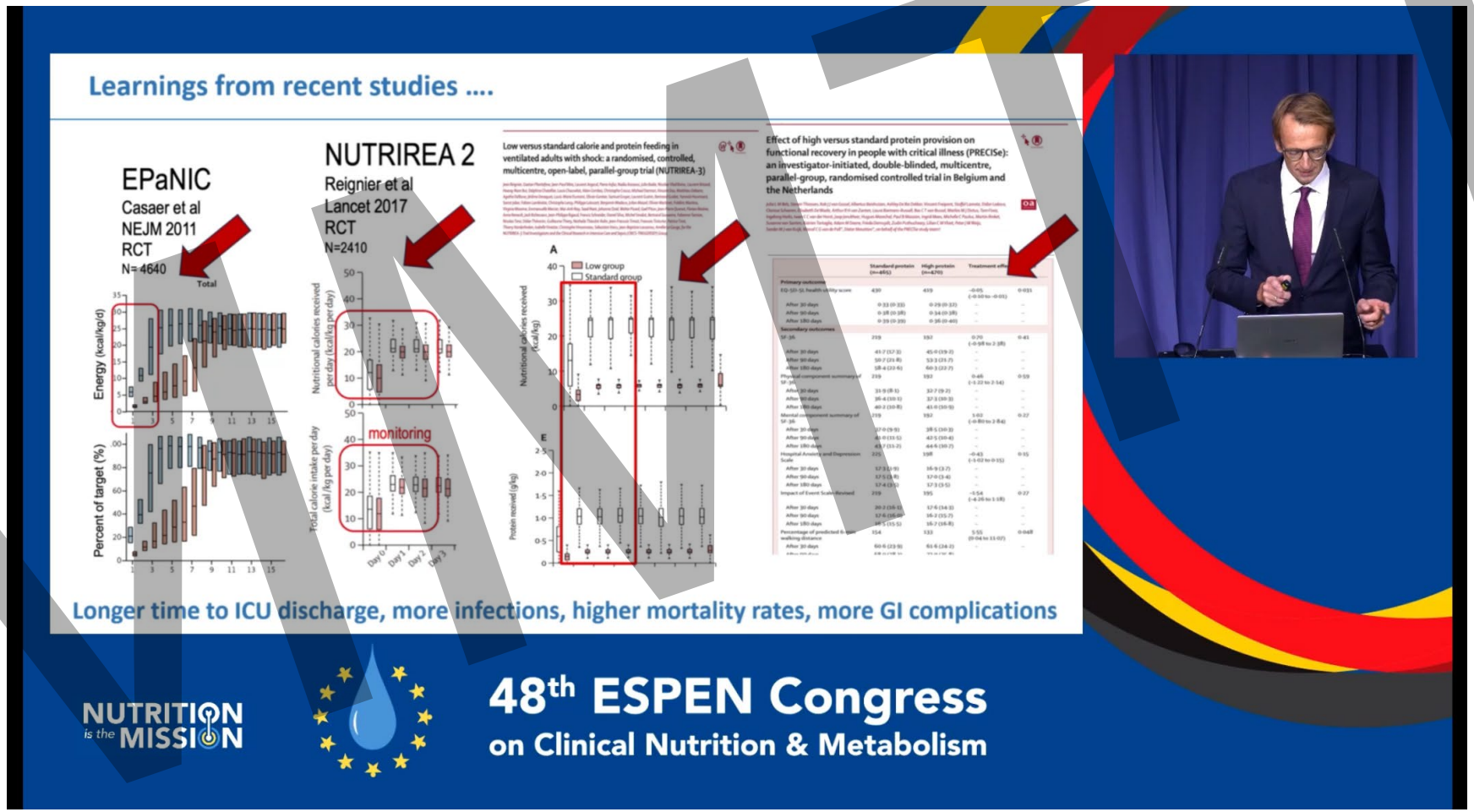
Precizitás a kritikus állapotú betegek táplálásában

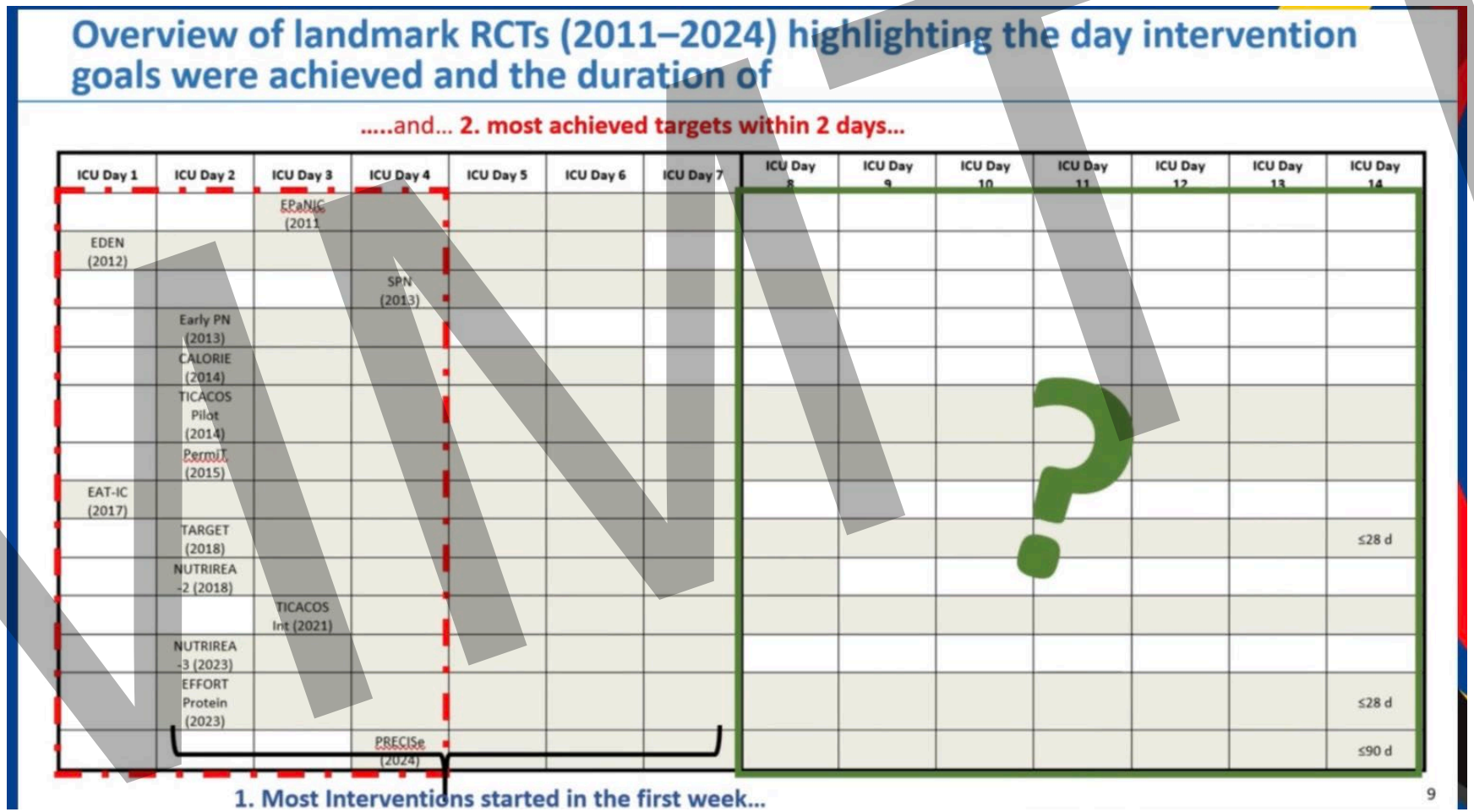
dr Tamási Péter
Budapesti Péterfy S utcai Kórház, KAITO

MMTT

Bajok a studykkal

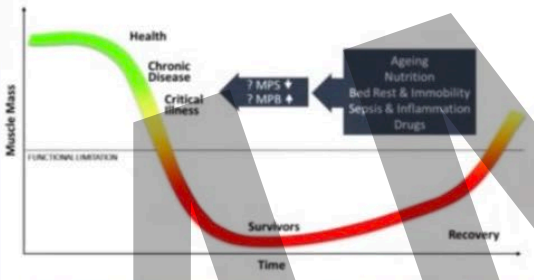


Jelentős vizsgálatok – hibák?



Az alultápláltság következményei

The consequences of malnutrition in critically ill patients









- Muscle loss is difficult to compensate
- Rehabilitation and post-hospitalization are difficult
- Cognition↓ and mobility↓, risk of infection↑
- An independent, self-determined life at home is no longer possible

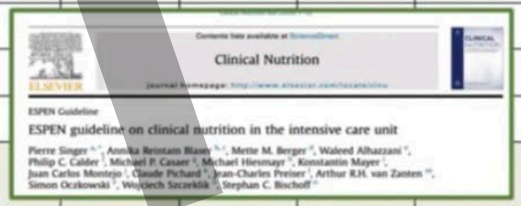
…These are the consequences that we have been fighting against for years…and are still doing so!

13

Óvatos és fokozatos….

Identifying the most appropriate strategy

ICU Day 1	ICU Day 2	ICU Day 3	ICU Day 4	ICU Day 5	ICU Day 6	ICU Day 7	ICU Day 8	ICU Day 9	ICU Day 10	ICU Day 11	ICU Day 12	ICU Day 13	ICU Day 14
		EPaNIC (2011)											
EDEN (2012)													
			SPN (2013)										
	Early PN (2013)												
	CALORIE (2014)												
	TICACOS Pilot (2014)												
	PermiT (2015)												
EAT-IC (2017)													
	TARGET (2018)												
	NUTRIREA -2 (2018)												
		TICACOS Int (2021)											
	NUTRIREA -3 (2023)												
	EFFORT Protein (2023)												≤28 d
			PRECISe (2024)										≤90 d


Contents lists available at ScienceDirect

Clinical Nutrition

journal homepage: http://www.elsevier.com/locate/clnu

ESPEN Guideline

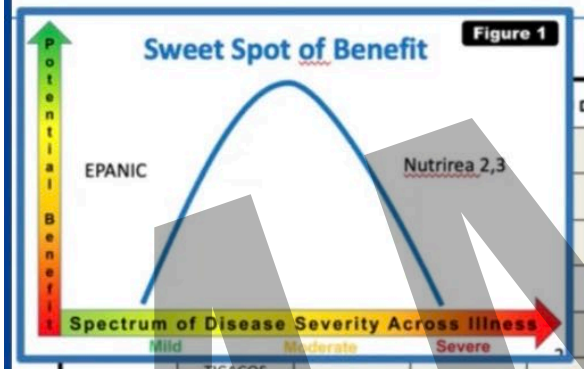
ESPEN guideline on clinical nutrition in the intensive care unit

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 Mayer [i], Juan Carlos Montejo [j], Claude Pichard [k], Jean-Charles Preiser [l], Arthur R.H. van Zanten [m], Simon Oczkowski [e], Wojciech Szczeklik [n], Stephan C. Bischoff [o]

….A careful and progressive enteral feeding strategy is recommended ..

A legjobb stratégia – precizitás?

Identifying the most appropriate strategy …& carefully evaluate!



	ICU Day 5	ICU Day 6	ICU Day 7	ICU Day 8	ICU Day 9	ICU Day 10	ICU Day 11	ICU Day 12	ICU Day 13	ICU Day 14
TICACOS Pilot (2014)										
PermiT (2015)										
EAT-IC (2017)										
TARGET (2018)										
NUTRIREA -2 (2018)										
TICACOS Int (2021)										
NUTRIREA -3 (2023)										
EFFORT Protein (2023)										
PRECISe (2024)										≤90 d


Clinical Nutrition

ESPEN Guideline

ESPEN guideline on clinical nutrition in the intensive care unit

….A careful and progressive enteral feeding strategy is recommended ..

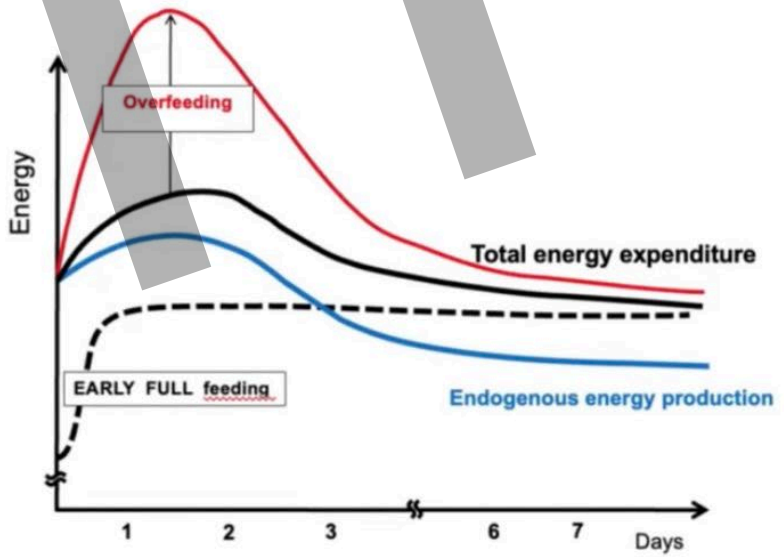
… BUT HOW precisely??

Mikor kezdjük a táplálást

The problem of timimg



- **When to start feeding …**
  - When to start EN or PN or SPN



Oshima et al Clin Nutr 2017

Mikor kezdjük a táplálást

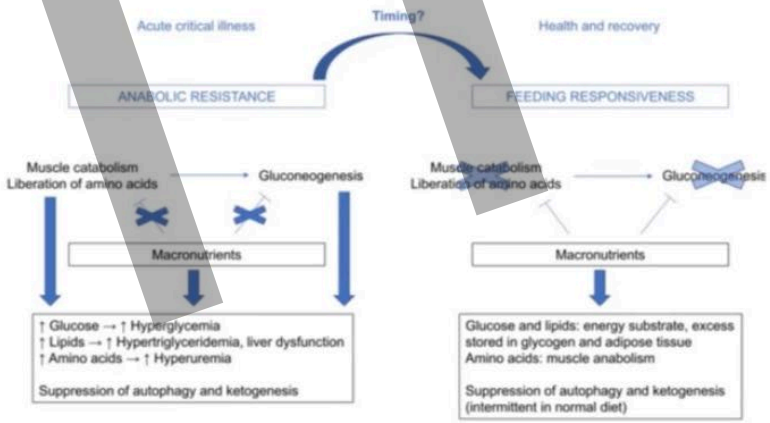
The problem of timing – the readiness for feeding..



Critical Care

REVIEW Open Access

Toward nutrition improving outcome of critically ill patients: How to interpret recent feeding RCTs?



The presence or absence of an anabolic response to feeding cannot be predicted or monitored and likely difers over time

32

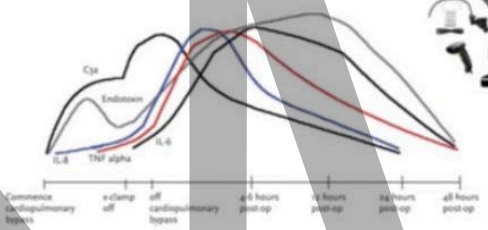
Példák az ágymelletti mérésre

Measuring at bedside is possible

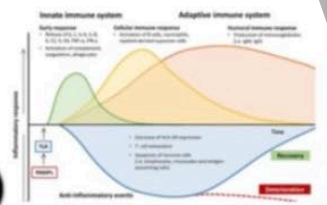














- Ischemia/Reperfusion
- Surgical Trauma
- Contact Activation
- Systemic Inflammatory Response to Extracorporeal Circulation
- Endotoxin and Cytokine
- .....

Monitor Success of Treatment





- In whom to start...
- When to start..
- Monitor it`s use ..
- When to wean..
- Assess it`s efficiacy
- **Risk for Organ Dysfunctions**

Inzulin rezisztencia

Biomarkers in our toolbox – the metabolic response

Critical Care Nutrition

Biomarker	Used for	Description	Valid in	Limitations	Major findings
Insulin resistance	To assess the metabolic tolerance	Indicates a biological mechanism related to the intervention and clinical outcome	• ICU patients		Underrecognized in the clinical practice

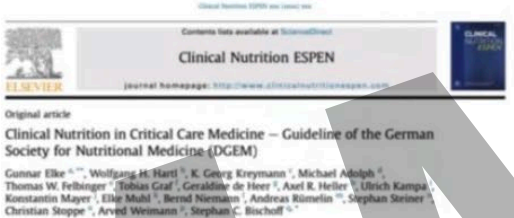
1. xx

MMTT

Inzulin rezisztencia – a gyakorlat

Biomarkers in our toolbox – the metabolic response

Critical Care Nutrition

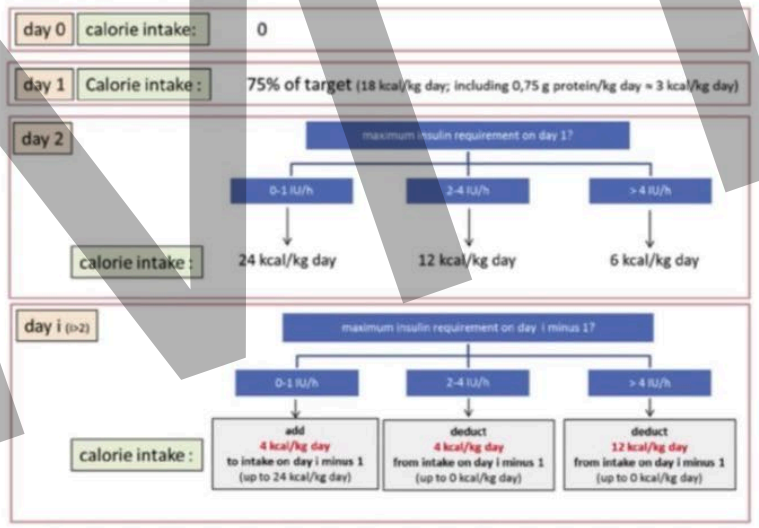

Clinical Nutrition ESPEN

Original article

Clinical Nutrition in Critical Care Medicine – Guideline of the German Society for Nutritional Medicine (DGEM)

Gunnar Elke [a, *], Wolfgang H. Hartl [b], K. Georg Kreymann [c], Michael Adolph [d], Thomas W. Felbinger [e], Tobias Graf [f], Geraldine de Heer [g], Axel R. Heller [h], Ulrich Kampa [i], Konstantin Mayer [j], Elke Muhl [k], Bernd Niemann [l], Andreas Rümelin [m], Stephan Striner [n], Christian Stoppe [o], Arved Weimann [p], Stephan C. Bischoff [q, *]

Individual control of calorie intake by insulin requirement; blood glucose concentration should not be > 180 mg/dl; day 0 indicates the day of disturbance of homeostasis.



Elke G et al., Clinical Nutrition in Critical Care Medicine e Guideline of the German Society for Nutritional Medicine (DGEM), Clinical Nutrition ESPEN, https://doi.org/10.1016/j.clnesp.2019.05.002

A magas adag fehérje sem jó

Biomarkers in our toolbox – in the clinical routine

Critical Care Nutrition

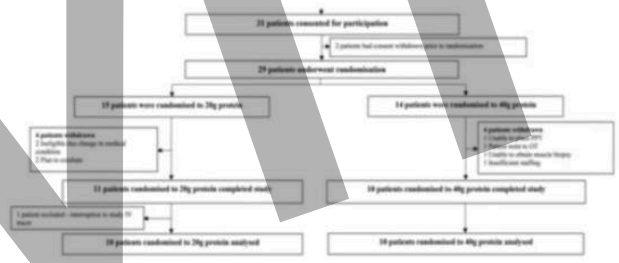
Biomarker	Used for	Description	Valid in	Limitations	Major findings
Whole body protein balance	Assess the real use and metabolization of proteins and amino acids	Valid measure of metabolic response to nutrition	• ICU patients • Hospitalised patients • Others	• Complex and expensive measures	Contributes to the understanding if administered AA are utilized or not

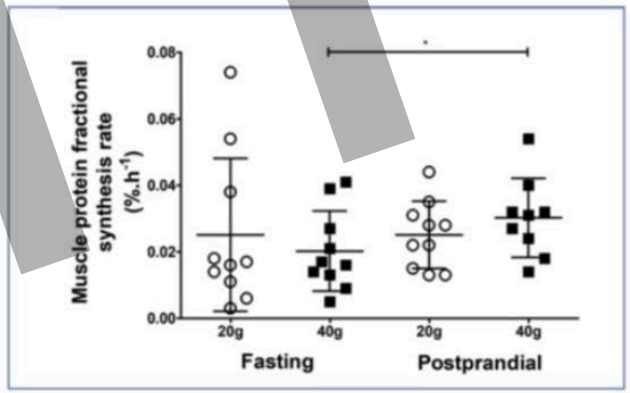
Published: February 24, 2025
Original Research | Critical Care

ATS thoracic.org OXFORD

Increasing protein dose does not further augment muscle protein synthesis in critical illness: a randomized, controlled clinical trial

Matthew J. Summers, Imre W.K. Kouw, Imogen E. Asser, Rhea Louis, Nilesh Anand Devanand, Tejaswini Arunachala Murthy, Mark P. Plummer, Adam M. Deane, Eamon Raith, Kylie M. Lange, Stefan Court-Kowalski, Naveen Yadav, Yee Chai, Luc J.C. van Loon, Marianne J. Chapman, Lee-anne S. Chapple





Higher enteral protein did not further augment postprandial muscle protein synthesis rates to overcome -anabolic resistance during critical illness, despite increased plasma amino acid availability

Providing greater amounts of protein does not overcome anabolic resistance

Karbamid/kreatinin arány

Biomarkers in our toolbox – others

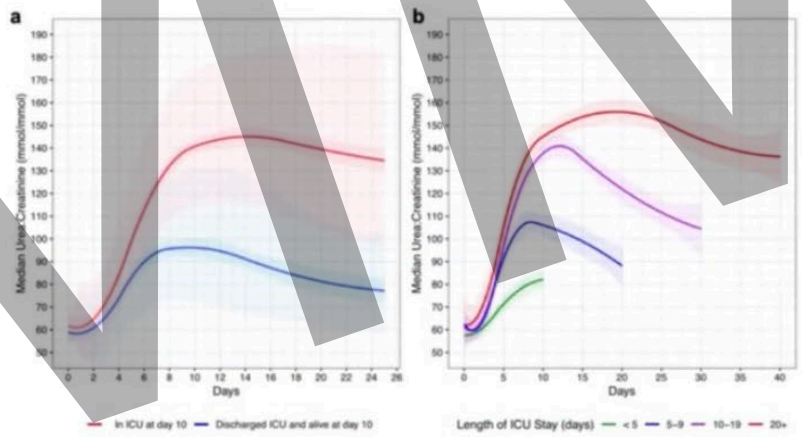
Biomarker
Urea – Creatinine ratio

Intensive Care Med (2019) 45:1718–1731
https://doi.org/10.1007/s00134-019-05760-5

ORIGINAL

Elevated urea-to-creatinine ratio provides a biochemical signature of muscle catabolism and persistent critical illness after major trauma

Ryan W. Haines[1,2], Parjam Zolfaghari[1,2], Yize Wan[1,2], Rupert M. Pearse[1,2], Zudin Puthucheary[1,2] and John R. Prowle[1,2,3*]

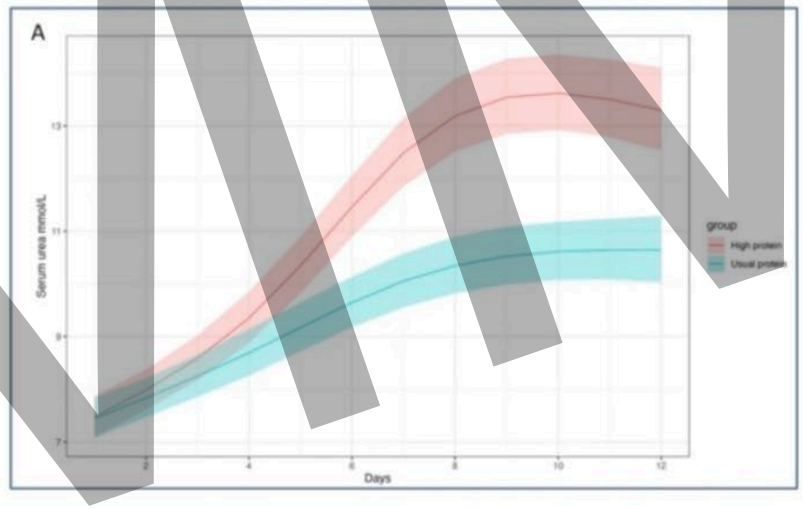


Elevated urea:creatinine ratio accompanies skeletal muscle wasting representing a biochemical signature of persistent critical illness after major trauma.

Miről beszél a karbamid…

Biomarkers in our toolbox – others

Biomarker
Urea – Creatinine ratio



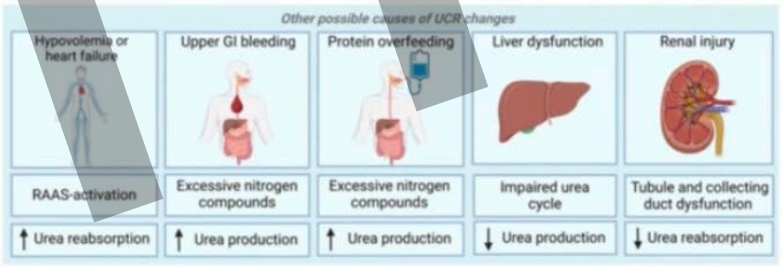
Haines et al. Critical Care (2024) 28:24
https://doi.org/10.1186/s13054-024-04799-1

Critical Care

RESEARCH Open Access

Association between urea trajectory and protein dose in critically ill adults: a secondary exploratory analysis of the effort protein trial (RE-EFFORT)

Ryan W. Haines[1,2*], John R. Prowle[1,2,3], Andrew Day[4], Danielle E. Bear[5], Daren K. Heyland[6†] and Zudin Puthucheary[1,2†]



Haines et al. Critical Care (2024) 28:24
Paulus *et al. Critical Care (2025) 29:175*

A foszfát – refeeding!

Biomarkers in our toolbox – others

Critical Care Nutrition

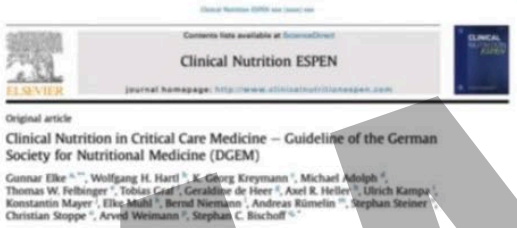
Biomarker	Used for	Major findings
Phosphate		• (< 0,65 mmol/l) – check signs of re-feeding syndrome resulting form previous reduced macronutrient intake (calories & proteins) • Commonly occurs after major surgeries In case of low levels - progressive feeding should occur carefully and stepwise

MMTT

Foszfát a gyakorlatban

Biomarkers in our toolbox – phosphate

Critical Care Nutrition



Clinical Nutrition ESPEN

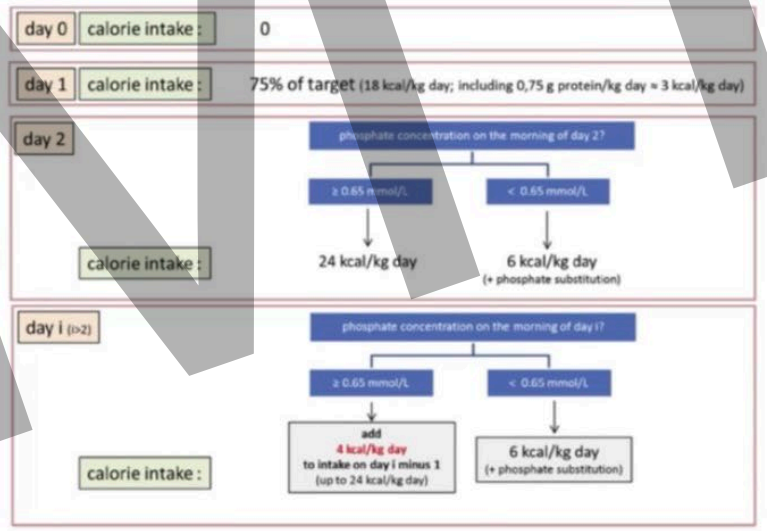
journal homepage: http://www.clinicalnutritionespen.com

Original article

Clinical Nutrition in Critical Care Medicine – Guideline of the German Society for Nutritional Medicine (DGEM)

Gunnar Elke [a, *], Wolfgang H. Hartl [b], K. Georg Kreymann [c], Michael Adolph [d], Thomas W. Felbinger [e], Tobias Graf [f], Geraldine de Heer [g], Axel R. Heller [h], Ulrich Kampa [i], Konstantin Mayer [j], Elke Muhl [k], Bernd Niemann [l], Andreas Rümelin [m], Stephan Steiner [n], Christian Stoppe [o], Arved Weimann [p], Stephan C. Bischoff [q, r]

Individual control of calorie intake by phosphate concentration; day 0 indicates the day of disturbance of homeostasis; flow diagram cannot be used in patients receiving renal replacement therapy (RRT).



Elke G et al., Clinical Nutrition in Critical Care Medicine e Guideline of the German Society for Nutritional Medicine (DGEM), Clinical Nutrition ESPEN, https://doi.org/10.1016/j.clnesp.2019.05.002

A túltáplálás következménye

Stop Feeding Inflammation

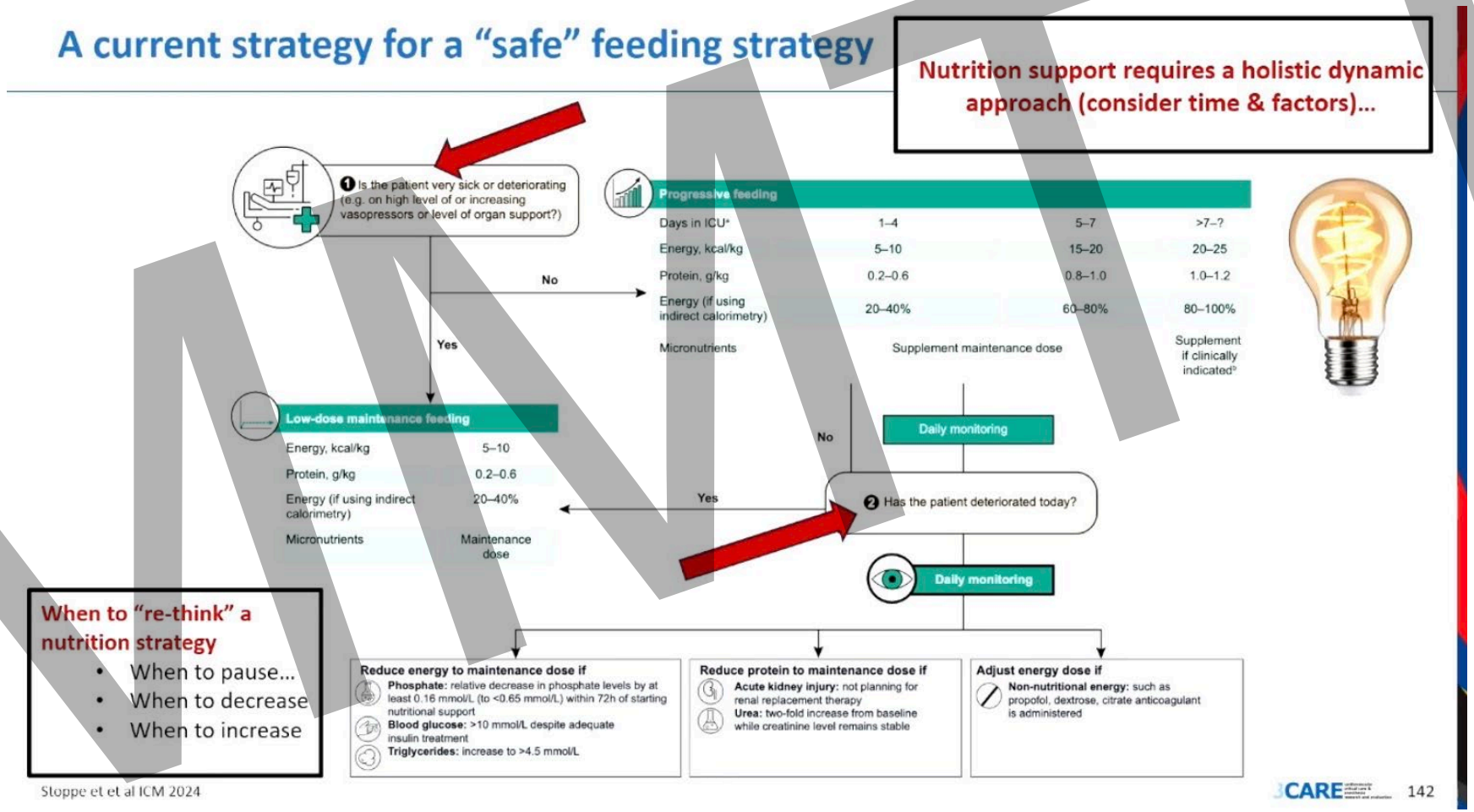


……..In the first days of critical illness, the body is catabolic, insulin resistant, and metabolically chaotic.

And we respond with… full feeding…

Early full feeding is not aggressive care. It may be aggressive ignorance.

Biztonságos táplálási stratégia



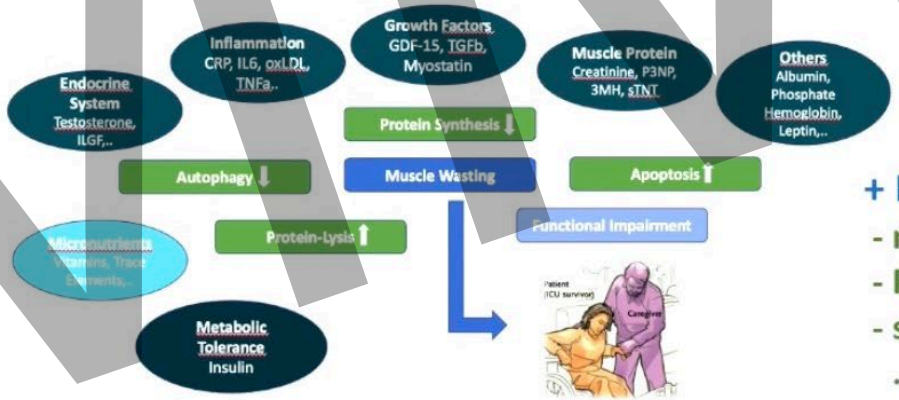
Tanulságok

Current learnings:

Critical Care Nutrition

- ***Precision medicine and personalized approaches are possible***
- *A strategy for more appropriate patient identification needs to be further established*
- ***The aspect of timing seems the most burning point as it has influence on the patients` phenotype***
- *The biological mechanisms need more recognition*

A more holistic and dynamic approach is needed to identify our target population



+ Patients baseline status

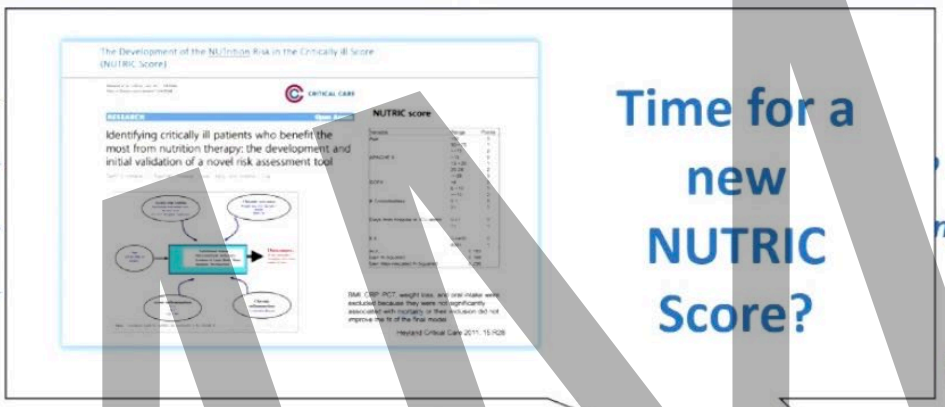
- nutritional status (GLIM, NRS,…)
- Frailty
- sarcopenia

….

Tanulságok - tervek

Current learnings:

Critical Care Nutrition

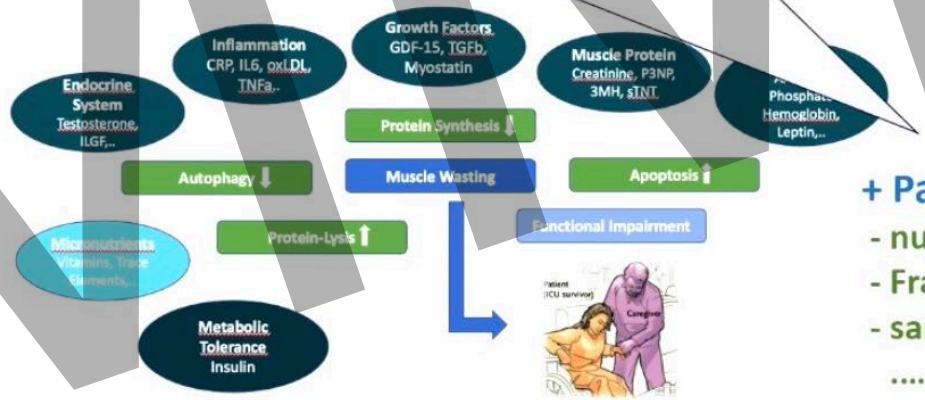


Time for a new NUTRIC Score?

be further established

influence on the patients` phenotype

to identify our target population



+ Patients baseline status

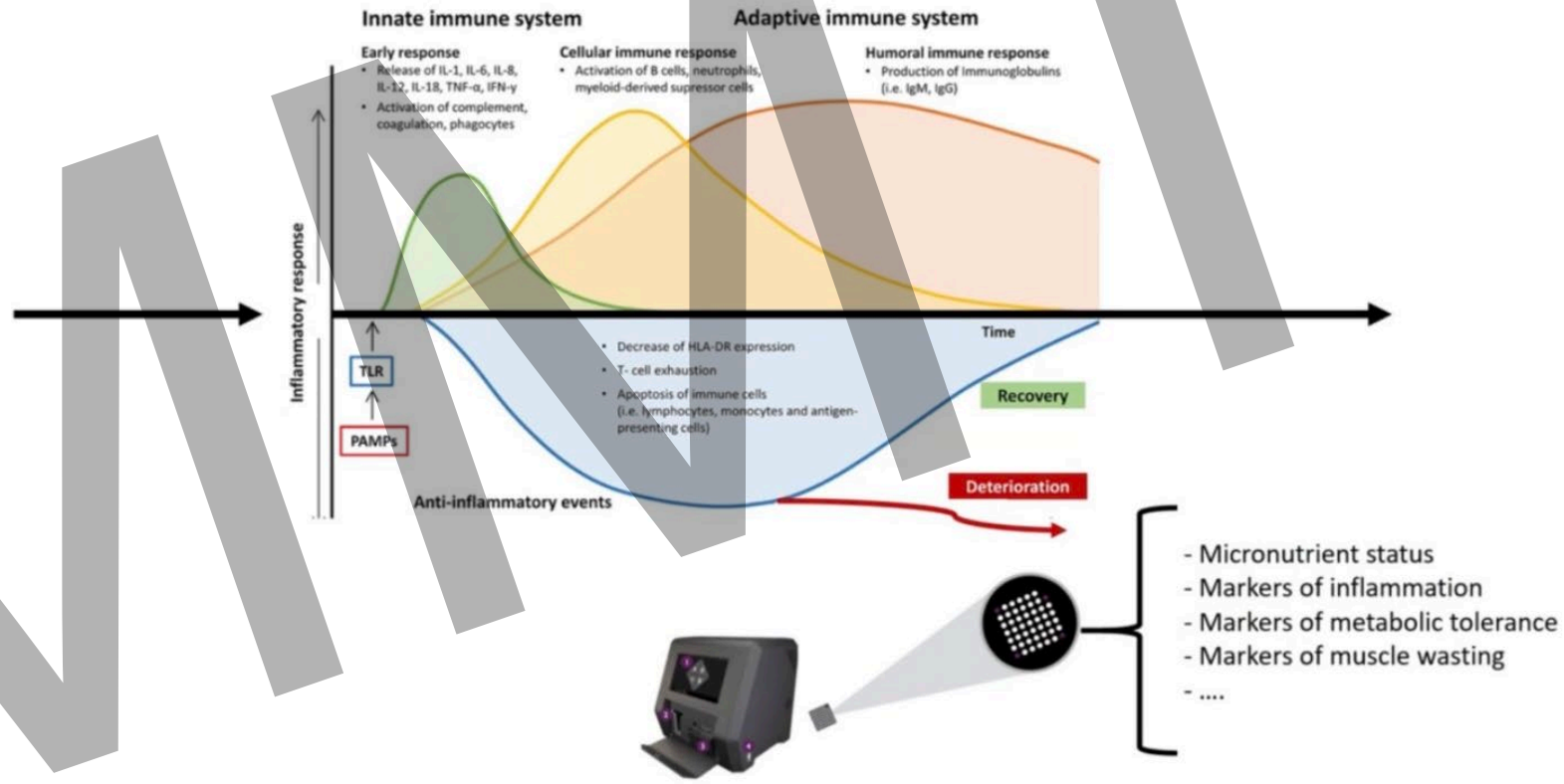
- nutritional status (GLIM, NRS,...)
- Frailty
- sarcopenia

....

KÖSZÖNÖM A LEHETŐSÉGET

My future vision for nutrition biomarkers

Critical Care Nutrition



New boundaries - the moderate study

Nutrition support requires a holistic dynamic approach (consider time & factors)…

COMING SOON

Dr. ZY Lee
Dr. W. Hartl
Dr. Ke Lu
Dr. L Gao
Dr. D. Bear
Dr. C. Lew
Dr. P. Schütz
..& many more..

MODERATE-Study

Intervention group:

- **Personalized fe… g strategy**
- Progressive in…ases of energy and protein delivery according to disease severity/metabolic to…ce until death, ICU discharg…or up to 8 days after randomization, whichever occurres first.
- Targets in th…table below depend on patients' disease severity/ metabolic tolerance, and the targ…may or may not be ach…ved.

Day of randomization	0 (randomization day)	1	2	3	4	5	6	7	8
Energy, kcal/k… day	(0.25 kcal/kg h)	10	15	20	25	25	25	25	25
Protein, g/kg d…	(0.01 – 0.02 g/kg h)	0.4	0.6	0.8	1.0	1.0	1.0	1.0	1.0



When to "re-think" a nutrition strategy

- When to pause…
- When to decrease
- When to increase

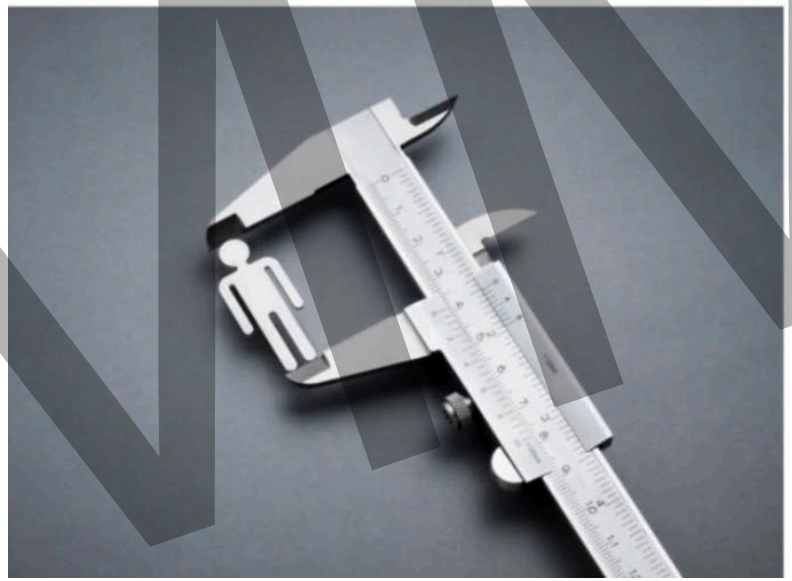
Individualized Therapy enabled by:

- SOFA Score
- Insulin requirements
- Phosphate levels

With kind support FRESENIUS KABI

Beteg kiválasztás

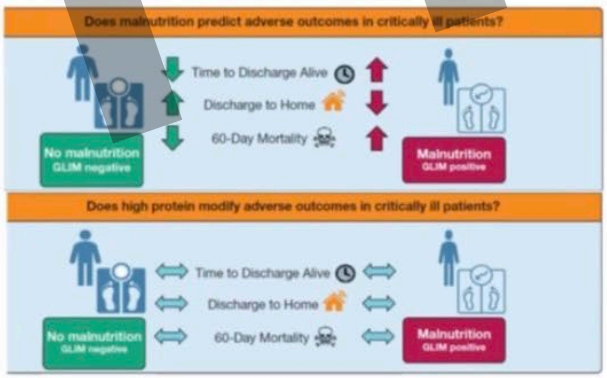
The problem of adequate patient identification



- **In WHOM to start…**
  - Baseline factors for patient identification (e.g. BMI, frailty…)

Post-hoc analysis of the EFFORT Protein trial

Lew et al. *Chest* 2024. DOI: 10.1016/j.chest.2024.02.008



Better strategies are needed to identify patients that benefit!

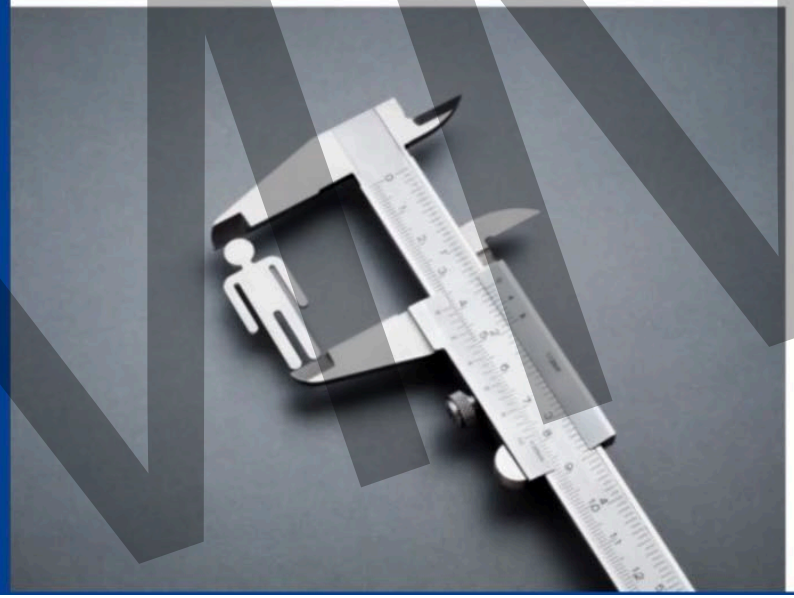
Beteg kiválasztás

The problem of adequate patient identification

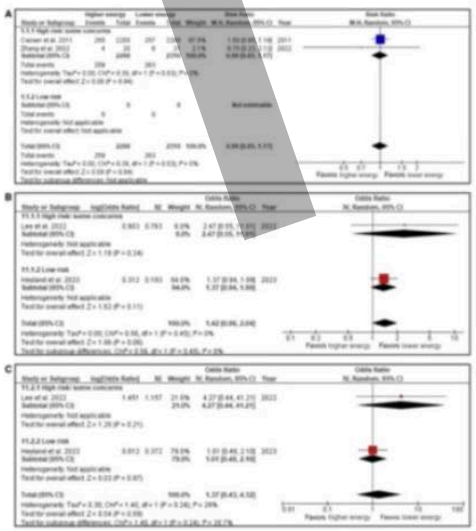
Meta-Analysis

Association Between Energy Delivery and Outcomes in Adult Critically Ill Patients Diagnosed With or At Risk of Malnutrition: A Systematic Review and Meta-analysis With Trial Sequential Analysis

Shu Han Chong, BSc (Hons) [1]; Yingxiao Huang, MSc [2]; Mei Shan Heng, BSc (Hons) [3]; Elizabeth Sin Tzun Chong, BSc (Hons) [4]; Cassandra D.Q. Lim, MSc [5]; Kok Wah Wong, MSc [6]; Hiu Nam Chan, MSc [7]; Daren K. Heyland, MD [8]; Christian Stoppe, MD [9,10]; Charlene Compher, PhD [11]; Zheng-Yii Lee, PhD [8,10,12]; Alvin Wong, PhD [2]; Charles Chin Han Lew, PhD [1,13,*]



- **In WHOM to start…**
  - Baseline factors for patient identification



These data do not support the prevailing belief that higher energy delivery improves survival in adult critically ill patients diagnosed with or at risk of malnutrition.

Biomarkerek

Biomarkers in our toolbox – in the clinical routine

Critical Care Nutrition

Biomarker	Used for	Decription	Valid in	Limitations	Major findings
CRP	Inflammatory State	good marker to assess inflammation and possible treatment response	• Hospitalized patients[1] • ICU patient[2]	• Slow kinetics • Unspecific to inflammation and infectious events	CRP (>100mg/dl) identified patients that benefit and not benefit form nutrition
IL6	Inflammatory State	Rapidly acting inflammatory marker	All types of patients	Limited availability, costly	
Albumin, pre-Albumin	Negative acute-phase protein	used to assess nutritional status or to evaluate progress of nutritional support	• As part of many risk scores • Low Albumin levels were associated with an increased risk to die	• Long half time • Influenced by several other factors than nutrition (e.g. liver function)	Albumin and pre-Albumin failed to identify patients that benefit from nutrition
Nitrogen loss	To indicate if nitrogen "protein" loss is higher tha upate	Collection of urine over 6-24 h and blood sampling	• ICU patients	• Influenced by many other factors	Indicates a biological mechanism related to the intervention and clinical outcome
GFR	Kidney function	Filtration capacity of kidneys	All patients, especially to asses prior kidney finction	• Influenced by several other factors	patients with a low GFR had showed a survival benefit after nutrition therapy

1. Merker M., et al. Association of Baseline Inflammation With Effectiveness of Nutritional Support Among Patients With Disease-Related Malnutrition: A Secondary Analysis of a Randomized Clinical Trial. JAMA Netw Open. 2020;3:e200663.
2. Ingels C et al. C- reactive protein rise in response to macronutrient deficit early in critical illness: sign of inflammation or mediator of infection prevention and recovery. Intensive Care Med. 2022;48:25-35.

IL6 – limitált hozzáférés

Biomarkers in our toolbox – in the clinical routine

Critical Care Nutrition

Biomarker	Used for	Decription	Valid in	Limitations	Major findings
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Nitrogen loss	To indicate if nitrogen "protein" loss is higher tha upate	Collection of urine over 6-24 h and blood sampling	• ICU patients	• Influenced by many other factors	Indicates a biological mechanism related to the intervention and clinical outcome
GFR	Kidney function	Filtration capacity of kidneys	All patients, especially to asses prior kidney finction	• Influenced by several other factors	patients with a low GFR had showed a survival benefit after nutrition therapy

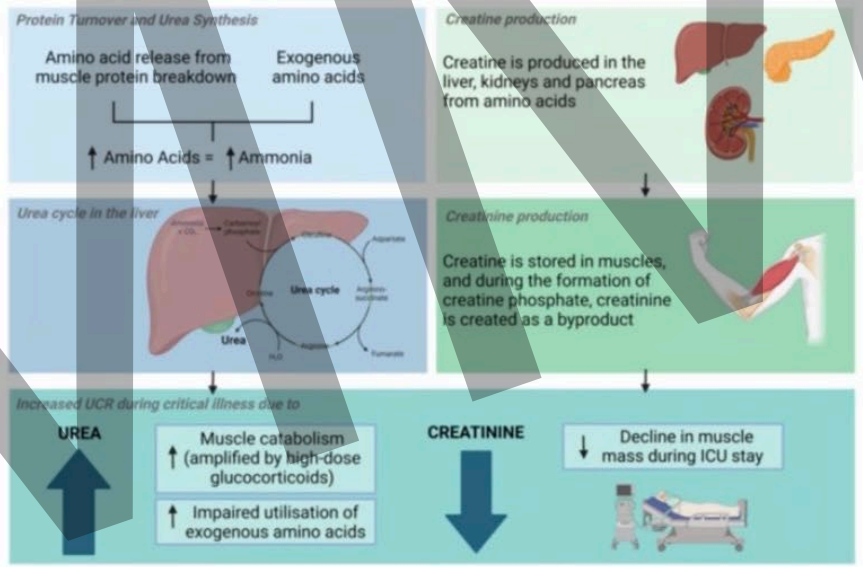
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2. Ingels C et al. C- reactive protein rise in response to macronutrient deficit early in critical illness: sign of inflammation or mediator of infection prevention and recovery. Intensive Care Med. 2022;48:25-35.

Karbamid/kreatinin arány

Biomarkers in our toolbox – others

Biomarker

Urea – Creatinine ratio



Paulus et al. Critical Care (2025) 29:175
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Critical Care

REVIEW Open Access

The urea-to-creatinine ratio as an emerging biomarker in critical care: a scoping review and meta-analysis

Michelle Carmen Paulus[1,2], Max Melchers[1,2], Anouck van Es[1], Imre Willemijn Kehinde Kouw[1,2] and Arthur Raymond Hubert van Zanten[1,2*]

Urea-to-creatinine ratio during critical illness.

Potential causes of increased UCR during critical illness and other factors that may contribute to this phenomenon.

Biztonságos táplálási stratégia

