Gastrointestinal tract (GIT) and Sequential Organ Failure Assessment (SOFA)

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Disclosures

- Advisory board or speaker fees
  - Nestlé
  - Fresenius
  - Nutricia
  - VIPUN Medical
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Multiple organ dysfunction – scoring

Organ system	Definition of dysfunction
Cardiovascular	Vasoactive drugs
Respiratory	Oxygenation
Neurological	Glasgow Coma Scale
Renal	Creatinine and urine output
Liver	Bilirubin
Hematological/coagulation	Platelet count

"The gut was felt to be very important, but too complex and therefore abandoned"

Vincent JL et al. SOFA score. Intensive Care Medicine 1996;707-710

Gastrointestinal functions

- Functions
  - Digestion and absorption (energy intake)
  - Endocrine
  - Immunological
  - Barrier

Biomarkers?

- Functioning motility [1] = prerequisite for absorption
  - Mixing = segmental contractions without propulsion
  - Propulsion = peristaltic contractions (incl. relaxation in-between)
  - Reservoir via sphincters and segmental contractions

1. Boron WF, Boulpaep EL. Medical physiology. Saunders 2012

GI Symptoms and outcome

- Univariate Analysis, number of patients (percentage)

	Total	Survivors	Nonsurvivors	P-value
Absent peristalsis	542 (41.3)	300 (30.3)	241 (75.3)	<0.001
Bowel distension	139 (10.6)	77 (7.8)	62 (19.4)	<0.001
GI Bleeding		53 (5.3)	44 (13.8)	<0.001
Large GRV*		210 (21.2)	88 (27.5)	0.013
Vomiting	501 (38.2)	370 (37.3)	131 (40.9)	0.139
Diarrhoea	184 (14.0)	135 (13.6)	49 (15.3)	0.251

Definitions?

- * GRV total per 24h
- None of the GI symptoms is an independent predictor of mortality

Reintam A et al. Acta Anaesthesiol Scand. 2009;53(3):318-24

An addition to GI symptoms

- Intra-abdominal pressure (IAP)
  - Assessment of the abdominal compartment
  - Numerical, reproducible
  - Associated with mortality (depending on severity of IAH)
  - Association with GI function unclear

	IAP <12 mmHg	IAP ≥ 12 mmHg
Vomiting / Regurgitation	28%	49%
GRV >500 ml / day	11%	22%
Feeding intolerance	16%	25%

Reintam Blaser et al. Crit Care Res Pract. 2011:982507

GIF score 2008

Points	Description
0	"normal" function
1	Enteral feeding <50% of needs
2	Feeding intolerance OR intra-abdominal pressure ≥ 12 mmHg
3	Feeding intolerance AND intra-abdominal pressure ≥ 12 mmHg
4	Abdominal compartment syndrome (intra-abdominal pressure >20 mmHg (with new or worsening organ dysfunction)

Feeding intolerance = enteral feeding stopped because of GI symptoms

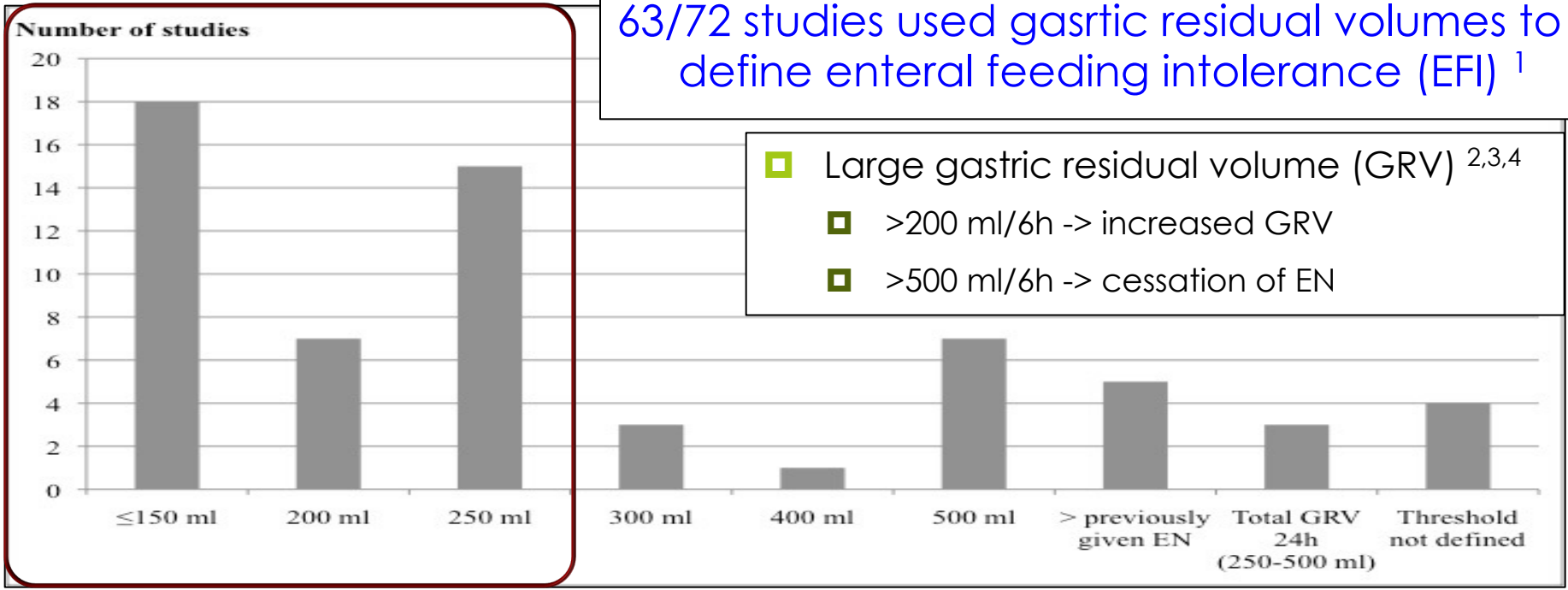
SOFA subscores and GIF score in regression analysis for prediction of ICU mortality

Score/subscore	*P*	OR	95% CI
Cardiovascular SOFA	<0.001	5.91	2.83–12.33
GIF score	0.004	2.20	1.28–3.78
Hepatic SOFA	0.024	1.75	1.075–2.86
Renal SOFA	0.087	1.39	0.95–2.04
Central nervous system SOFA	0.159	1.23	0.92–1.65
Haematological SOFA	0.712	0.92	0.57–1.47
Respiratory SOFA	0.518	0.84	0.48–1.44

CI, confidence interval; GIF, Gastrointestinal Failure (score); OR, odds ratio; SOFA, Sequential Organ Failure Assessment.

Reintam A et al. Crit Care 2008;12:R90
Reintam A. Dissertationes Medicinae Universitas Tartuensis 150; 2008

Definition of feeding intolerance



63/72 studies used gasrtic residual volumes to define enteral feeding intolerance (EFI) [1]

- Large gastric residual volume (GRV) [2,3,4]
  - >200 ml/6h -> increased GRV
  - >500 ml/6h -> cessation of EN

1. Reintam Blaser A. Acta Anaesth Scand 2014;58(8):914–922
2. McClave S. 2016;40(2):159–211
3. Reintam Blaser A. Int Care Med 2017;43(3):380–398
4. Singer P. Clin Nutr 2019;38(1):48–79

EDITORIAL

Editorials represent the opinions of the authors and *JAMA* and not those of the American Medical Association.

Rice TW. JAMA 2013;309:283-284

Gastric Residual Volume
End of an Era

Todd W. Rice, MD, MSc

GASTRIC DYSMOTILITY IS COMMON IN CRITICALLY ILL patients. The pathophysiology is multifactorial including the severity and etiology of the underlying critical illness, use of narcotic analgesia and other sedatives, decreased blood flow from shock, and use of vasopressors. Gastric dysmotility results in delayed gastric emptying that may place patients at risk of developing complications such as vomiting, aspiration, and ventilator-associated pneumonia (VAP). To manage this risk, guide-

An Editorial announced an “End of an Era” for measurements of Gastric residual volumes after the study by Reignier et al. was published in JAMA 2013.

Too early, too generalized and without substitute/alternative?

of mechanical ventilation and ventilator-free days, intensive care unit (ICU) lengths of stay, and ICU and hospital mortality, were also similar. These data prompted many to increase their GRV threshold to between 300 mL and 500 mL or to require additional signs of gastrointestinal intolerance before interrupting enteral feedings.[7,8]

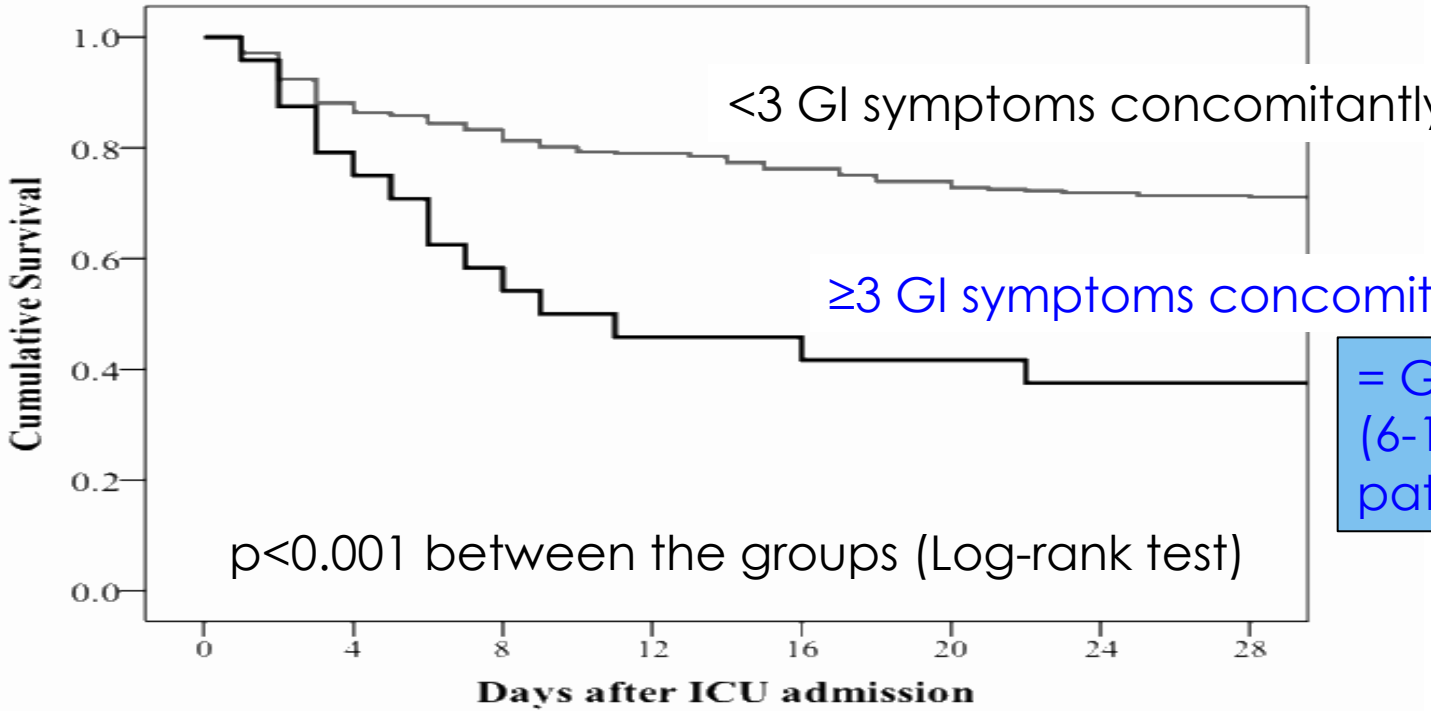
However, it still was not clear that GRVs alone were clinically important, that they were correlated with gastrointestinal intolerances, or that holding enteral feedings for some arbitrary volume provided any protection from feeding complications. Mentec et al[9] found that more than half of criti-

tients randomized to 200 mL and 400 mL of GRV thresholds. Again, enteral feedings were interrupted significantly more with lower thresholds.

Mentejo et al[6] took the concept of higher GRV thresholds further by comparing clinical outcomes of patients randomized to 200- vs 500-mL thresholds. Patients managed with higher thresholds received a higher percentage of prescribed enteral nutrition over the first week and reached goal

cal question was whether monitoring GRVs conferred any clinical benefit. In this issue of *JAMA*, the clinical trial by Reignier and colleagues[12] provides an answer to this question. The investigators randomized 449 adults receiving enteral nutrition via gastric tubes within 36 hours of initiation of mechanical ventilation, 222 of whom were randomized to a protocol in which GRV was checked every 6 hours, with adjustment of enteral feeding rates if the

Coincident GI symptoms



= GI failure (6-10% of ICU patients)

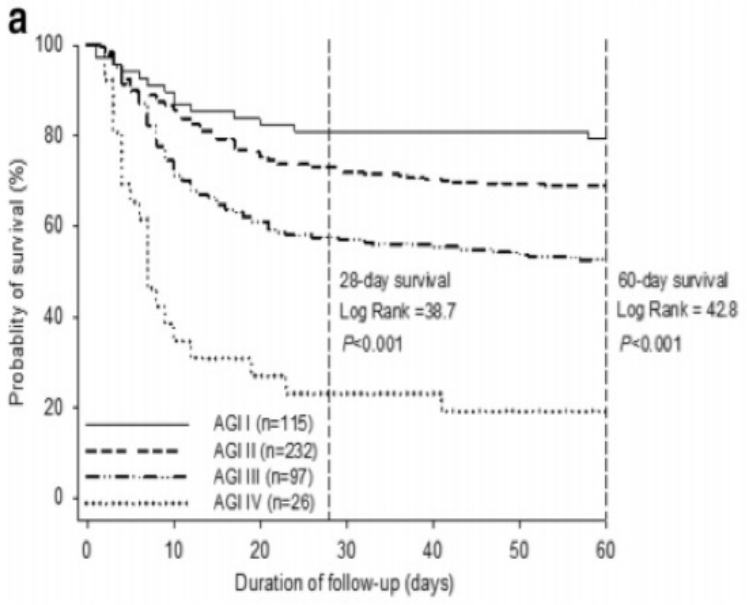
Reintam Blaser A. Intensive Care Med 2013; 39(5):899-909

Padar M. J Crit Care 2019;52:103-108

Visualization by J. Starkopf

AGI Grading = subjective and descriptive

Despite that validated in several studies (increasing AGI grade is independently associated with mortality)



Reintam Blaser A et al. Intensive Care Med 2012;38(3):384-94

I = symptoms after an insult, self-limiting (e.g. vomiting or absence of peristalsis postop.)

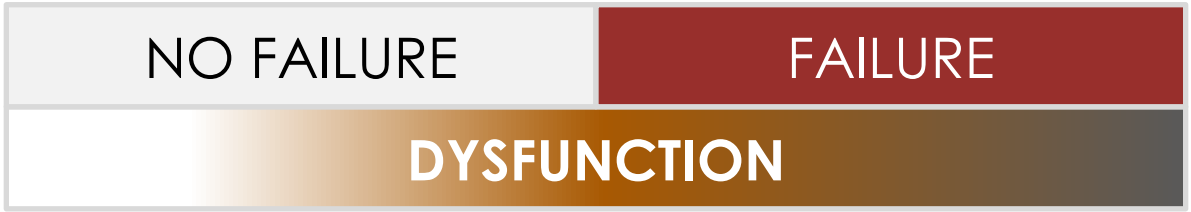
II = requires interventions, several/severe symptoms

III = feeding intolerance persists/progresses despite interventions, worsening multiple organ failure

IV = dramatically manifested GI failure, immediately life-threatening

Zhang D. Medicine (Baltimore) 2018;97(43):e12970
Hu B. Crit Care 2017;21(1):188

iSOFA study



CLINICAL DATA + CITRULLINE – enterocyte function
I-FABP – enterocyte damage = Variables in the score

28- and 90-d mortality, in a model with SOFA score

Reintam Blaser A et al. Clin Nutr 2021;40(8):4932-4940

Association of GI symptoms & biomarkers with mortality

Univariate analyses	28-day mortality		90-day mortality	
	HR (95%CI)	P-value	HR (95%CI)	P-value
Absent bowel sounds	2.44 (1.39; 4.28)	**0.002**	2.26 (1.34; 3.82)	**0.002**
Vomiting/regurgitation	1.28 (0.40; 4.15)	0.677	0.96 (0.30; 3.09)	0.941
Diarrhea	1.47 (0.69; 3.17)	0.320	1.44 (0.73; 2.86)	0.293
Abdominal distension	3.95 (2.35; 6.64)	**<0.001**	3.88 (2.43; 6.20)	**<0.001**
GI bleeding	0.94 (0.23; 3.81)	0.932	0.85 (0.21; 3.48)	0.821
GI paralysis	3.47 (1.79; 6.73)	**<0.001**	3.52 (1.97; 6.31)	**<0.001**
Large gastric residual volume	3.56 (1.66; 7.62)	**0.001**	2.97 (1.45; 6.07)	**0.003**
Intra-abdominal hypertension	1.42 (0.76; 2.65)	0.265	1.26 (0.72; 2.20)	0.411
Citrulline (continuous variable)	1.00 (0.97; 1.03)	0.861	1.00 (0.97; 1.03)	0.800
Citrulline below reference	0.94 (0.35; 2.51)	0.896	1.17 (0.50; 2.71)	0.717
I-FABP (continuous variable)	1 (1; 1)	0.088	1 (1; 1)	0.114
I-FABP above reference	2.95 (1.18; 7.38)	**0.021**	2.11 (0.88; 5.08)	0.096

I-FABP = intestinal fatty acid binding protein

Reintam Blaser A et al. Clin Nutr 2021;40(8):4932-4940

Multivariate analysis with SOFA subscores

	28-day mortality		90-day mortality	
Variable	**Hazard ratio (95% CI)**	**P-value**	**Hazard ratio (95% CI)**	**P-value**
Absent bowel sounds	1.34 (0.78; 2.32)	0.287	1.28 (0.77; 2.13)	0.349
Vomiting/Regurgitation	1.78 (0.57; 5.59)	0.321	1.25 (0.39; 4.04)	0.704
Oral Intake	0.33 (0.17; 0.64)	**0.001**	0.38 (0.22; 0.66)	**0.001**
Diarrhea	1.33 (0.60; 2.93)	0.482	1.37 (0.69; 2.72)	0.367
Abdominal Distension	1.71 (0.92; 3.16)	0.090	1.77 (1.03; 3.03)	**0.038**
GI bleeding	1.04 (0.20; 5.44)	0.960	0.97 (0.19; 4.89)	0.972
GI Paralysis/Ileus	1.86 (0.87; 4.00)	0.111	2.20 (1.15; 4.19)	**0.017**
GRV over 200	1.54 (0.68; 3.48)	0.300	1.25 (0.58; 2.71)	0.565

Number of symptoms important

Reintam Blaser A et al. Clin Nutr 2021;40(8):4932-4940

A single symptom/sign is not sufficient

	GI dysfunction present	GI dysfunction absent
Positive test Bowel sounds absent	**TRUE Positive** **No bowel sounds detected AND** **patient has GI dysfunction and EFI**	**FALSE positive** **No bowel sounds detected BUT** **patient does not have GI dysfunction/EFI**
Negative test Bowel sounds present	**FALSE negative** **Bowel sounds heard BUT** **patient has GI dysfunction and EFI**	**TRUE negative** **Bowel sounds heard AND** **patient does not have GI dysfunction/EFI**

EN should not be withheld

EN should be applied carefully or even withheld (**depending on other signs and symptoms**)

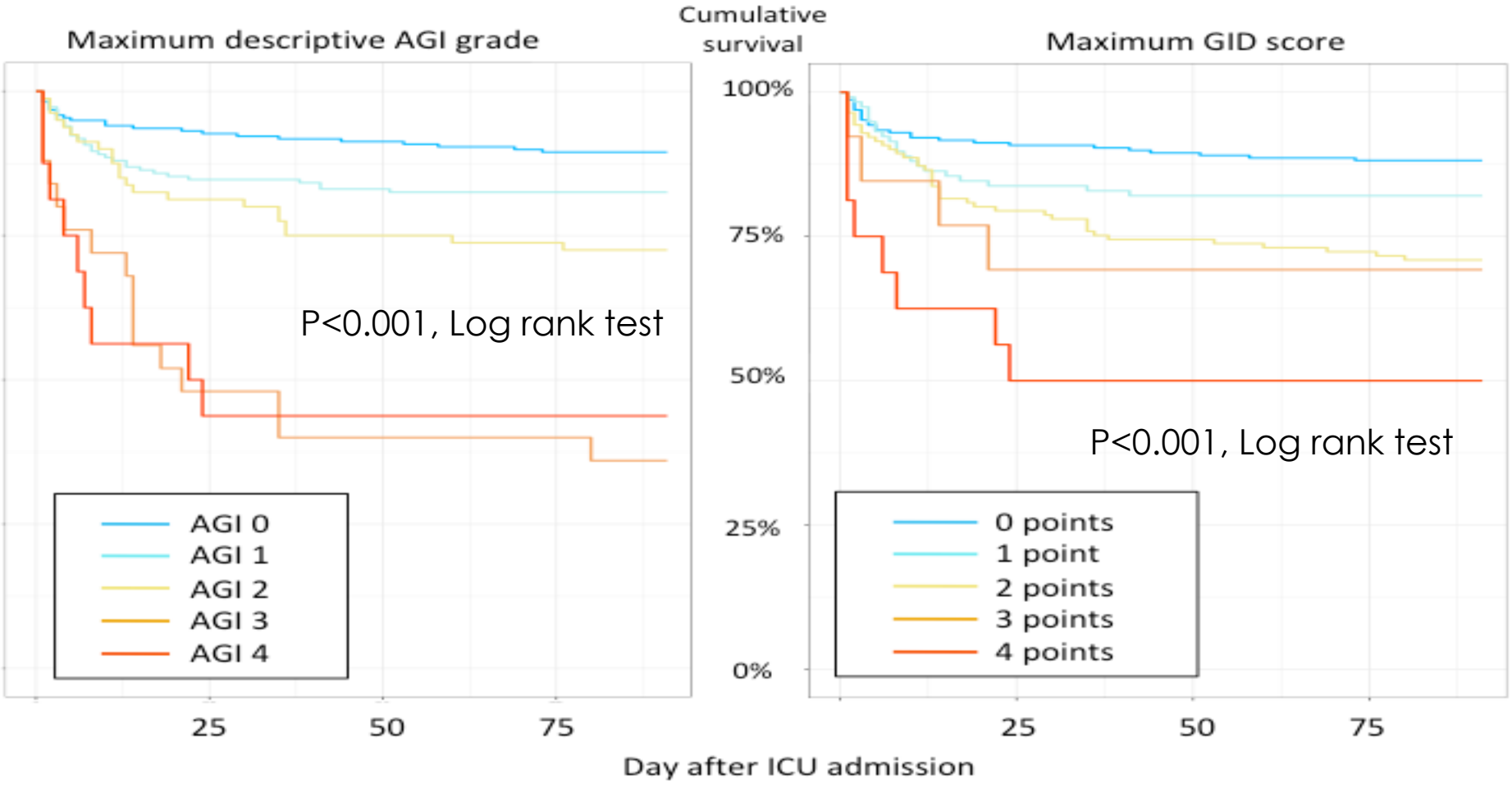
EFI = enteral feeding intolerance

1 single symptom in a patient WITH oral intake is NOT sufficient to define GI dysfunction	1 single symptom in a patient WITHOUT oral intake is sufficient to define the risk of GI dysfunction	More symptoms or single severe symptoms define GI dysfunction	Several severe symptoms (under treatment) define failure	One immediately life-threatening condition
- Absent bowel sounds - Vomiting - GRV > 200 ml - GI paralysis/ileus - Abdominal distension - Diarrhoea (not severe) - GI bleeding without transfusion - IAP 12-20 mmHg	- No oral intake - Vomiting - Absent bowel sounds - GRV >200 ml - GI paralysis/ileus - Abdominal distension - Diarrhoea (not severe) - GI bleeding without transfusion - IAP 12-20 mmHg	- Severe diarrhoea - GI bleeding with transfusion - IAP > 20 mmHg	- Prokinetic use - GI paralysis/ dynamic ileus - Abdominal distension - Severe diarrhoea - GI bleeding with transfusion - IAP > 20 mmHg	- GI bleeding leading to hemorrhagic shock - Mesenteric ischaemia - Abdominal compartment syndrome

Reintam Blaser A et al. Clin Nutr 2021;40(8):4932-4940

GIDS - independent impact on mortality

Multivariate Cox Model: SOFA subscores + GIDS				
	28-day mortality		90-d mortality	
SOFA cardiovascular	1.15 (0.95; 1.41)	0.136	1.13 (0.95; 1.34)	0.162
SOFA respiratory	1.20 (0.92; 1.56)	0.167	1.25 (1.01; 1.54)	**0.036**
SOFA hematological	0.88 (0.65; 1.20)	0.422	0.89 (0.67; 1.18)	0.425
SOFA renal	1.48 (1.22; 1.80)	**<0.001**	1.37 (1.14; 1.65)	**<0.001**
SOFA hepatic	1.00 (0.72; 1.40)	0.994	1.05 (0.77; 1.43)	0.758
SOFA neurological	1.59 (1.30; 1.94)	**<0.001**	1.58 (1.31; 1.89)	**<0.001**
GIDS	1.48 (1.13; 1.92)	**0.003**	1.47 (1.15; 1.87)	**0.001**


Maximum descriptive AGI grade
Cumulative survival
Maximum GID score
100%
75%
50%
25%
0%
P<0.001, Log rank test
P<0.001, Log rank test
AGI 0
AGI 1
AGI 2
AGI 3
AGI 4
0 points
1 point
2 points
3 points
4 points
25
50
75
25
50
75
Day after ICU admission

Validation of GIDS?

Table 3
Multi-factor regression analysis with 28-day mortality and GIDS.

	OR (95% CI)	*P value*
Age	1.025 (0.999; 1.052)	0.059
Principal pathology–Cardiovascular	3.0093 (1.097; 8.718)	**0.033**
Principal pathology–Neurological	0.828 (0.334; 2.052)	0.684
Principal pathology–Renal	1.443 (0.340; 6.131)	0.619
Principal pathology–Metabolic disorders	6.132 (0.993; 35.873)	0.051
GIDS group	2.946 (1.188; 7.307)	**0.020**
AGI	1.224 (0.668; 2.242)	0.513
APACHE II	1.051 (0.989; 1.117)	0.106
SOFA	1.082 (0.9626; 1.217)	0.191
Start enteral nutrition within 48 h	0.817 (0.375; 1.777)	0.610
Septic shock	1.053 (0.333; 3.328)	0.929
Sepsis	1.604 (0.708; 3.634)	0.258
Duration of mechanical ventilation, hours	1.003 (1.000; 1.005)	**0.031**

All variables except duration of mechanical ventilation are reported here for admission day. GIDS, Gastrointestinal Dysfunction Score; AGI, acute gastrointestinal injury; APACHE II, Acute Physiology and Chronic Health Evaluation II; SOFA, Sequential Organ Failure Assessment.

← GIDS 0-1 vs GIDS 2-4

Liu X et al. Clinical Nutrition 42 (2023) 700e705

Future

Planned in 2023-2024

- Define core set of daily monitoring of GI function in critically ill
  - COSMOGI (Delphi process >200 panel members)
- Validate GIDS (together with epidemiology of dysphosphatemia)
  - GUTPHOS (observational study with 1500 patients)
- SOFA 2.0 consensus process within ESICM

Not yet planned in detail

- Test GIDS for management of GI dysfunction and guiding EN

www.cosmogi.site (Kaspar Bachmann) annika.reintam.blaser@ut.ee

Summary

- The clinical score (GIDS) is far from perfect, but as good as it gets
  - Performs similarly to AGI grading but with reduced subjectivity
  - Includes upper and lower GI dysfunction
  - Focused on motility, not directly GI function
  - Includes GI symptoms that are subjective/observer-dependent
  - Not externally validated (developed with the mortality outcome)

GIT and SOFA??