Martin Padar on Anestesiologian ja tehohoidon erikoislääkäri Tartossa. Hän väitteli tohtoriksi 12.11.2021 aiheenaan "Enteral nutrition, gastrointestinal dysfunction and intestinal biomarkers in critically ill patients". SAY:n puheenjohtaja Matti Reinikainen toimi Martinin vastaväittäjänä. Martin ystävällisesti kirjoitti Finnanestiin katsauksen väitöskirjatyönsä aiheesta.

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Quantifying gastrointestinal dysfunction

Managing single or multiple organ dysfunction is a cornerstone of modern intensive care. Despite rapid advances in the diagnostic capabilities and treatment or replacement therapies of other organ systems, functioning of the gastrointestinal (GI) tract in critically ill patients continues to be assessed mainly using observer-dependent clinical examination.

The GI tract is not included in currently used illness severity and multiple organ dysfunction assessment scores, impeding research in the field. Partly as a consequence, treatment options tageting the GI tract, other than enteral nutrition (EN), are few.

Functions of the GI tract include digestion and absorption of nutrients and water, and barrier, endocrine and immune functions. Adequate perfusion, secretion, motility and coordinated gut-microbiome interactions are necessary for normal functioning (1). Some adaptations related to critical illness are well recognized, such as loss of appetite, anorexia and decreased bowel motility (2,3). However, normal functioning of the GI tract in critical illness is difficult to identify and no unified definition exists. Nevertheless, it is important to recognize and to be able to diagnose abnormal functioning of the GI tract to assess and manage GI problems in critically ill patients.

Clinical assessment remains the main method to monitor GI function in critical illness. No imaging strategy, biomarker nor method to assess absorption or barrier function has been sufficiently validated or is available for everyday use. Therefore, previous attempts at quantifying GI dysfunction in intensive care patients have mostly centred around assessment of gastrointestinal or abdominal signs and symptoms. These notably varying and numerous attempts over the last decades are summarized in Table 1, hinting at >>

Name or acronym, year	Components / rationale	Gradation	Research-derived	External validation*	Comments / problems
GI failure, 1985 (10) Specific diseases (cholecystitis, stress ulcer etc)	Yes, 2 grades	Yes	Yes	Initially included in MOF score	
GI dysfunction, 1987 (11)	FI defined through 4 abdominal/ GI symptoms	None	Yes	No	Poorly defined, subjective GI features
GI dysfunction, 2006 (12)	Prolonged ileus or GI bleeding	None	Yes	No	GI failure in 2.6% of patients, not a predictor of mortality
GI failure, 2006 (13)	FI, GI bleeding, ileus	None	Yes	No	FI and ileus poorly defined
GIF score, 2008 (5)	Amount of EN, FI, IAH, ACS	Yes, 4 grades	Yes	Yes	Poor continuity
LIFE score, 2008 (14)	IAP, lactic acidosis, progression of enteral feeding, GI symptoms	Yes, 5 grades	No	No	Never validated
Acute GI Injury, 2012 (1)	Descriptive grading. Rationale: 1. risk/self-limiting condition 2.GI dysfunction 3. GI failure 4. life-threatening GI failure	Yes, 4 grades	No	Yes	Developed with consensus. FI poorly defined. Other organ dysfunctions play important role
GI failure, 2013 (6)	≥ 3 coincident GI symptoms	None	Yes	Yes	Poorly defined, subjective GI features
Intestinal failure, 2015 (15)	Descriptive categorization, rationale: 1. Acute, short-term condition 2. Prolonged acute condition 3. Chronic condition	No	No	Partial	Based on duration = not well applicable at any time point
Gut failure 2013/2016 (16,17)	Plasma citrulline and I-FABP	No	Yes	No	Relation to clinical features and EN not included
Modified GIF score, 2019 (18)	0–4 points for each category: daily energy balance, gastric residual volumes and vomiting, stool passage	Yes, 0–12 points	Yes	No	Retrospective; link between GI dysfunction and energy balance not certain*

Table 1. GI – gastrointestinal; MOF – multiple organ failure; FI – feeding intolerance; GIF – Gastrointestinal Failure (score); EN – enteral nutrition; IAH – intra-abdominal hypertension; ACS – abdominal compartment syndrome; LIFE – Lausanne Intestinal Failure Estimation; IAP – intra-abdominal pressure; MODS – Multiple Organ Dysfunction Score; I-FABP – intestinal fatty acid binding protein.

*The score has been tested (for prediction of outcome) in a general adult ICU population other than the development cohort.

the complexity of this organ system and also of its task. Indeed, in 1996, when for the first time proposing the Sepsis-related Organ Failure Assessment (SOFA) score to describe multiple organ dysfunction, authors noted that "attempting to include dysfunction/failure of the gut was felt to be very important, but also too complex and was therefore abandoned" (4). Below, a short overview is given on some approaches to define GI dysfunction, with emphasis on the work performed by the University of Tartu research group.

Previous attempts to define GI dysfunction / failure

In 2008, the Gastrointestinal Failure (GIF) score was created based on feeding intolerance (FI) and intra-abdominal hypertension (IAH) (5). FI was defined as the need to discontinue EN due to vomiting, high gastric residual volume (GRV), ileus, severe diarrhoea, abdominal pain or distension. Among 264 consecutive mechanically ventilated patients in a single centre, FI developed in 58 % and IAH in 27 % of patients. A clinical score with 4 grades of severity was created: 0 – normal gastrointestinal function; 1 – EN possible but achieving < 50 % of calculated needs or no feeding during 3 days after abdominal surgery;

0 No risk	1 Increased risk	2 GI dysfunction	3 GI failure	4 Life threatening
No symptoms OR one of the following with oral intake	Two of the following	Three or more symptoms of score 1 OR up to two of the following	Three or more of the following	One of the following
▪ Absent bowel sounds ▪ Vomiting ▪ GRV > 200 ml ▪ GI paralysis/ dynamic ileus ▪ Abdominal distension ▪ Diarrhoea (not severe) ▪ GI bleeding without transfusion ▪ IAP 12–20 mmHg	▪ No oral intake ▪ Absent bowel sounds ▪ Vomiting ▪ GRV > 200 ml ▪ GI paralysis/ dynamic 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 haemorrhagic shock ▪ Mesenteric ischaemia ▪ Abdominal compartment syndrome

Table 2. Gastrointestinal Dysfunction Score (GIDS), Adapted from (8).

2 – FI or IAH; 3 – FI and IAH; 4 – abdominal compartment syndrome. The average GIF score during the first 3 days of ICU appeared as an independent risk factor for ICU mortality and slightly improved the predictive ability of the Sequential Organ Failure Assessment (SOFA) score. Nevertheless, while the GIF score can be easily assessed using readily available clinical data, major limitations include the subjective nature of determining FI and the fact that the score does not reflect a continuum of function.

In a subsequent attempt to create a GI dysfunction score, 377 mechanically ventilated adult patients from 40 ICUs were included in a prospective study collecting data on prespecified GI symptoms (absent bowel sounds, vomiting/ regurgitation, GRV, diarrhoea, bowel distension, GI bleeding), feeding and IAH (6). Based on daily comparisons between survivors and non-survivors with different number of GI symptoms, a cut-off for GI failure was identified at the presence of 3 or more concomitant symptoms in one day. GIF diagnosed this way occurred in 6.4 % of patients and if present on admission day, was associated with a threefold independent increase in mortality. In addition, a score based on 6 aforementioned GI symptoms, named similarly the GIF score, was proposed, with the severity gradation as follows: 0 – no GI symptoms; 1 – 1 symptom; 2 – 2 symptoms; 3 – 3 symptoms; 4 – ≥4 symptoms. Even though an increasing GIF score was associated with higher mortality, it was not able to add any value to the SOFA score in terms of mortality prediction. Addition of feeding-related variables or IAH did not improve the performance of the GIF score. In a later single-centre study with the same approach, the number of GI symptoms on admission day appeared as an independent predictor of 90-day mortality alongside SOFA subscores for other organ failures (7). Problems with this approach include the subjective nature of its components and failure to appreciate different impact of each single symptom.

In 2012, the Working Group on Abdominal Problems of the European Society of Intensive Care Medicine produced a consensus document unifying the terminology and definitions of acute GI failure and GI symptoms (1). The Acute Gastrointestinal Injury (AGI) grading was developed based on expert opinion. This descriptive grading includes five degrees of severity, with AGI 0 corresponding to normal functioning of the GI tract; AGI 1 – risk; AGI 2 – GI dysfunction; AGI 3 – GI failure; AGI 4 – life-threatening condition arising from the GI tract causing distant organ failure, with examples given for each grade. Although the AGI grading has later been externally validated against mortality, its limitations include inability to apply it retrospectively, subjectivity and likely effect from other organ dysfunctions.

Gastrointestinal dysfunction score (GIDS)

To address the shortcomings of previous approaches and to produce an objective and >>

reproducible score to quantify GI dysfunction, a multicentre prospective observational study including 540 consecutive intensive care patients was conducted (8). The emphasis of data collection during the patients' first week of ICU stay was placed on gastrointestinal and abdominal signs and symptoms as well as feeding and intra-abdominal pressure. In a subset of patients, biomarkers citrulline and intestinal fatty acid-binding protein (I-FABP) were measured. A stepwise statistical process taking into account the impact of the number and severity of different single symptoms and conditions towards mortality prediction yielded the Gastrointestinal Dysfunction Score (Table 2). When added to the SOFA score, GIDS was independently associated with 28- and 90-day mortality and slightly improved the predictive power of the SOFA score.

Following the rationale of the AGI grading (1), the GIDS is composed of 4 grades of severity, with 0 points corresponding to a normal functioning of the GI tract in an intensive care patient. The situation where a patient is able to eat and experiences just one GI symptom or grade I-II IAH was best categorised as normal GI function. As in the GIF score (6,7), the importance of simultaneously occurring signs and symptoms is emphasised in the constitution of GIDS. IAH, although not a measure of GI function per se, likely increases the objectivity of the score being a measurable value and complements the assessment of GI function. The highest grade of severity was defined as certain life-threatening conditions arising from the GI tract – bleeding with haemorrhagic shock, mesenteric ischaemia and abdominal compartment syndrome. With this approach, influence from other organ systems is introduced, however no particular symptom or combination of symptoms could satisfactorily describe such a state. Another critique may be that the ability or inability to eat is also affected by consciousness, respiratory function etc. Although inclusion of more objective components is desirable, adding citrulline and I-FABP to the score did not improve its performance.

Although many of the single symptoms included in the score remain subjective, for the time being the components included seem the most practical. Being developed on a prospective multicentre population of consecutively admitted ICU patients, GIDS could be a valuable tool to assess GI dysfunction either on its own or as a part of multiple organ dysfunction. Before accepting the score for clinical and research use, validation studies are needed. ■

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