

# The black box revelation: monitoring gastrointestinal function

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## Abstract

The gastrointestinal tract comprises diverse functions. Despite recent developments in technology and science, there is no single and universal tool to monitor GI function in intensive care unit (ICU) patients. Clinical evaluation is complex and has a low sensitivity to diagnose pathological processes in the abdomen. We performed a MEDLINE and Pubmed search connecting abdominal assessment and critical care. Based on these findings we defined the following major categories of monitoring and diagnostic measures: clinical investigation; assessment of motility and digestive function; microbiome monitoring; perfusion monitoring; laboratory biomarkers and hormonal function; intra-abdominal pressure measurement; and imaging techniques. Only a few of these monitoring and assessment tools have found their way into clinical practice, as most of them have one or more significant objections preventing broad implementation in daily clinical practice. Further research should be directed to reaffirm and define the use of current techniques to ascertain their validity and usefulness to monitor gastrointestinal function in ICU patients.

Anaesthesiology Intensive Therapy 2018, vol. 50, no 1, 72–81

**Key words:** gastrointestinal function, monitoring, assessment, imaging, biomarkers, abdominal pressure, perfusion

Gastrointestinal (GI) function comprises digestion, barrier control to modulate absorption, endocrine, and immune functions, whereas perfusion, secretion, motility and coordinated gut-microbiome interaction are prerequisites for an adequate function. In accordance with its diverse functions, a large variety of monitoring and diagnostic measures have been developed over the past decades. New techniques have been explored, and elder knowledge reaffirmed and refined (eg. intra-abdominal pressure). In the current review, we summarize methods that can be considered for monitoring of GI function in critically ill patients. Furthermore, we will address their advantages and disadvantages as well as usefulness in daily practice.

## METHODS

A MEDLINE and PubMed search were performed using the search terms 'gastrointestinal function', 'gastrointestinal

failure', 'gastrointestinal dysfunction', 'intestinal failure', 'acute gastrointestinal injury', 'abdominal problems', 'gastrointestinal symptoms' AND 'monitoring', 'assessment' AND ('critically ill' OR 'intensive care' OR 'critical care' OR 'critical illness'). The reference lists of identified papers were screened to identify other relevant articles. Based on the search results more in-depth search was performed using specific search terms.

## RESULTS AND DISCUSSION

### STANDARD CLINICAL ASSESSMENT

Approximately 60% of all patients in ICU will develop at least one GI problem during their ICU stay [1]. GI symptoms outside the ICU include nausea and vomiting, pain and bloating, feeding intolerance, constipation and diarrhea. Within the ICU, GI symptoms always need to be considered being a sign of GI dysfunction, however, some (e.g. post-

operative nausea and vomiting) may also occur without clinically relevant impairment of GI function.

Large variability of definitions has been used for GI symptoms in critically ill [2]. Moreover, some definitions from outside of ICU do not fit well to critically ill patients. To overcome this variability that makes comparison of different studies difficult, we have suggested unification of definitions for ICU patients, including combining them into descriptive grading system for Acute Gastrointestinal Injury (AGI) [2]. However, assessment of GI symptoms and AGI as a part of multiple organ failure is based on subjective evaluations. Clinical assessment is complex, but still subjective and often unreliable, especially in the ICU [3]. Therefore, all alternatives and additional tools to assess GI function beyond clinical evaluation need to be considered and further investigated.

Thorough clinical assessment with inspection, palpation and auscultation of the abdomen, assessment of gastric contents and stool, and evaluation of the effect of feeding challenge should guide the clinician in ordering appropriate technical investigations and subsequent treatment [4–9].

Abdominal pain is difficult to assess since patients may be sedated, mechanically ventilated or receiving high dose peripheral (IV) or central analgesia (epidural catheter). The postoperative abdomen is more sensitive to touch than in normal circumstances and in the post-operative phase diminished bowel sounds on auscultation can be expected. Therefore, alternatives and additives to assess GI function beyond clinical evaluation as described below need to be considered and further searched.

Feeding intolerance (FI) could be considered being a manifestation of GI dysfunction in critical illness [10]. Assessment of feeding intolerance has commonly been based on gastric residual volumes, sometimes in combination with GI symptoms, whereas a large variability in definitions exists [2, 11].

## **MOTILITY AND DIGESTIVE FUNCTIONS**

### **GASTRIC EMPTYING**

One of the most frequently assessed parameter in follow up of intestinal motility is the rate of gastric emptying (GE). Using this parameter, we try to apprehend if any form of feeding intolerance (FI) is present. Gastric residual volume (GRV) is still widely used as surrogate measure for GE. Two main approaches are commonly used (aspiration or gravity drainage) to assess GRV. These two techniques have recently been compared in a clinical setting [12]. However, the usefulness and accuracy of this practice is being questioned since it is neither validated nor standardized and can be influenced by numerous factors [13].

Recently, measurement of gastric residual volumes (GRV) has become questioned after one study showing that routine GRV monitoring is not associated with increased

prevalence of ventilator associated pneumonia [14]. Importantly, this study was performed in mechanically ventilated (MV) patients with already established enteral nutrition (EN), whereas GI surgery patients were excluded [14]. Moreover, a large proportion of patients experienced vomiting in this study (42 vs. 27% in no-GRV vs. GRV-group,  $P = 0.02$ ) [14]. Therefore, we think that current evidence is insufficient to omit GRV measurements in all ICU patients unless routine gastric ultrasound is used instead to monitor gastric filling. Avoidance of distended stomach is especially important in patients after upper GI surgery and in spontaneously breathing patients with impaired protective reflexes against aspiration.

Other means to measure GE such as scintigraphy, gastric impedance monitoring, carbohydrate absorption (3-O-methylglycose) and breath tests (e.g. 13C) have been shown to accurately estimate GE and FI [15–18]. However, these investigations are time consuming, costly, require specific equipment and expertise and thus not suited for daily practice [13, 19]. Paracetamol absorption test (PAT) has been proven to give an accurate measure for GE. However, PAT has its limitations since patients cannot receive paracetamol during at least 24 hours prior to investigation. Thereby it is less appropriate in the perioperative stage. Two other bedside and readily accessible investigations have been proposed; refractometry and bedside ultrasound measurement. The advantage of refractometry (the measurement of substances' refractive index (breaking of light) in order to assess their composition or purity) is that it is cheap, can be easily performed and takes gastric contents into account [20, 21]. Ultrasound assessment can be performed to assess GE and provides an accurate measurement of volume [18, 22–24]. Ultrasound is highly investigator dependent and can be influenced by patient-related and liquid nutrient factors.

Based on these findings and the most recent literature, regular measurement of GRV is still recommended in post-operative abdominal surgical patients and in patients with high risk of GI dysfunction and aspiration. Considering local expertise, ultrasound and/or refractometry can be used as measures for GE in daily practice.

### **INTESTINAL MOTILITY**

Recently the use of an Acoustic Gastrointestinal Surveillance Biosensor (AGIS) has been proposed to detect the presence of postoperative ileus (POI). POI remains a prevalent and expensive condition following abdominal surgery. The AGIS sensor contains an adhesive micro-electric microphone that measures abdominal vibration and acoustic signals; a bedside computer unit calculates motility scores and visually presents the result. A scale from 0-10 was proposed where a score of 2 or lower was consistent with POI. This can prove to be an additional measure to detect and

timely treat POI, however its application in ICU has not been studied yet [25, 26].

Small intestinal motility has also been measured after major abdominal surgery by using perfused manometric assemblies. This technology showed continued small intestinal activity almost immediately after surgery, but revealed persisting abnormalities in this activity. Its use is mainly restricted to experimental research and has not yet found its way to clinical practice [27].

#### ABSORPTION/MALABSORPTION

Malabsorption is an underdiagnosed problem in critically ill patients. Monosaccharide tests with 3-O-methylglucose measurement and  $^{13}\text{CO}_2$  breath analyses have been used to estimate small intestinal absorption capacities, barrier function and transit time [28, 29]. Although these studies were able to show reduced absorption and increased permeability, the mechanisms are still not yet well clarified and confounding factors make it hard to interpret the results. This type of investigations is, however, currently only relevant in a clinical research setting.

Fecal weight and energy content measured by bomb calorimetry has been proposed as a practical and reliable biomarker for malabsorption [30, 31]. According to these findings a fecal output of  $> 350 \text{ g day}^{-1}$  would indicate a significantly lower intestinal absorption of energy and macronutrients. There have been no other studies so far confirming these results. Visual aspect of feces may help to suspect malabsorption of fat and initiate further examination in the laboratory with determination of fat or fecal elastase-1 (suggestive for pancreatic insufficiency). However, also these examinations have limitations in critically ill, especially if diarrhea is present.

#### MICROBIOME MONITORING

In recent years increasing attention has been paid to the role of the gut flora and more specifically the microbiome in critically ill patients. Evaluation of stool samples can be used to document and characterize changes in gut flora. The normal gut flora has a symbiotic relationship to the human host where commensal microbes stimulate immunity and suppress inflammation [3, 32, 33]. Recent studies have pointed out that major shifts in the microbiome to a dys- or pathobiome can lead to various diseases and is driven by antibiotic use or by sudden insult (such as abdominal surgery) with disruption of key protective elements of the intestinal microbiota [34, 35]. Especially a decrease in obligate anaerobes and increase of (hospital acquired) pathogen bacteria would eventually lead to increased septic complications and mortality [36, 37]. Fecal gram staining is possible and can be used to classify fecal bacteria into several patterns. These patterns appear to represent different states of the gut flora

and environment and were associated with septic complications and mortality in patients with systemic inflammation. The pattern of fecal Gram-stained bacteria could eventually be used as a quick diagnostic marker for gut flora to predict septic complications prior to treatment [37]. Fecal surveillance cultures can help to prescribe patient-tailored preemptive antibiotics.

Evaluation of stool samples can be used to document and characterize changes in gut flora. This can be used as an indication of patient status and guide for appropriate treatment (probiotics, antibiotics). In critically ill patients, stool samples can be used to indicate presence of bacterial overgrowth, which may lead to bacterial translocation and bacteremia [33, 38]. However, passage of stool is often not present in critically ill patients with GI dysfunction. Moreover, it is not known whether and how the use of laxatives in these patients may alter the results once passage occurs.

#### PERFUSION

Splanchnic perfusion is challenged in shock states and in the perioperative phase after (abdominal) surgery. Gastrointestinal mucosal hypoperfusion is an important marker and probably a cause of poor prognosis in the critically ill patient. Early measurement of hypoperfusion can be used to direct and adapt therapeutic measures against tissue hypoperfusion and improve oxygenation.

#### REFRACTANCE SPECTROPHOTOMETRY

Refractance spectrophotometry (RS) is used to measure mucosal perfusion (e.g. via a rectal probe). RS uses the refraction of light to measure the average haemoglobin (Hb) oxygen saturation of blood in the gastrointestinal tract. The average Hb Saturation is approximately 70% in normal circumstances. Since measurements are superficial (on the mucosal capillaries) these are considered to yield a reliable estimate of Hb oxygen saturation in the mucosal capillaries. The advantages of this technique are that it allows real-time monitoring and gives a direct estimate of oxygen delivery. However, it does not measure blood flow. Several factors can influence correct measurements such as presence of bile, stool and other optically active materials. Also, the probe has to approach the mucosa very closely in 90 degrees (or close to) angle. Other light sources can also influence measurement (during placement, intraoperative, etc.). Several other indications outside critical care have been researched such as ulcer disease and inflammatory bowel disease [39–41].

#### INFRA-RED SPECTROSCOPY

A variant of RS is a near-infrared spectroscopy (NIRS). It uses near infrared (NI) light to measure haemoglobin oxygenation. NI infiltrates tissue more deeply — up until the *muscularis propria* — enabling measurement of deeper struc-

tures. Transcutaneous NIRS has been used to assess liver perfusion in critically ill children. However, there are several limitations, such as accessibility of the liver, inter-individual variation of single point tissue oxygenation, subcutaneous fat and edema. It is not sure whether liver oxygenation is a good marker for splanchnic perfusion because of the dual blood supply and lack of autoregulation [40, 41].

#### GASTROINTESTINAL TONOMOMETRY

Gastrointestinal tonometry uses the diffusion of carbon dioxide ( $\text{CO}_2$ ) from the surrounding tissue into the gastric lumen to estimate the perfusion and oxygenation of the gut. Consistent with the principles of diffusion the partial pressure of  $\text{CO}_2$  ( $\text{pCO}_2$ ) of the surrounding tissues and intraluminal  $\text{pCO}_2$  should be in a state of equilibrium. As such  $\text{pCO}_2$  in the gastrointestinal mucosa should theoretically be the same as the intraluminal  $\text{pCO}_2$  (e.g. within the balloon positioned against the mucosa). Different techniques have been used to measure the  $\text{pCO}_2$ . Whereas in earlier days intragastric balloon catheters filled with normal saline (or other fluid) were used to measure  $\text{pCO}_2$  intermittently newer devices have been developed (using infrared spectrophotometry) which are able to semi-continuously measure  $\text{pCO}_2$ . Tonometry is prone to several pitfalls such as technical and measurement errors (either continuous or in blood gas analyzer), procedural errors, catheter position, influence of enteral feeding, medications such as antacids, increased  $\text{CO}_2$  production through buffering of hydrochloric acid by bicarbonate. The use of  $\text{pHi}$  (gastric intramucosal pH) has also been questioned since it relies heavily on two key assumptions: that the  $\text{CO}_2$  measured by the tonometer will approximate the  $\text{CO}_2$  of the GI mucosa and that the arterial bicarbonate will be the same as the bicarbonate in the mucosa. The  $\text{CO}_2$  gap or gradient (the difference between intraluminal and arterial  $\text{pCO}_2$ ) seems to be a more accurate measure (higher sensitivity and specificity) indicating gut hypoxia. A normal gradient should be smaller than 10 mm Hg, whereas a gradient of  $> 20$  mm Hg is indicative of gut hypoxia. At this time, semi-continuous measurement seems to be the method of choice [40, 42, 43]. Studies have shown an inverse relation between gastric  $\text{pCO}_2$  and intra-abdominal pressure (IAP) [44, 45].

#### INDOCYANINE GREEN PLASMA DISAPPEARANCE RATE

Indocyanine green (ICG) is a water soluble inert anionic compound which is excreted almost completely into the bile by the hepatocytes without any metabolism or enterohepatic circulation. It has been proposed as a dynamic marker for liver function and splanchnic perfusion, but in the setting of septic shock it preferentially relates to hepatosplanchnic perfusion. Measurements can be done either by serial blood samples, or continuously by a transcutaneous pulse dye

densitometer (commercially available as LiMON, Maquet Getinge Group, Munich, Germany). These measurements are used to derive the ICG plasma disappearance rate (ICG-PDR). Normal values of ICG-PDR are over 18% per minute. ICG has been proven to be a valuable method for dynamic assessment of the liver function and can be used as a prognostic tool in the critically ill and patients with acute liver failure (sensitivity 85.7%, specificity 88.9%) [40, 46–49]. The ICG values are inversely related to IAP [48]. However its role in detection of splanchnic hypoperfusion is unclear and subject to several limitations: results are dependent on perfusion – hepatic uptake and excretion [50].

#### LASER DOPPLER FLOWMETRY

Laser Doppler flowmetry provides a measurement of microcirculatory blood flow using the principle of Doppler shift. The laser penetrates the tissue for approximately 1-3mm allowing the study of mucosal blood flow without interference of the greater *lamina muscularis* blood flow. The main limitation of this technique is that it is unable to measure absolute blood flow, but flow is measured in a variable volume of tissue being thus unable to detect flow in individual vessels [40, 41]. The method requires almost direct access to the splanchnic blood vessels, and is therefore inapplicable in context of ICU. The use of this technique during abdominal surgery is beyond the scope of this review.

#### VIDEOMICROSCOPIC IMAGING TECHNIQUES

Orthogonal polarization spectral (OPS) and sidestream darkfield (SDF) are two videomicroscopic imaging techniques that can be applied at the bedside. With both techniques, the selected wavelength (530 nm) is absorbed by the haemoglobin contained in the red blood cells, independently of its oxygenation state, so that these can be seen as black/gray bodies. These techniques are used to measure vascular density, heterogeneity of perfusion and microvascular blood flow. The technique also has several limitations as secretions, pressure and movement artifacts influence imaging of the microvessels [40, 41, 51]. Similar to flowmetry, the technique requires direct contact to the mucosa at the area of interest. Therefore, it is generally limited to the sublingual area, which is only feasible in sedated or cooperative patients and may not be representative for splanchnic perfusion [52]. Access to GI mucosae is possible in patients with stomas, but this limits the generalizability of the method [53].

#### BIOMARKERS

Experimental and clinical studies have demonstrated that plasma levels of different biomarkers may well reflect various aspects of GI function. Further research should evaluate if and which of the biomarkers described below could be used for GI monitoring in routine setting of intensive care.

## ENTEROHORMONES

Several enterohormones, such as Cholecystokinin (CCK), Peptide YY (PYY), Ghrelin, Motilin and Glucagon-like peptide 1 and 2 (GLP1, GLP2) have been subject of interest of researchers the last years. CCK and PYY appear to be increased in critically ill patients and this increase seems to be more prominent in patients with delayed gastric emptying or with feeding intolerance [54, 55]. Ghrelin is secreted from the stomach during fasting and its secretion is suppressed by meal ingestion. Ghrelin is an acute stimulant of appetite and stimulates GE [56, 57]. In critical illness, fasting plasma concentrations seem to be markedly reduced whereas patients with FI demonstrated higher amounts of Ghrelin but lower concentrations of acyl Ghrelin (active form) [57]. This suggests a role of reduced Ghrelin excretion in delayed GE in ICU patients [58]. Motilin, secreted in the small intestine, has a similar role in stimulation of GE and has a role in propagation of the Migrating Motor Complex. In critically ill, motilin production seems to increase after small intestinal nutrient stimulation, whereas production may increase in health [59].

GLP1 is a so-called incretin and is produced within the intestinal tract as a response to the presence of nutrition. GLP1 has a function in glucose metabolism and stimulates insulin secretion. GLP1 was shown to have immunomodulatory functions and has been proven to increase the number of T helper and T regulatory cells, whereas T-cytotoxic cells were shown to decrease. GLP1 fasting-concentrations appear to be higher in critically ill patients than in healthy subjects [60]. These results were recently questioned by Bakiner *et al.*, who were unable to confirm a link between GLP1 and change in immune function, however enteral feeding did in some way stimulate immunomodulation [61]. GLP2 is co-secreted with GLP1. It has a more glucagonotropic effect and has no effect on insulin secretion. A potential role for GLP2 has been suggested in patients with short-bowel syndrome [62, 63].

## BIOMARKERS BASED ON PROTEIN SYNTHESIS AND DEGRADATION IN ENTEROCYTES

Citrulline is an amino acid synthesized by enterocytes of the intestinal mucosa from glutamine [64, 65]. Reduced plasma citrulline concentration is considered as a marker of loss of enterocyte mass, intestinal dysfunction and mucosal barrier injury [66]. Piton *et al.* [67] showed that a citrulline concentration of  $< 10 \mu\text{mol L}^{-1}$  is associated with increased mortality and can be used as a prognostic biomarker for mortality during ICU stay. However, normal plasma citrulline concentrations ( $> 20 \mu\text{mol L}^{-1}$ ) observed in critically ill patients, cannot rule out decreased citrulline synthesis due to two conditions: first, acute and/or chronic renal failure; second, inducible nitric oxide synthesis in SIRS. Thus, the use and prognostic value of citrulline in the ICU can be questioned [68].

A potential biomarker for loss of enterocyte integrity is Intestinal Fatty acid-binding protein (I-FABP), also known as FABP2. These are small proteins present in mature enterocytes at the tip of the villus. They are released when enterocyte integrity is lost. I-FABP is a sensitive marker for intestinal ischemia and there appears to be a correlation between the serum level of I-FABP and the extent of ischemia/epithelial damage [69–71]. In post-trauma patients I-FABP was detected in all patients, but with highest values in patients in shock and patients with severe abdominal trauma [70]. Although specificity and sensitivity of I-FABP was suboptimal ( $< 80\%$ ) it has a high negative predictive value of 96.3% [71, 72]. Until now, I-FABP is one of the most sensitive biomarkers in the detection of enteric ischemia and this parameter can be used to follow up progression of intestinal injury. Despite these findings I-FABP has not yet found its way to the general ICU and emergency setting. I-FABP or FABP2 should not be confounded with FABP1 (Fatty Acid-Binding Protein 1), also known as liver-type fatty acid-binding protein (L-FABP). L-FABP is primarily expressed in the liver where it is involved in the binding, transport and metabolism of long-chain fatty acids (LCFAs), endocannabinoids, and other hydrophobic molecules. Altered expression of this protein has been linked to metabolic conditions such as obesity. L-FABP is also expressed in the cytoplasm of human renal proximal tubules and Urinary L-FABP levels accurately reflect the degree of tubulointerstitial damage and are strongly correlated with the prognosis of chronic kidney disease patients in clinical studies.

## D-LACTATE

D-lactate is a lactate enantiomer produced by colonic bacteria. Under normal conditions concentrations are very low. In case of increased permeability and mucosal barrier damage large amounts of D-lactate are released into peripheral blood. D-lactate has been suggested as a biomarker for barrier function, and presence and severity of intestinal ischemia. D-lactate has a high sensitivity (90%) and specificity (85.9%) for the diagnosis of intestinal ischemia [71, 73, 74]. However a more recent study by Hong *et al.* [75] was unable to show convincing evidence that D-lactate is useful in differentiating between patients with and without intestinal infarction in post-cardiac surgery patients requiring laparotomy based on suspicion of intestinal ischemia. However, continuous rise in D-lactate after the first laparotomy was associated with mortality. Important limitation of D-lactate is its poor stability, which demands specific handling of blood samples.

Recently  $\alpha$ -smooth muscle actin (SMA) was proposed as a marker for severe intestinal ischemia based on studies in infants with necrotizing enterocolitis [76, 77]. Hong *et al.* [75] recently compared D-lactate, I-FABP and SMA and found

SMA diagnostically superior to the other biomarkers. SMA has a distinct time course in comparison to I-FABP (I-FABP exhibits rapid elevation during ischemia whereas SMA increases more during the reperfusion phase). SMA is proposed as a biomarker for transmural necrosis and may provide information about the need to operate [75, 77]. Further research is needed to confirm the use of SMA.

D-dimer and L-lactate have been used in the diagnostic process of intestinal ischemia. L-lactate seems an interesting parameter in follow up of patients with suspected ischemia whereas D-dimer does not seem to be a good marker for early diagnosis of intestinal ischemia [73, 78]. D-lactate levels and D-over-L-lactate ratio will also typically be increased in patients with short bowel syndrome and bacterial overgrowth.

### **INTRA-ABDOMINAL PRESSURE**

Intra-abdominal pressure (IAP) has been proposed decades ago and is being more and more accepted as a measurable parameter to facilitate the monitoring of GI function. Reintam *et al.* [9, 79] pointed out that IAP measurement is probably not obligatory in all ICU patients, however in high-risk patients (severe burns, severe trauma, severe acute pancreatitis, liver failure, ruptured aortic aneurysms, gastrointestinal bleeding, shock and recent laparotomy), measurement of IAP is indicated. Critically ill patients should be screened for risk factors known to be associated with increased IAP and a baseline IAP measurements is recommended if 2 or more risk factors are present [80, 81]. Several methods have been proposed using either invasive direct intraperitoneal measurement and non-invasive indirect measurements. Sugrue *et al.* [82, 83] recently updated historical publications and provided an overview of all available techniques. IAP should be measured at the end of expiration with the patient in supine position and the zero position at the level where the mid-axillary line crosses the iliac crest [81]. Direct measurement is theoretically the most accurate but due to its invasive nature, requiring direct access to the peritoneal cavity with risk of contamination or infection, this technique is not broadly used, but limited for research purposes.

At this moment intra-bladder measurement of the IAP, either continuous or intermittent, has been accepted as the gold standard measurement method due to its ease in use and minimally invasive nature. Intermittent measurement is performed by instilling a maximum of 20–25 mL of saline into the bladder — in line with WSACS guidelines [84]. Continuous measurement has the advantage that it is able to show a continuous trend showing daily fluctuations and peak pressures, respiratory variations can be more easily identified and less nurse interventions are needed [85]. If possible, continuous measurements are advised. Con-

tinuous IAP measurement can be performed either via a 3-way Foley catheter with continuous irrigation or via a balloon-tipped nasogastric probe [82, 83]. The Abdominal Compartment Society (WSACS, [www.wsacs.org](http://www.wsacs.org)) has provided definitions regarding normal IAP and a grading system to interpret and treat intra-abdominal hypertension [81]. Normal values range between 5–7 mm Hg, intra-abdominal hypertension is defined as a sustained increase of IAP to or above 12 mm Hg [81]. Measurements can be influenced by several factors (such as body position, transducer position, bowel function, analgesia and sedation, ventilation method), which should be taken into account while interpreting IAP measurements [86, 87].

In case of contra-indication for intra-vesical measurement (cystectomy, traumatic bladder injury, pelvic packing) intra-gastric techniques can be used. Other available techniques such as intra-rectal and intra-uterine measurements are seldom used in critically ill and will not be discussed in further detail.

Inferior vena cava pressure measurement has been shown to have a good correlation with IAP, but only when IAP is above 20 mm Hg [88, 89].

Intragastric measurement of IAP can be performed intermittently with a Gastromanometer (Holtech Medical, Charlottenlund, Denmark) [12] or continuously with a Spiegelberg (Spiegelberg, Hamburg, Germany) or CiMon (Maquet Getinge Group, Munich, Germany) technique using a balloon-tipped nasogastric probe [90, 91]. In the past, intragastric pressure was deemed inaccurate because of confounding gastric contractions. However continuous measurements may be able to bypass these contractions and give accurate IAP measurements [91, 92].

### **IMAGING**

Static radiological imaging (ultrasound, abdominal plain X-ray, computed tomography (CT) and magnetic resonance imaging) can be used in evaluation of structural and perfusion pathologies. Each of these investigations has its benefits and limitations. Ultrasound, with or without Doppler imaging, is a readily available first line investigation in the assessment of all (perioperative) patients and is able to give a quick bedside image on intra-abdominal free fluid, perfusion, solid and hollow organ status. On the down side the quality of this investigation is strongly researcher dependent and can be influenced by postoperative presence of intra-abdominal air or CO<sub>2</sub>.

Plain X-ray of the abdomen is the least sensible investigation and has lost most of its indications in ICU setting, except for follow up of enteral tube positioning and assessment of bowel diameter in case of e.g. colonic pseudo-obstruction.

CT scans with or without intravascular or enteral contrast have gone through major improvements with evolution to multislice CT with enhanced imaging quality, reduced radiological exposure and reduced scanning times. However, patients have to be transported to the radiological ward with all inherent risks.

MRI can provide more clear imaging in some cases but has a long investigation time, requires special monitoring equipment and, as for CT, patients have to be transported for the investigation.

Some guidelines and reviews have been issued on the use of imaging in the acute abdomen and in case of mesenteric ischemia [93–95]. However, it is unclear whether these guidelines can be extrapolated to the ICU population. Importantly, specific recommendations do not exist with regard to administration of enteral contrast media via gastric or jejunal tube in ICU patients with overt passage problems. Based on our experience, we strongly recommend against administering the usual dosage (1500 mL) of enteral contrast media to ICU patients with clinically overt passage problems prior the CT scan and recommend reducing this dose.

## CONCLUSIONS

The abdominal compartment is still a black box with respect to monitoring of processes it conceals. Researchers have been trying hard to bring light into this box. Although different monitoring tools and diagnostic measures for the different gastrointestinal functions have been developed, only a few are being effectively used at the bedside in daily clinical practice. The search for appropriate laboratory biomarkers for detection and quantification of splanchnic hypoperfusion and/or enterocyte dysfunction in critical illness needs to continue. Work on the gut microbiome, using fecal samples, shows promising results and may find its way into clinical practice after proper validation. Many techniques, which are already practiced in the ICU, are still subject to debate (such as GRV, refractometry, indocyanine green plasma disappearance rate, IAP measurements and imaging) due to their questionable direct relation with complex GI function or lack of specific guidelines (especially for the imaging techniques). Therefore, before developing new tools, a critical appraisal of existing techniques needs to be undertaken while establishing a rationale for their appropriate use. The ability to monitor GI function is crucial for development of future treatment modalities improving GI function and thereby possibly also outcome of critically ill patients.

## ACKNOWLEDGEMENTS

1. This article is endorsed by the International Fluid Academy (IFA). The mission statement of the IFA is to foster education, promote research on fluid management and hemodynamic monitoring, and thereby improve

survival of critically ill by bringing together physicians, nurses, and others from throughout the world and from a variety of clinical disciplines. The IFA is integrated within the not-for-profit charitable organization iMERiT, International Medical Education and Research Initiative, under Belgian law. The IFA website (<http://www.fluidacademy.org>) is now an official SMACC affiliated site (Social Media and Critical Care) and its content is based on the philosophy of FOAM (Free Open Access Medical education — #FOAMed). The site recently received the HONcode quality label for medical education (<https://www.healthonnet.org/HONcode/Conduct.html?HONConduct519739>).

2. Conflict of interest: Annika Reintam Blaser received honoraria for advisory board participation or speaker's fee from Fresenius, Nestlé and Nutricia. Heleen M. Oudemans-van Straaten has received honoraria for advisory board meetings from Baxter and B Braun; lecture fees from Fresenius Kabi, Danone-Nutricia and Baxter; congress support from Baxter; and Funding for research from Fresenius Kabi, Nestlé, Danone-Nutricia and AstraZeneca. Manu Malbrain is founding President of WSACS (The Abdominal Compartment Society) and current Treasurer, he is also member of the medical advisory Board of Pulsion Medical Systems (part of Maquet Getinge group) and consults for ConvaTec, Acelity, Spiegelberg and Holtech Medical. Manu Malbrain is co-founder of the International Fluid Academy (IFA). The other authors have no possible conflicts of interest in relation to the content of this review article.

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*Received: 10.10.2017*

*Accepted: 15.11.2017*