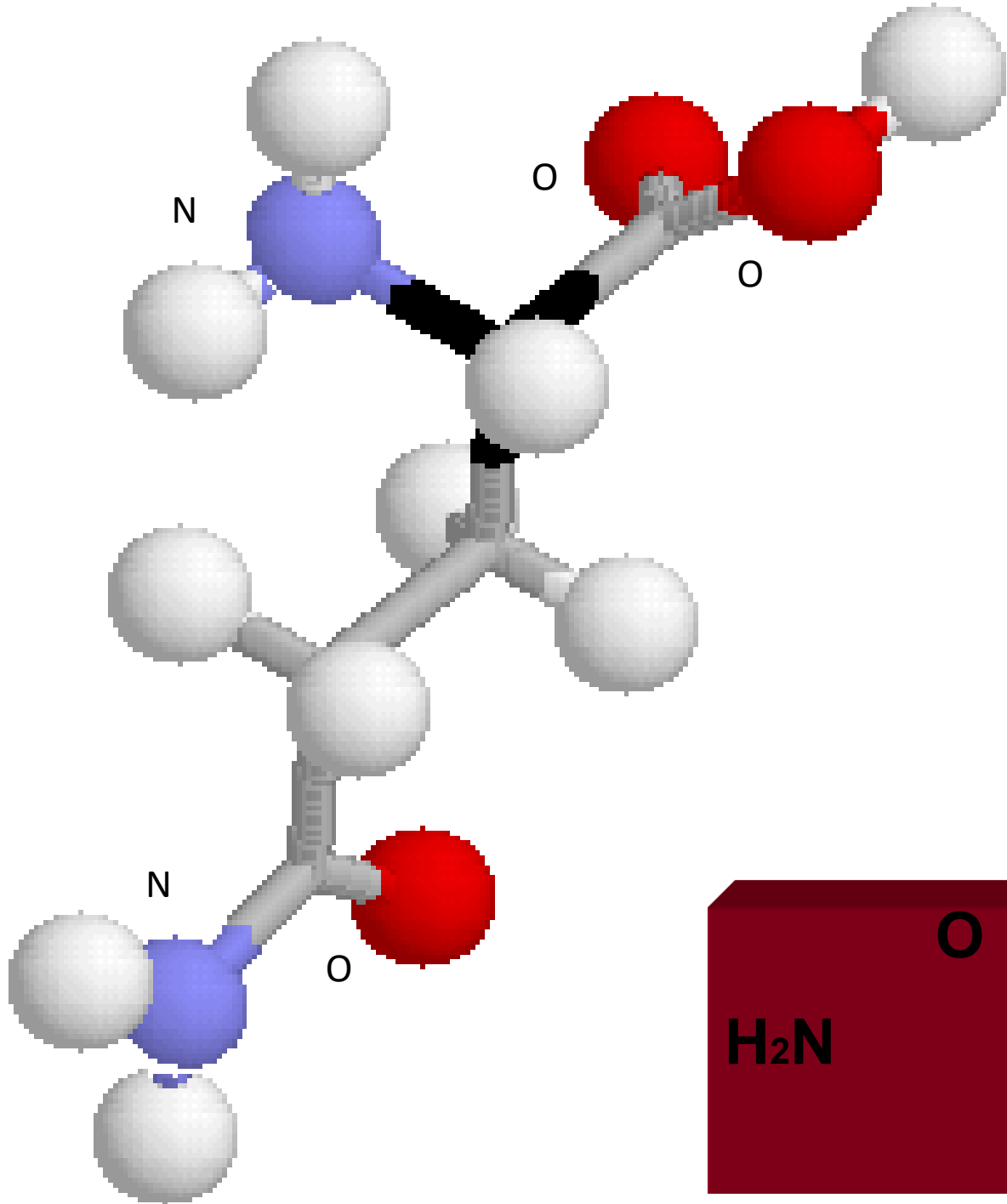
3 Fibras

3 Arginina

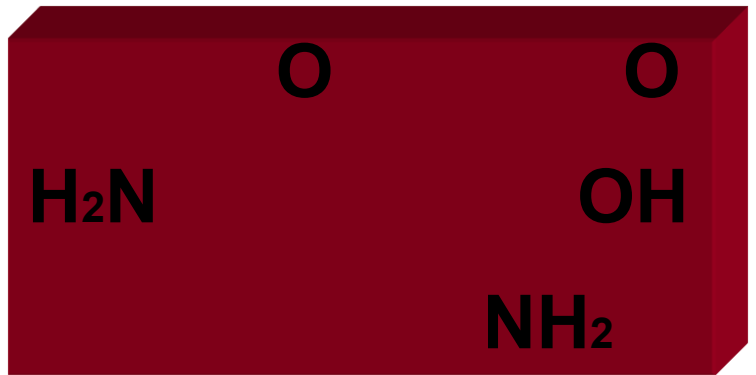
3 Nucleotídeos

3 w-3/w-6

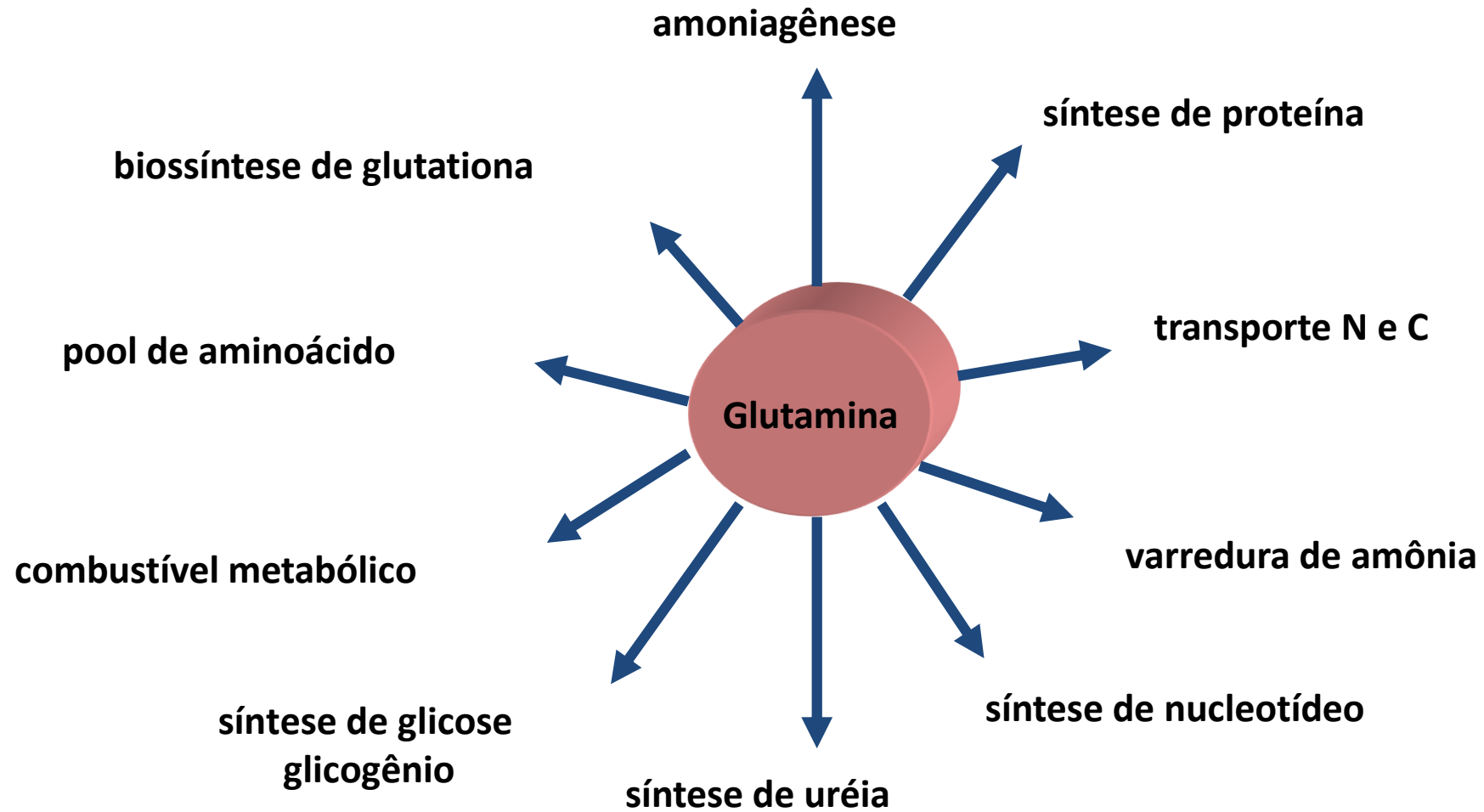
“Pacote Immunomodulador”



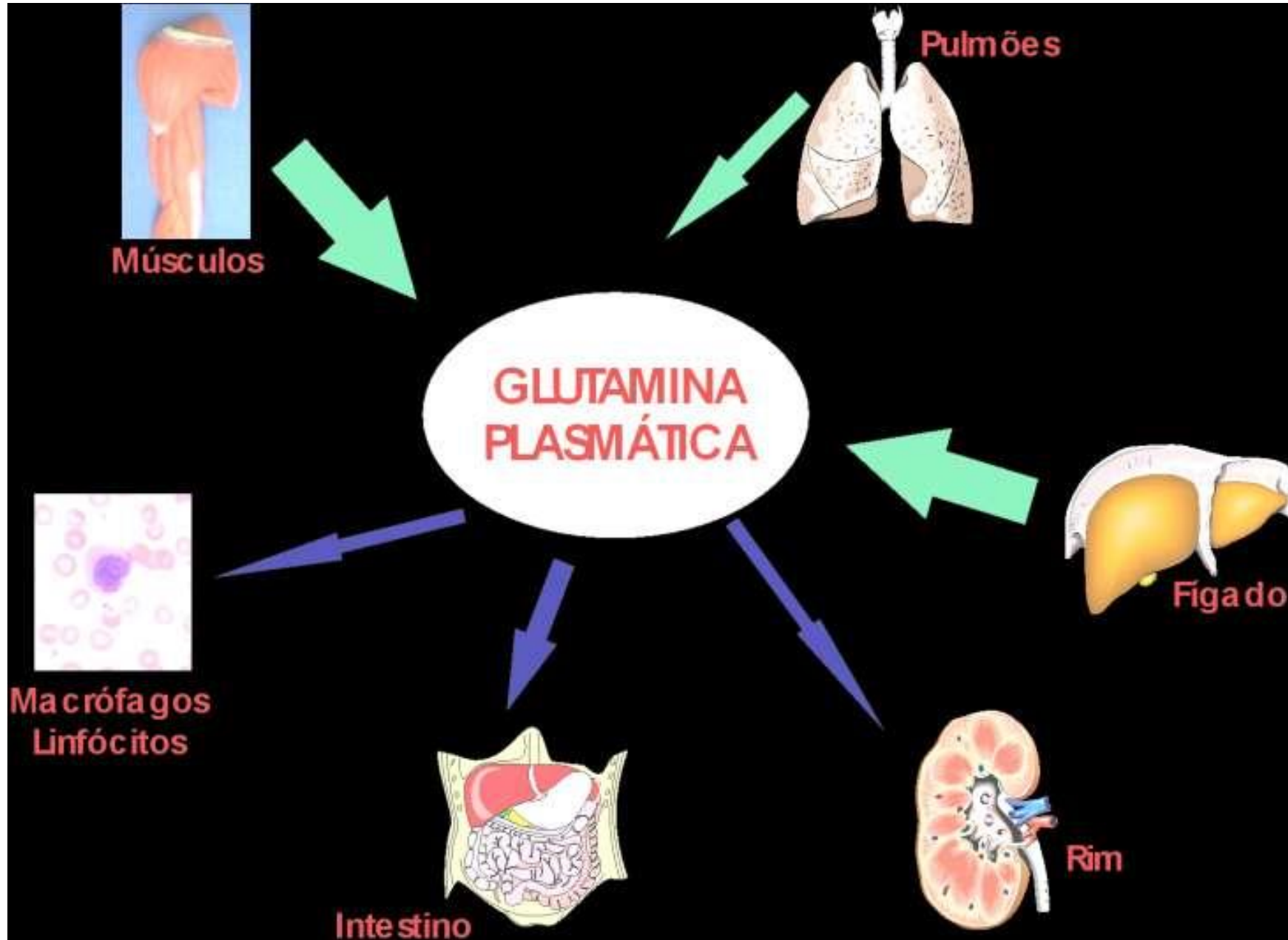
Glutamina



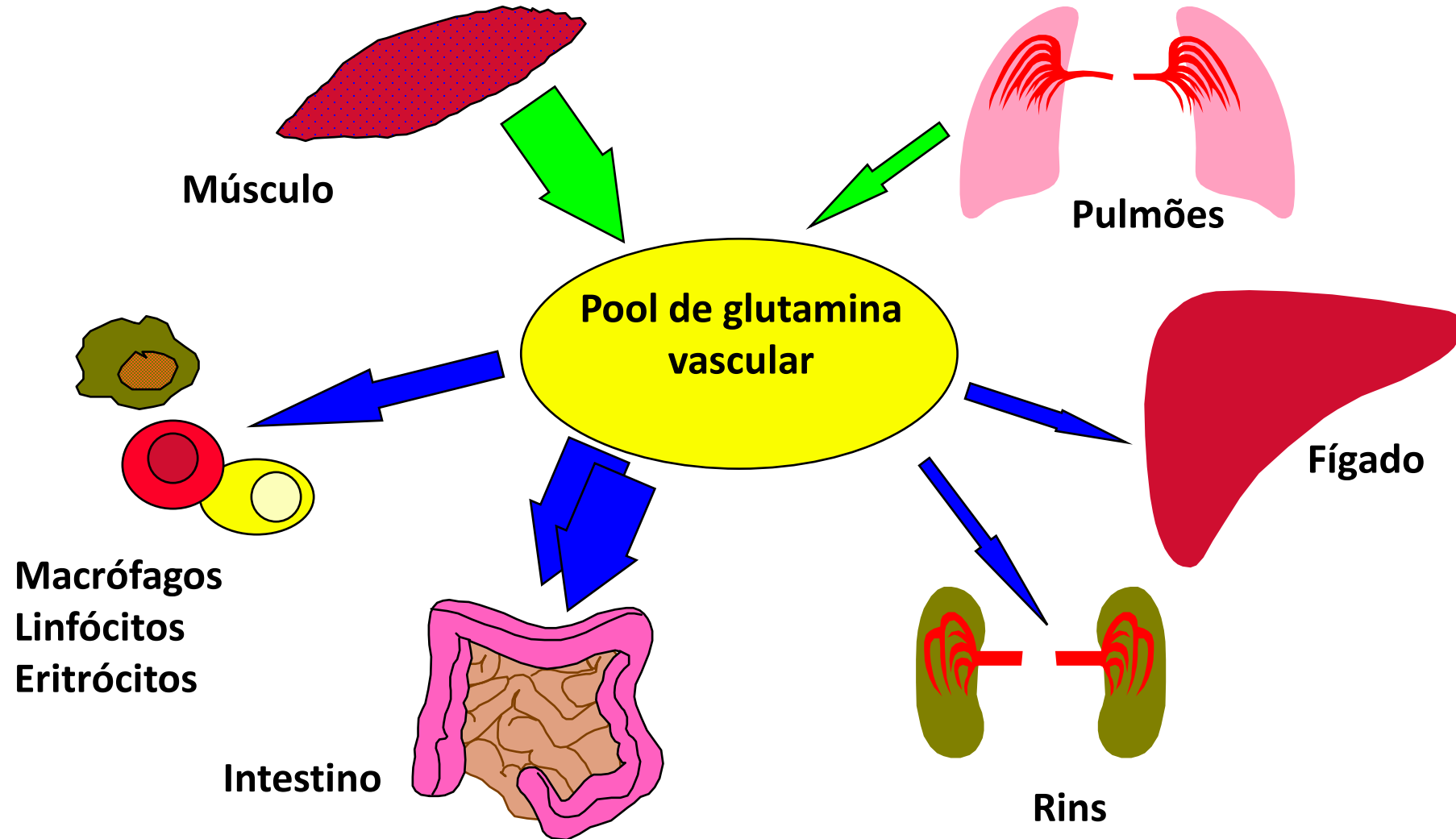
Glutamina



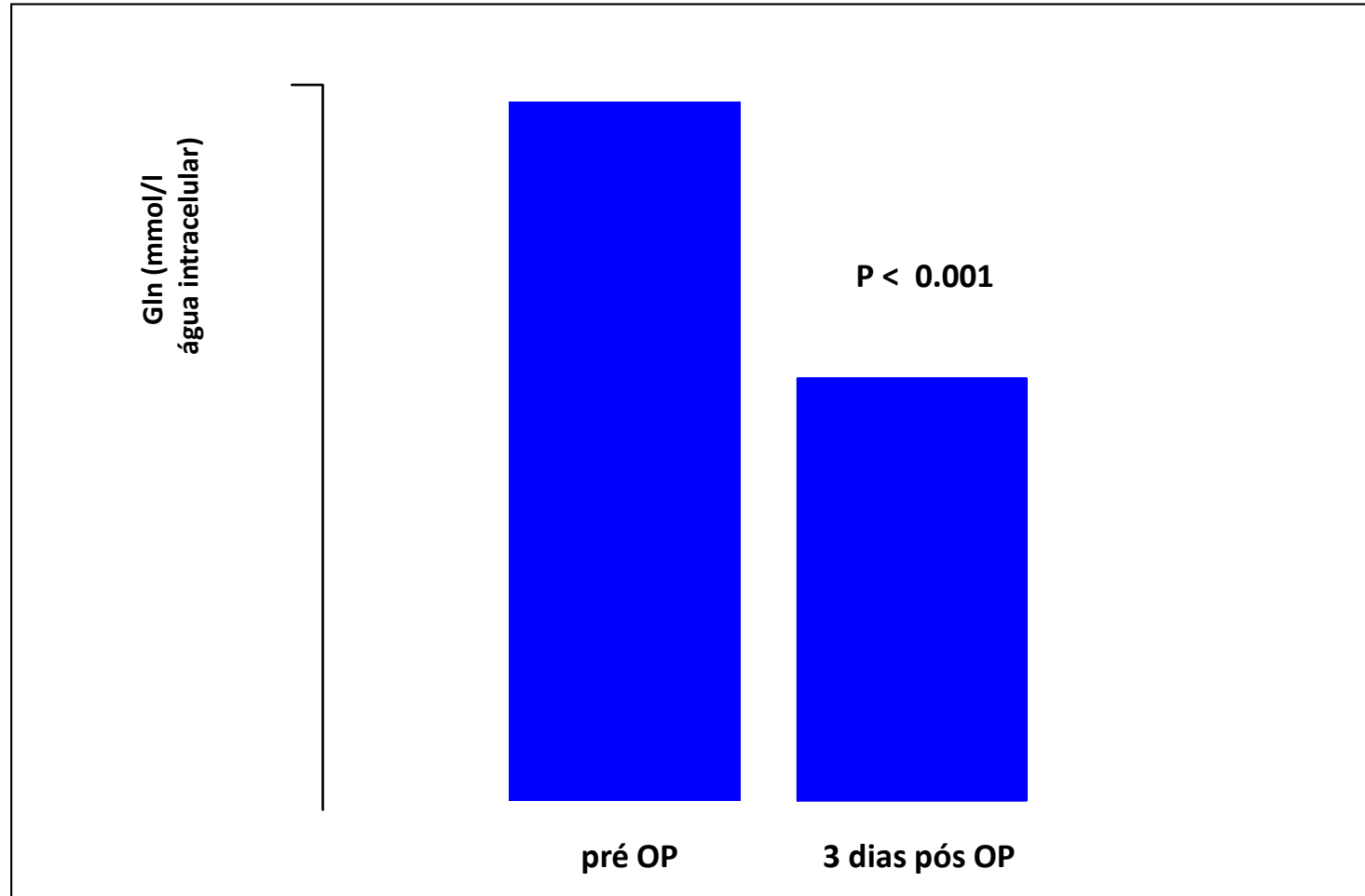
Fluxo da Glutamina no Indivíduo Sadio



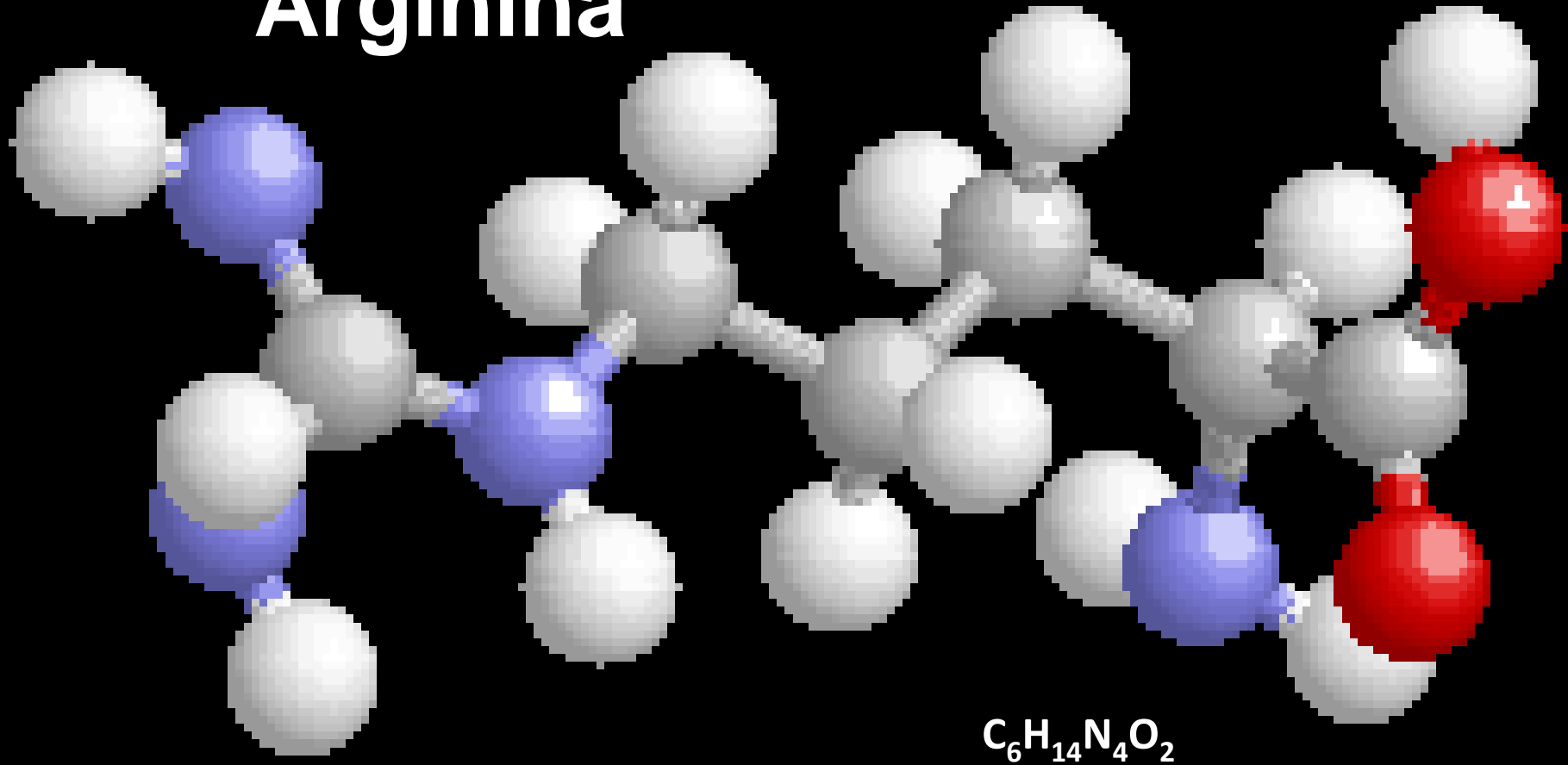
Fluxo de glutamina no catabolismo



Depleção de glutamina no tecido muscular após grandes operações



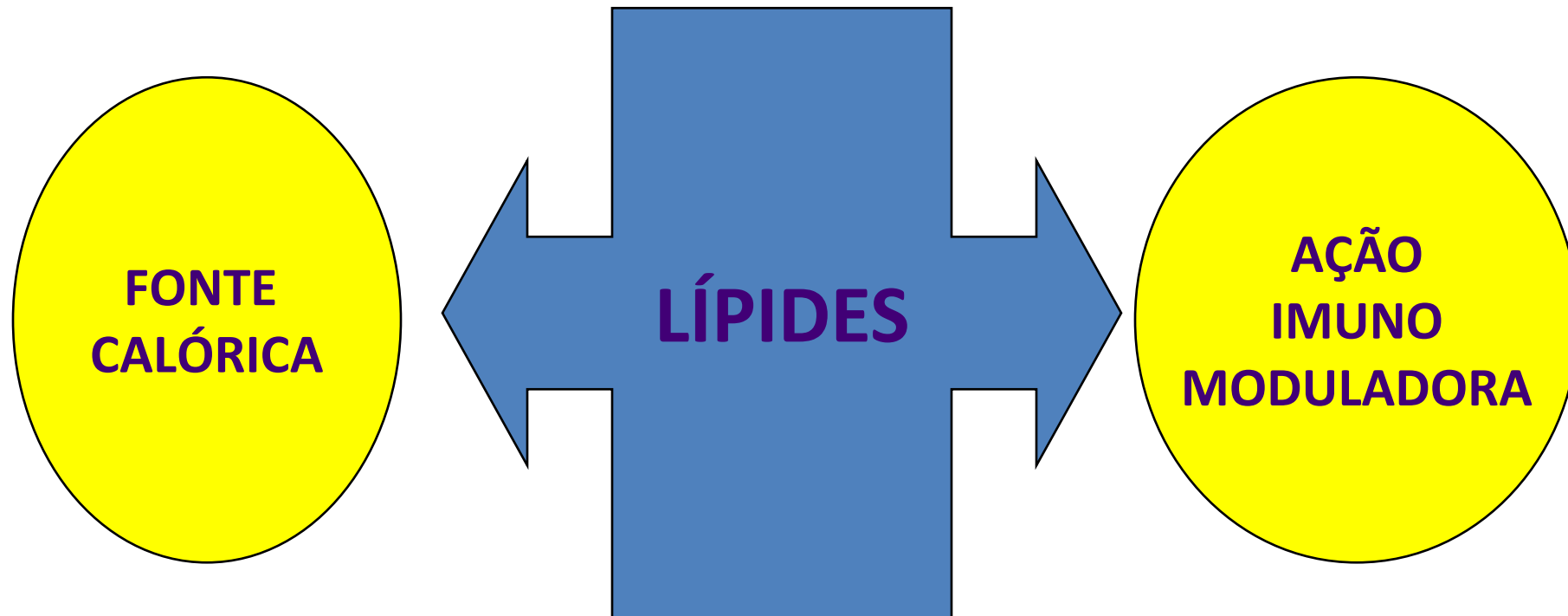
Arginina



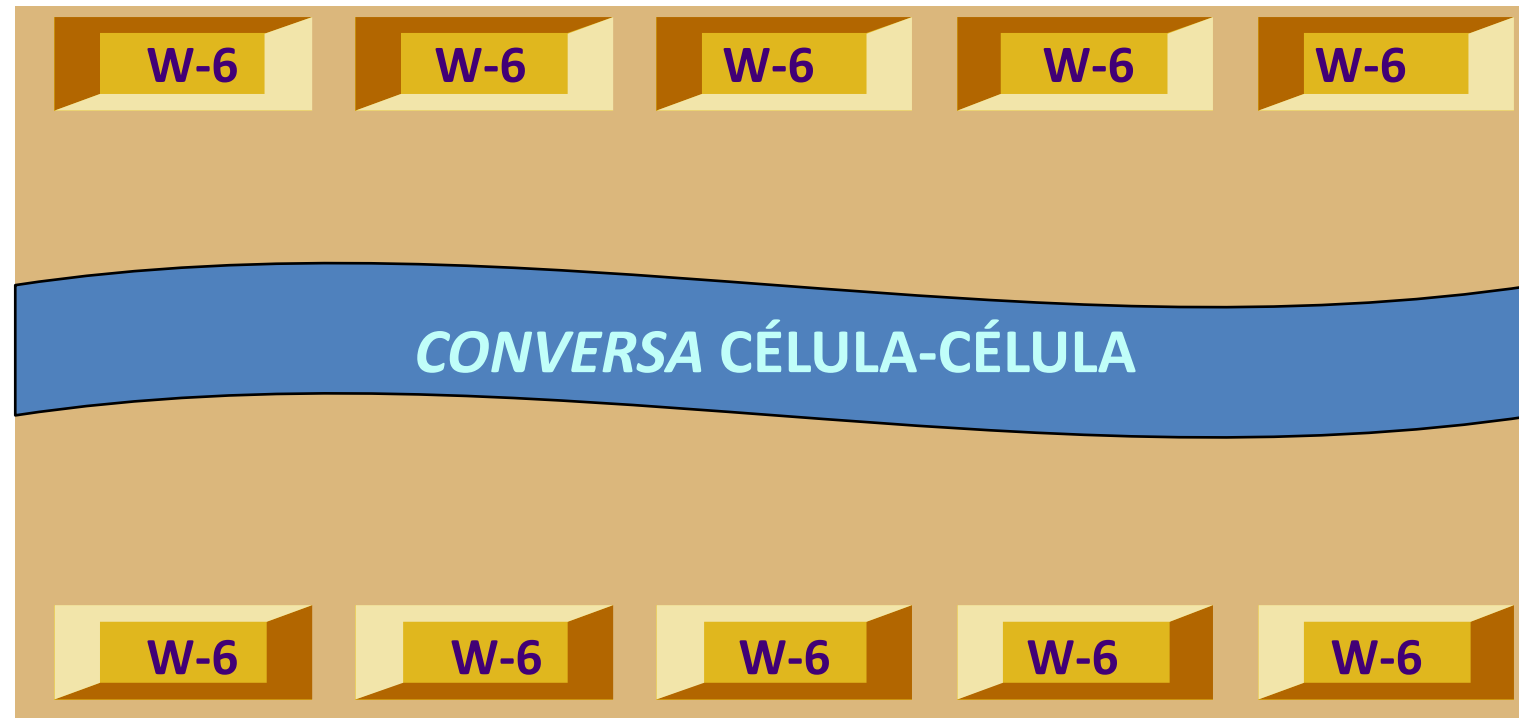
Arginina

Witte e Barbul, 2003





COMPOSIÇÃO DE MEMBRANA CELULAR



Omega-6 Series

$\Delta 6$ Desaturase

Arachidonic Acid

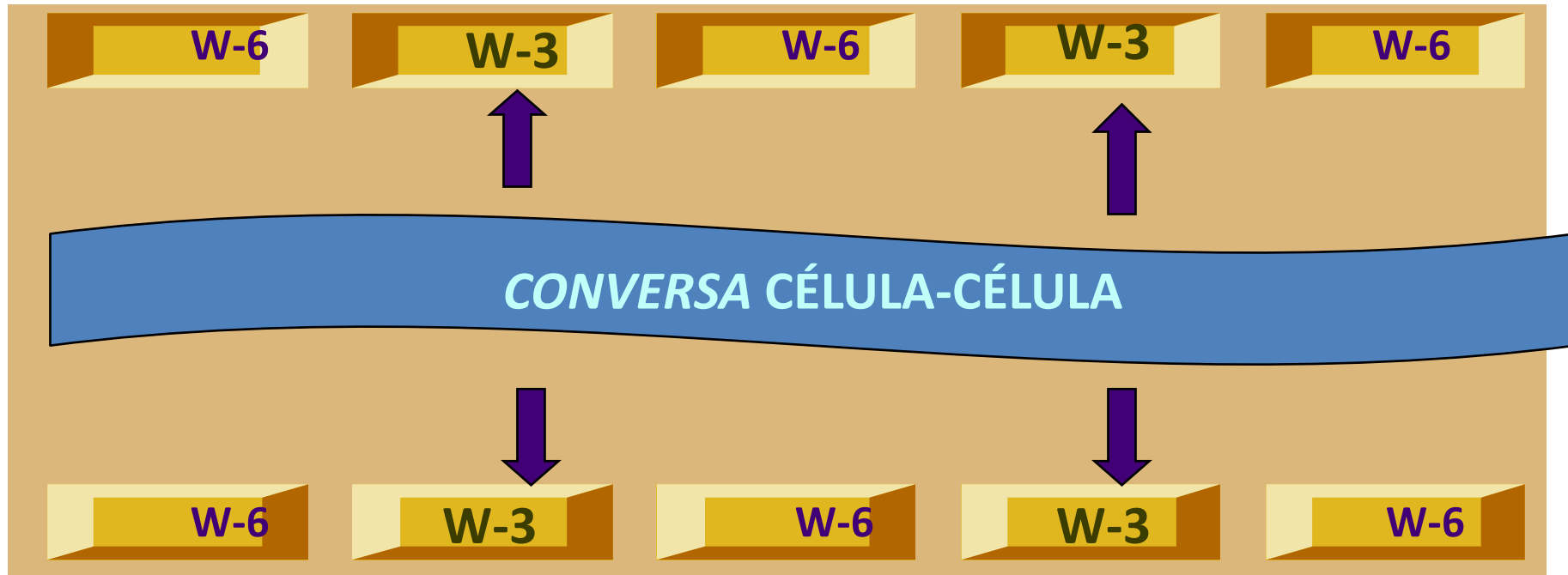
Cyclooxygenase

Immune Suppression

Inflammation

Vasoconstriction

COMPOSIÇÃO DE MEMBRANA CELULAR



Omega-3 Series

α - Linolenic acid

$\Delta 6$ Desaturase

Fish oil ----- EPA \rightleftharpoons DHA

Cyclooxygenase

Anti-platelet

Vasodilatory

Anti-inflammatory

Nucleotídeos

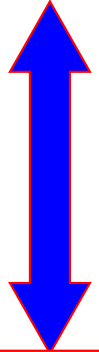


Nucleotídeos

- ↑ integridade da barreira intestinal
- ↑ concentração de RNA e DNA + proteína intestinal
- ↑ atividade enzimática das bordas em escova
- Estímulo da resposta proliferativa à antígenos das cels. T
- Estímulo da ativação de macrófagos pelas cels. T
- Reversão da imunossupressão

PACIENTE CRÍTICO

**Hipermetabólico
35-65%**



**Hipometabólico
15-20%**



POPULAÇÃO HETEROGÊNEA

Glutamine and Antioxidants in the Critically Ill Patient: A Post Hoc Analysis of a Large-Scale Randomized Trial

Daren K. Heyland, MD¹; Gunnar Elke, MD²; Deborah Cook, MD³;
Mette M. Berger, MD, PhD⁴; Paul E. Wischmeyer, MD⁵; Martin Albert, MD⁶;
John Muscedere, MD¹; Gwynne Jones, MD⁷; and Andrew G. Day, MSc¹,
on behalf of the Canadian Critical Care Trials Group

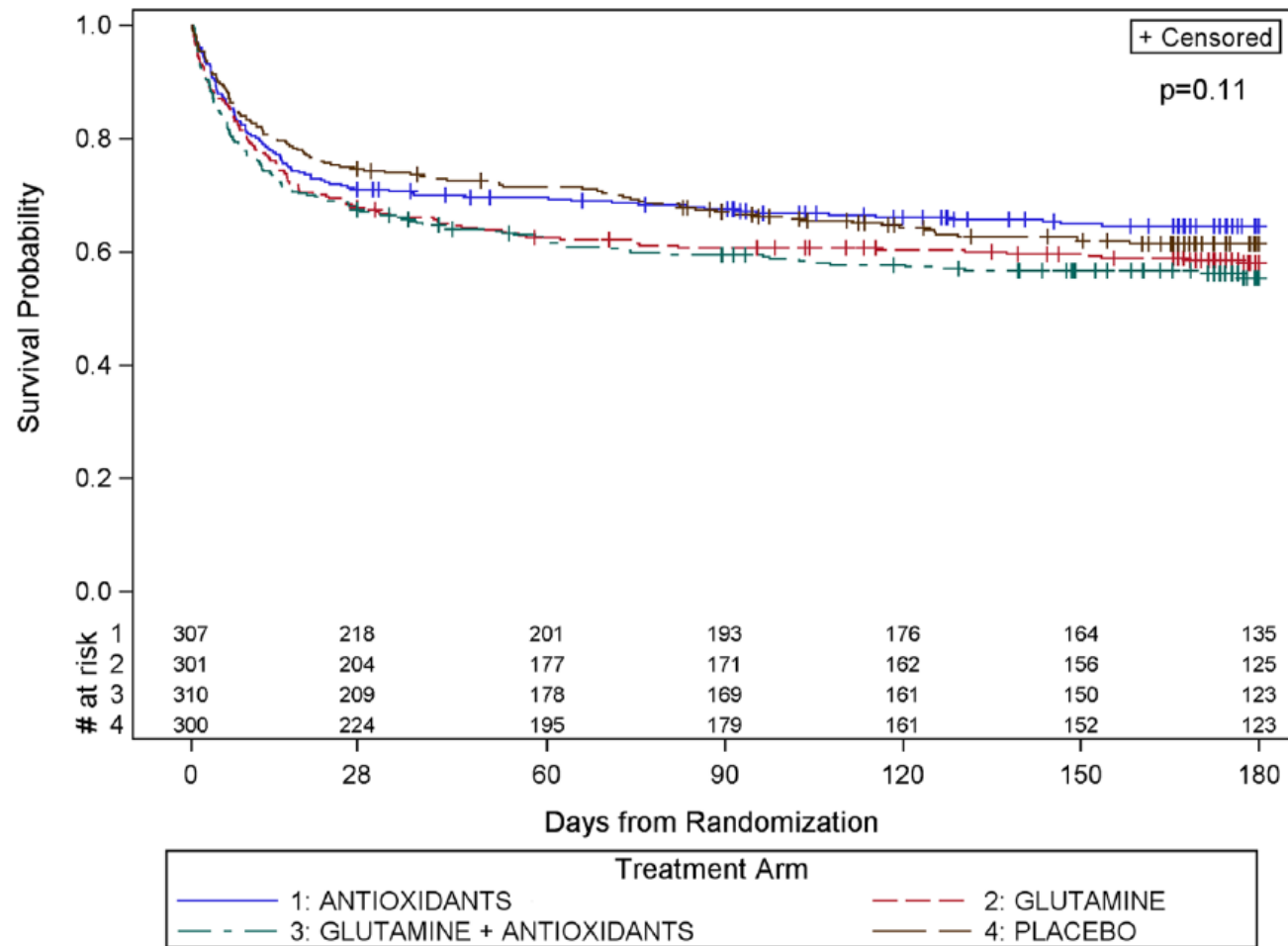
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40 UTIS – América e Europa - 1223 pac. VM
com MOF
GLN - Antioxidantes - GLN + Antioxidantes –
Placebo – 28 dias de Mortalidade

was 1.5 (95% confidence interval, 1.0–2.1, $P = .05$), 1.2 (0.8–1.8, $P = .40$), and 1.4 (0.9–2.0, $P = .09$) for glutamine, antioxidant, and glutamine plus antioxidant arms, respectively. In the post hoc subgroup analysis, both glutamine and antioxidants appeared most harmful in patients with baseline renal dysfunction. No subgroups suggested reduced mortality with supplements. *Conclusions:* After adjustment for baseline covariates, early provision of high-dose glutamine administered separately from artificial nutrition was not beneficial and may be associated with increased mortality in critically ill patients with multiorgan failure. For both glutamine and antioxidants, the greatest potential for harm was observed in patients with multiorgan failure that included renal dysfunction upon study enrollment. (*JPEN J Parenter Enteral Nutr.* 2015;39:401-409)

Keywords

randomized clinical trials; glutamine; antioxidants; post hoc analysis; critical care



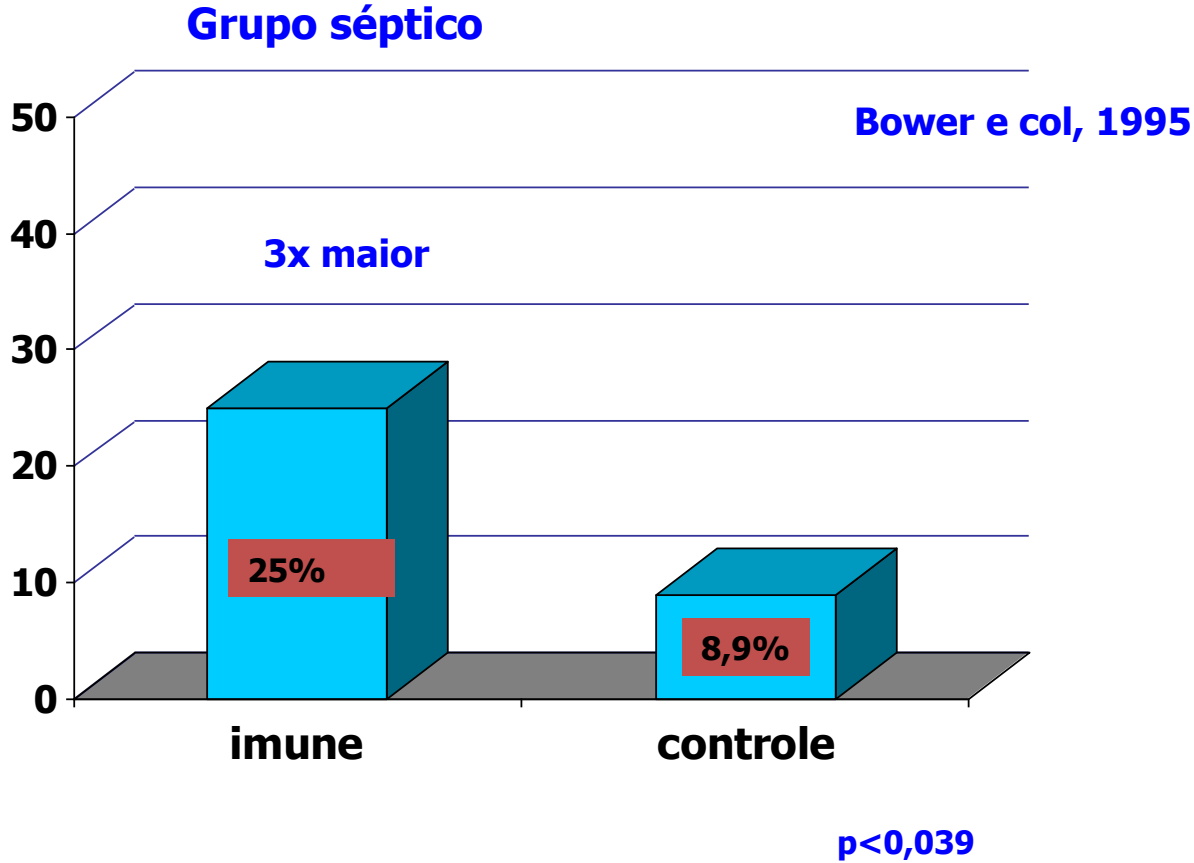
28 dias de mortalidade: Placebo 25% - 32% GLN - 29% antiox – 33% GLN + antiox.

Glutamina

- Será que todos os pacientes na UTI são candidatos ao tratamento com glutamina ou apenas aqueles que apresentem deficiência de glutamina?
- Qual é a dose correta para suplementação de glutamina?
- Todos os pacientes da heterogênea população da UTI têm as mesmas necessidades, ou subpopulações específicas têm necessidades específicas?

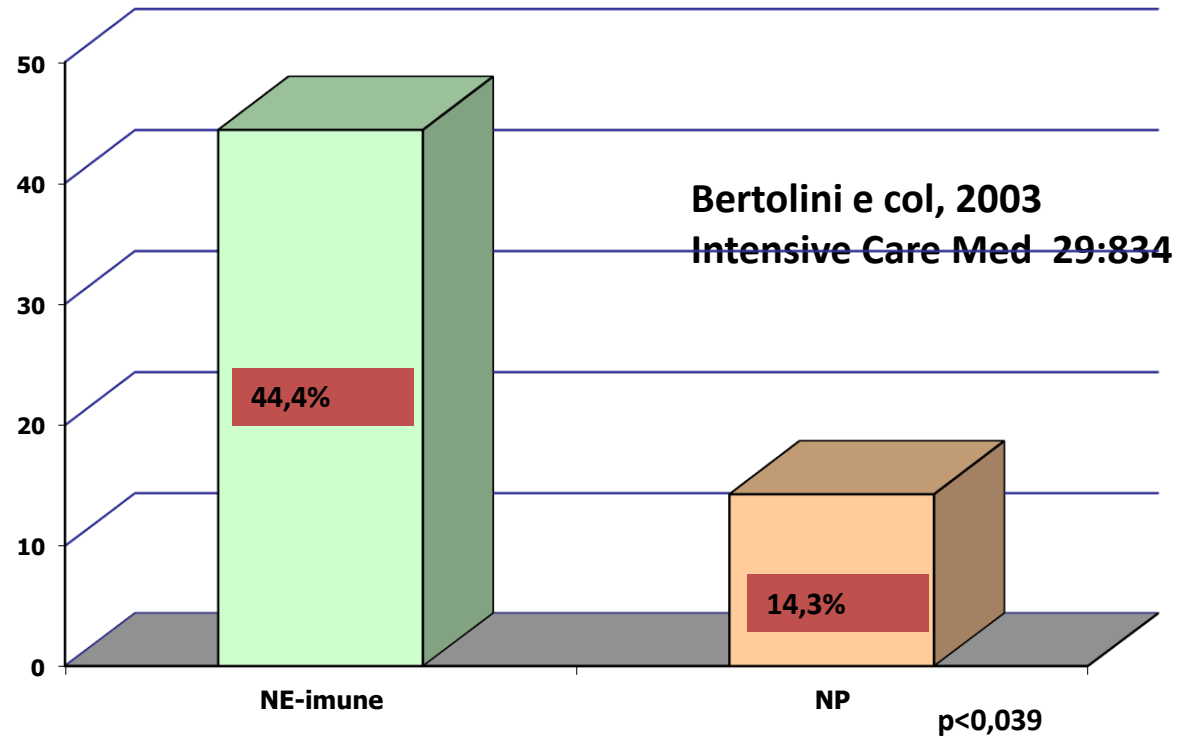
Arginina - Sepse grave

Culpada por determinar aumento da mortalidade

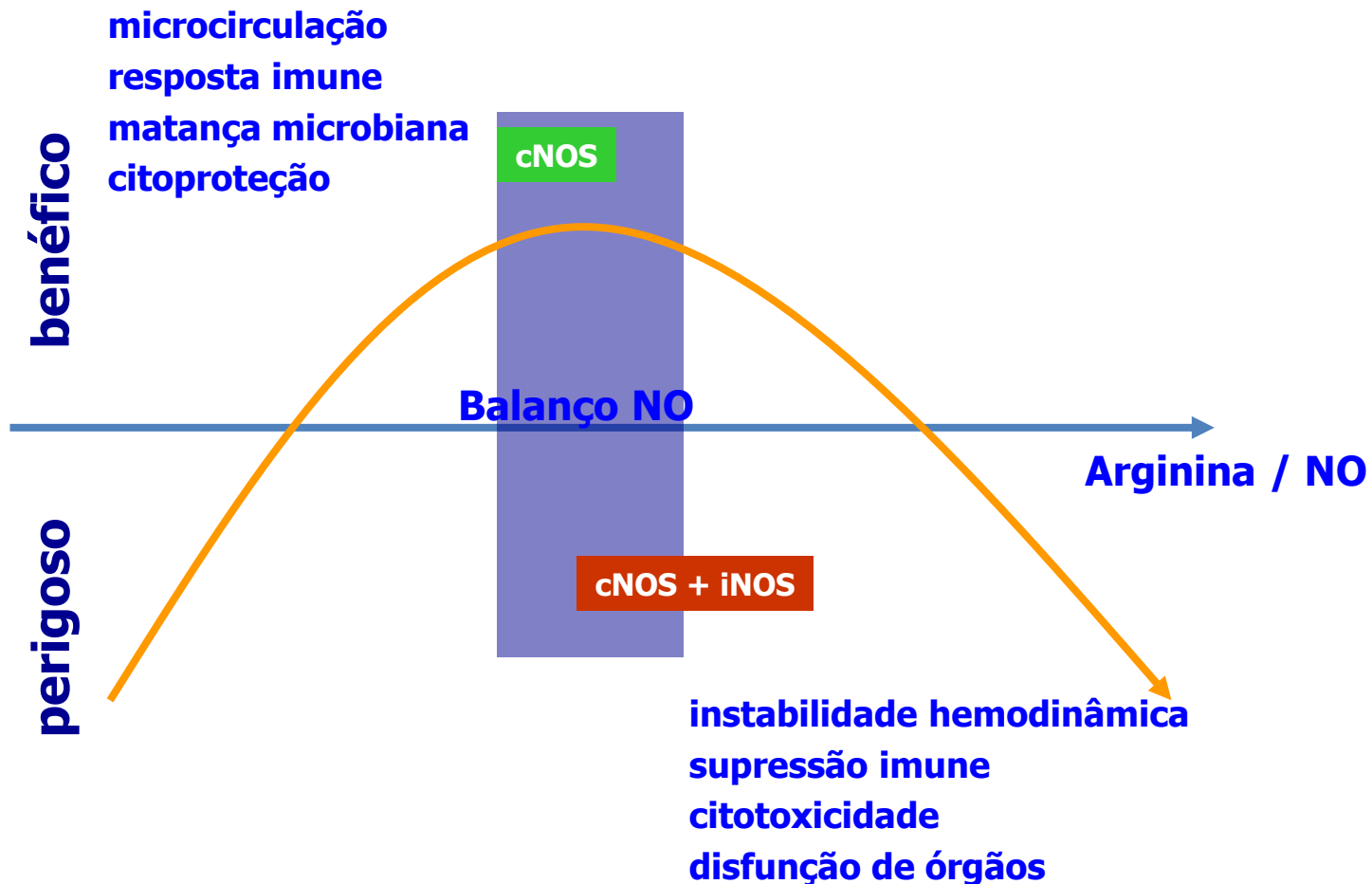


Arginina - Sepse grave Culpada por determinar aumento da mortalidade

Desenho do Estudo = 1500 pacientes
Interrompido com 237



Conseqüências do desequilíbrio da oferta de NO



High-protein enteral nutrition enriched with immune-modulating nutrients vs standard high-protein enteral nutrition and nosocomial infections in the ICU: a randomized clinical trial.

van Zanten AR¹, Sztark F², Kaisers UX³, Zielmann S⁴, Felbinger TW⁵, Sablotzki AR⁶, De Waele JJ⁷, Timsit JF⁸, Honing ML⁹, Keh D¹⁰, Vincent JL¹¹, Zazzo JF¹², Fijn HB¹, Petit L², Preiser JC¹¹, van Horssen PJ¹³, Hofman Z¹³.

Author information

Abstract

IMPORTANCE: Enteral administration of immune-modulating nutrients (eg, glutamine, omega-3 fatty acids, selenium, and antioxidants) may reduce the incidence of nosocomial infections and improve recovery from critical illness. However, controversy exists on the use of immune-modulating enteral nutrition because of the lack of consensus in guidelines.

OBJECTIVE: To determine whether high-protein enteral nutrition enriched with immune-modulating nutrients (IMHP) reduces the incidence of infections compared with standard high-protein enteral nutrition (HP) in mechanically ventilated critically ill patients.

DESIGN, SETTING, AND PARTICIPANTS: The MetaPlus study, a randomized, double-blind, multicenter trial, was conducted from February 2010 through April 2012 including a 6-month

Não houve diferença entre os 2 grupos e o grupo IMHP sugeriu ↑ de mortalidade qdo ajustado para 6 meses.

or HP (n = 149) group and included in an intention-to-treat analysis, performed for the total population as well as predefined medical, surgical, and trauma subpopulations.

INTERVENTIONS: High-protein enteral nutrition enriched with immune-modulating nutrients vs standard high-protein enteral nutrition, initiated within 48 hours of ICU admission and continued during the ICU stay for a maximum of 28 days.

301 pacientes UTI
Randomizados

152 IMHP

149 HP

Omega-3 Fatty Acids as a Putative Treatment for Traumatic Brain Injury

Linda Hasadsri,¹ Bonnie H. Wang,² James V. Lee,² John W. Erdman,³ Daniel A. Llano,⁴ Aron K. Barbey,^{2,5,6} Tracey Wszalek,⁷ Matthew F. Sharrock,² and Huan (John) Wang⁸

Os ácidos graxos ômega-3 restauram a energia celular, reduzem o estresse oxidativo e a inflamação, reparam os danos celulares e atenuam a ativação dos processos apoptóticos após a TBI.

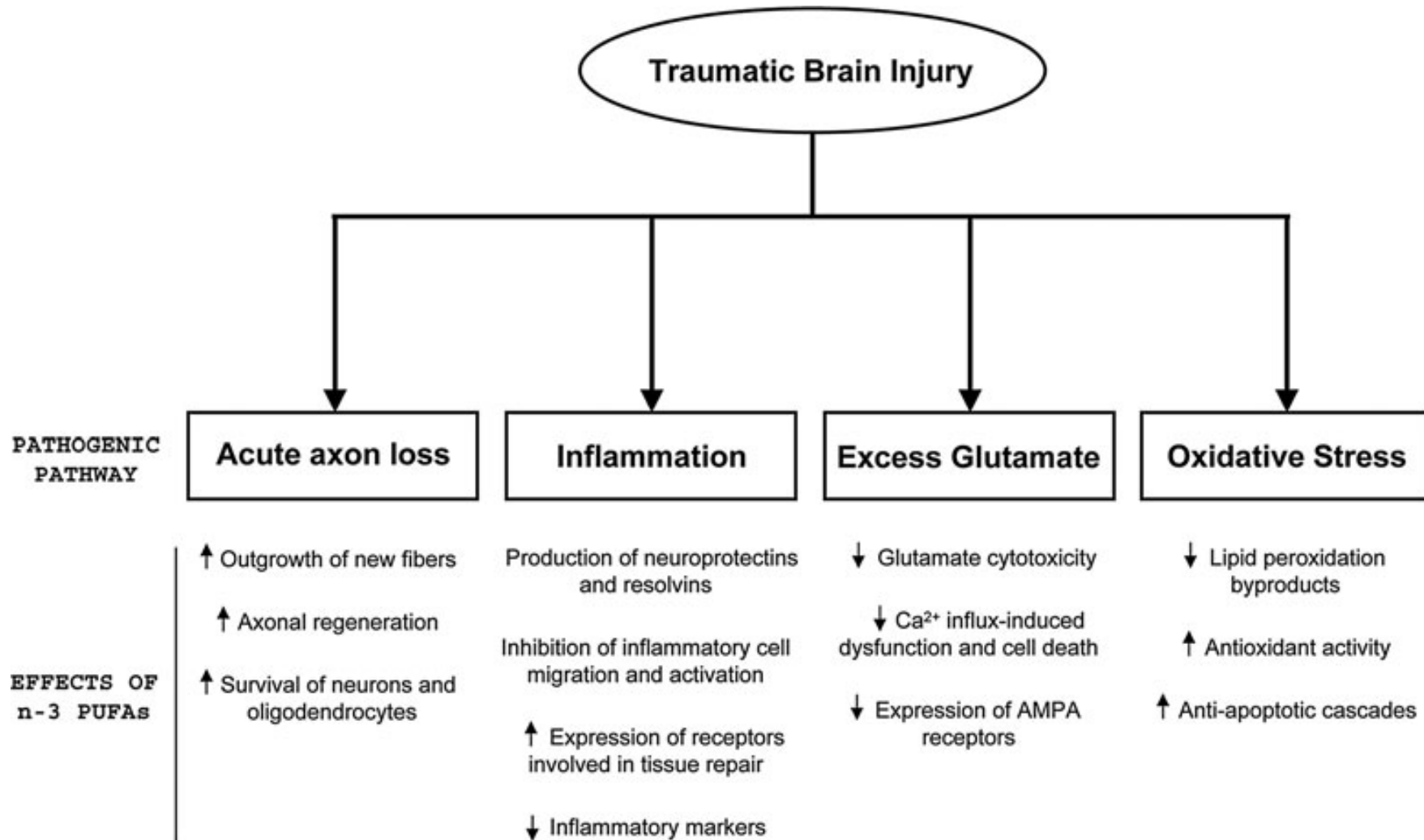
Key words: encephalopathy; omega 3 fatty acids, plasma membrane; therapeutic approaches to CNS injury; traumatic brain injury

Introduction

TRAUMATIC BRAIN INJURY (TBI) remains a significant cause of death and permanent disability in the United States. Drawing

Repetitive head impacts add another level of complexity to the characterization of TBI because the emergence and duration of pathogenic events can overlap. This is particularly relevant in athletes and military personnel. Recent evidence suggests that

Impacto do Ômega 3 sobre diferentes mecanismos de injúria cerebral



A Meta-Analysis of the Effect of Combinations of Immune Modulating Nutrients on Outcome in Patients Undergoing Major Open Gastrointestinal Surgery

Kanagaraj Marimuthu, MRCS, Krishna K. Varadhan, MSc, MRCS,* Olle Ljungqvist, MD, PhD,†
and Dileep N. Lobo, MS, DM, FRCS, FACS**

Background: Immune modulating nutrition (IMN) has been shown to reduce complications after major surgery, but strong evidence to recommend its routine use is still lacking.

Immune modulators such as L-arginine, L-glutamine, ω -3 fatty acids, and nucleotides is thought to modify immune and inflammatory responses favorably and result in reduced postoperative infective

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26 estudos com 2496 pacientes

1252 dieta Immunomoduladora e 1244

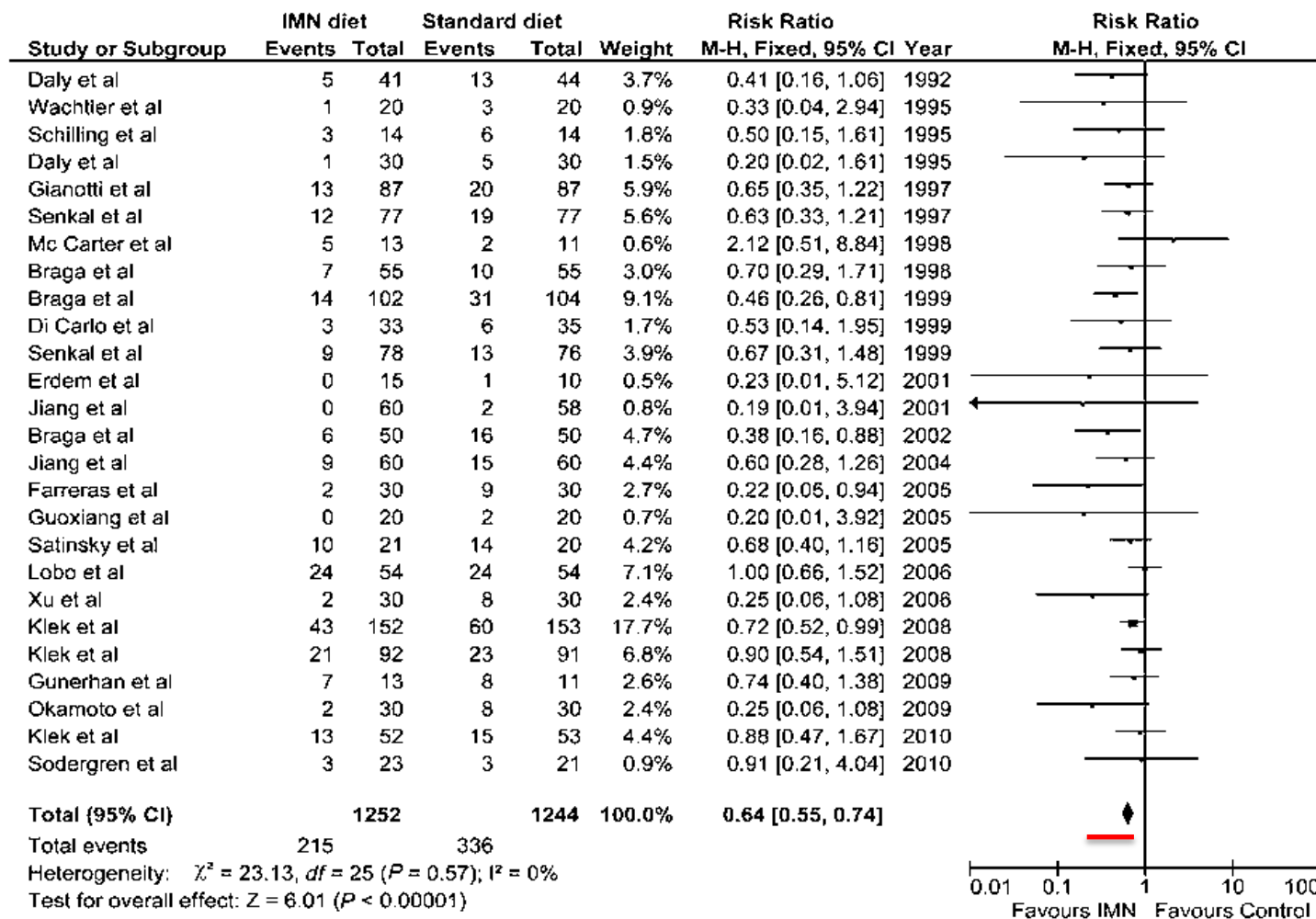
padrão

Results: Twenty-six randomized controlled trials enrolling 2496 patients (1252 IMN and 1244 control) were included. The meta-analysis suggests strong evidence in support of decrease in the incidence of postoperative infectious [risk ratio (RR) (95% confidence interval [CI]): 0.64 (0.55, 0.74)] and length of hospital stay [mean difference (95% CI): -1.88 (-2.91, -0.84 days)] in those receiving IMN. Even though significant benefit was observed for noninfectious complications [RR (95% CI): 0.82 (0.71, 0.95)], the quality of evidence was low. There was no statistically significant benefit on mortality [RR (95% CI): 0.83 (0.49, 1.41)].

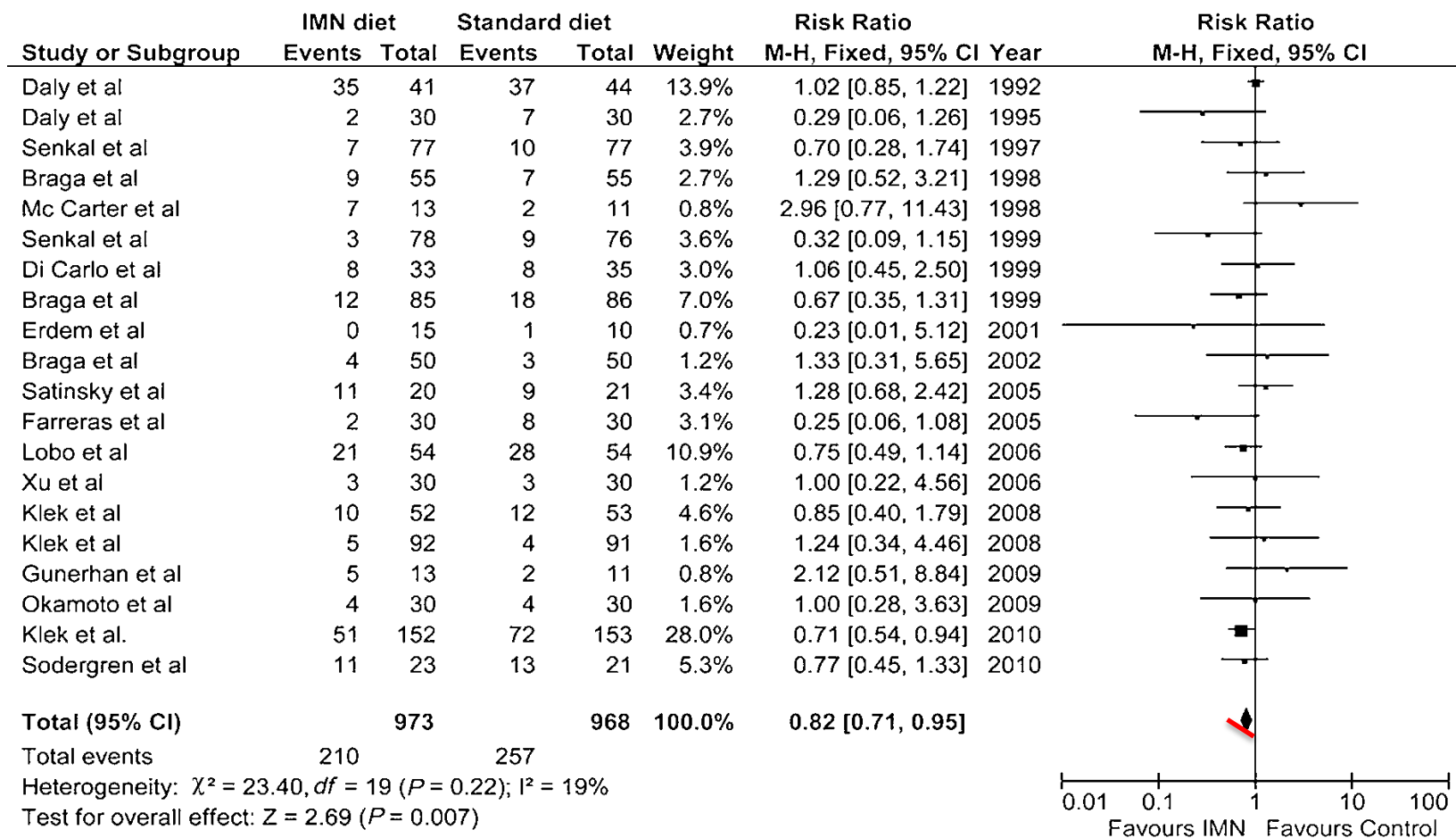
Conclusions: IMN is beneficial in reducing postoperative infectious and non-infectious complications and shortening hospital stay in patients undergoing major open gastrointestinal surgery.

effects of individual components of IMN in modifying immune and inflammatory responses. Furthermore, combinations of 2 or more IMN have been shown to enhance host defenses to a significantly greater extent than when used alone.^{4,17-19} Currently available meta-analyses^{6,7} of IMN in surgical patients have included RCTs supplementing both single and multiple IMN in the experimental group, making the treatment effect of either of them difficult to interpret. Moreover, since the publication of the most recent meta-analysis of RCTs up to September 2009,⁷ additional studies using IMN on surgical patients and guidance for rating the quality of evidence and strength of recommendations using the "Grading of Recommendations Assessment, Development, and Evaluation (GRADE) system"

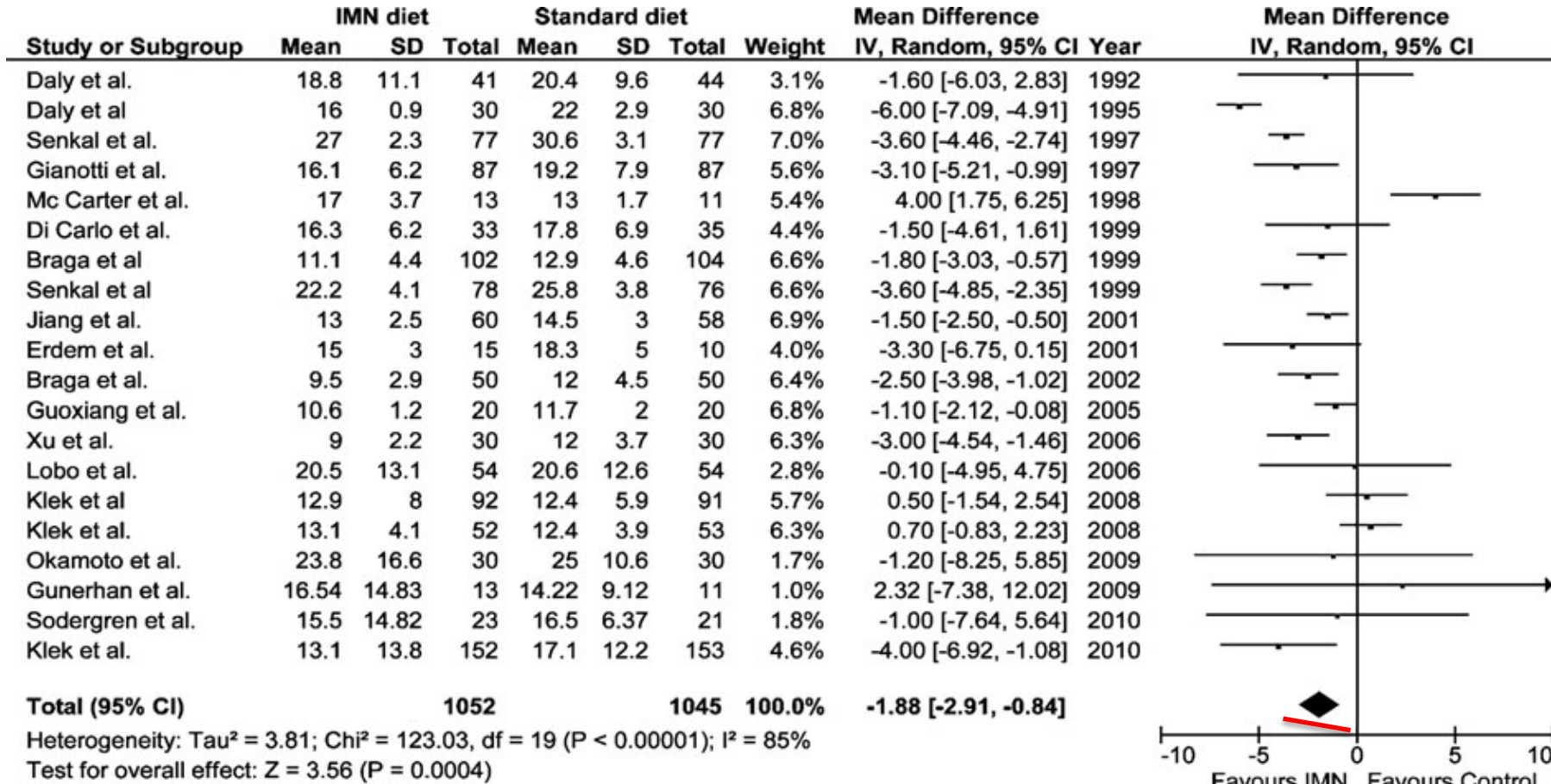
Dieta imunomoduladora X padrão X Infecção



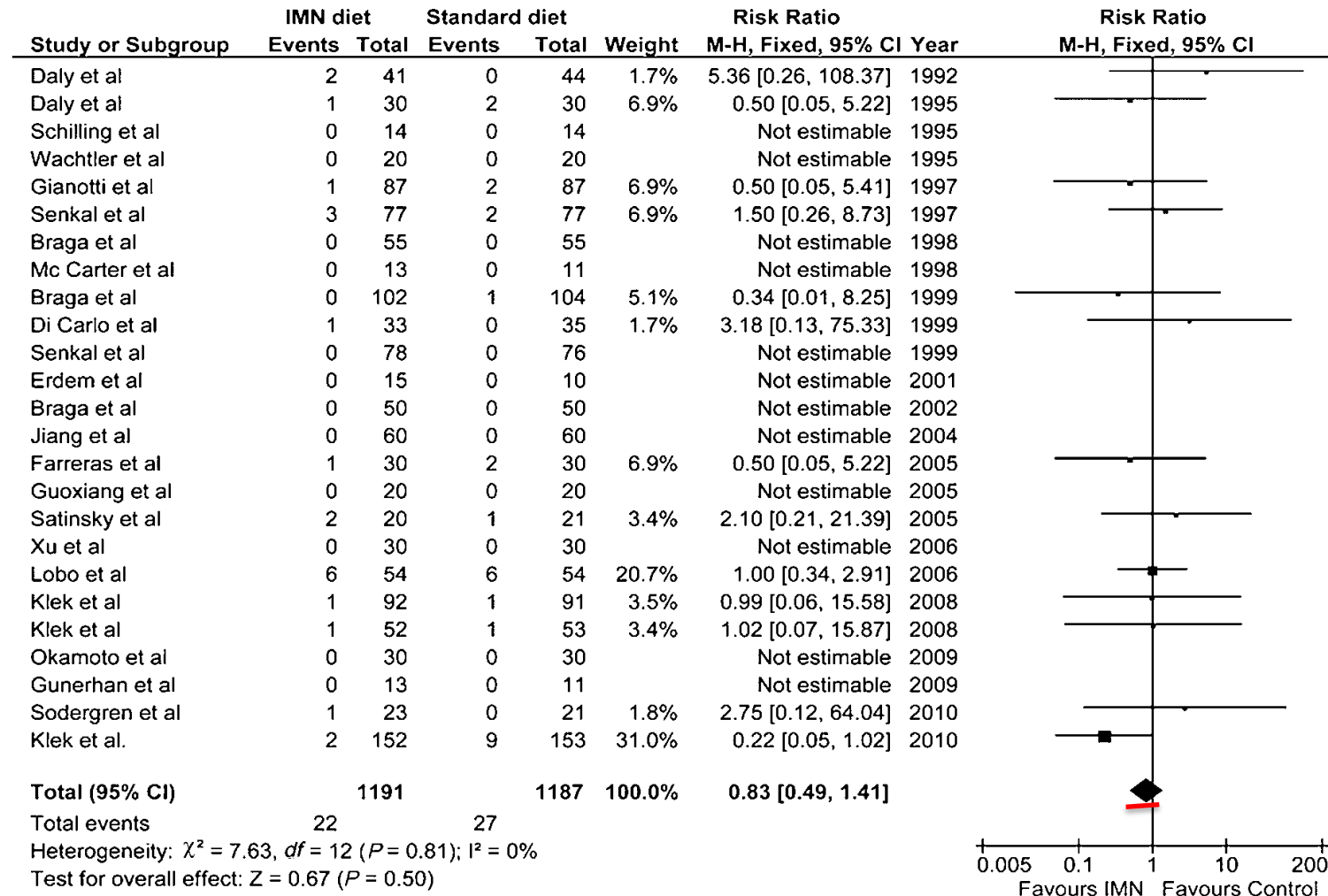
Dieta imunomoduladora X padrão X complicações não infecciosas



Dieta imunomoduladora X padrão X Dias de Hospital



Dieta imunomoduladora X padrão X Mortalidade



Guidelines Society of Critical Care Medicine (SCCM) and American Society for Parenteral and Enteral Nutrition (ASPEN)

Sugere Uso de rotina de formula
imunomoduladora (contendo arginina e w3) em
pacientes em Pós-operatório que requer TNE.

Guidelines Society of Critical Care Medicine (SCCM) and American Society for Parenteral and Enteral Nutrition (ASPEN)

Sugere o uso de formula imunomoduladora
(contendo arginina e w3) em pacientes com
severo trauma .

Guidelines Society of Critical Care Medicine (SCCM) and American Society for Parenteral and Enteral Nutrition (ASPEN)

Sugere formula imunomoduladora contendo arginina ou EPA/DHA com formula padrão em pacientes com TCE.

Guidelines Society of Critical Care Medicine
(SCCM) and American Society for Parenteral and
Enteral Nutrition (ASPEN)

Sugere que formula imunomoduladora não deve ser utilizada rotineiramente em pacientes com sepse severa.

Obrigada!