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COMMENTARY

Bio-electrical impedance analysis in critically ill patients: are we ready for prime time?

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1 The burden of fluid overload

Fluid overload in critically ill patients is defined as a 10% increase in cumulative fluid balance (CFB) from baseline body weight and represents a well-known problem which detrimentally affects intensive care unit (ICU) patient's clinical course and their outcome [1–3]. Therefore, timely recognition and correction of fluid overload, or even better, identification of patients at risk for fluid accumulation in an early stage is of great importance. However, this remains challenging in clinical practice, as we miss an accurate and reliable tool for correct assessment of fluid status [4]. Current methods include the calculation of daily and CFB, by recording fluid inputs and outputs, the use of clinical or biochemical signs of fluid overload, monitoring filling pressures, however, none of these methods allow for a close monitoring for fluid balance, and intercompartmental fluid shifts [1, 5].

2 The promise for BIA

Bio-electrical impedance analysis (BIA) has gained increased interest to help physicians to determine volume status and fluid distribution in critically ill patients (see Table 1) [1, 2, 4, 6–21]. Indeed, several data published in the last decade suggest that BIA may provide useful information not only in different well-established patient groups (dialysis, AIDS, malnutrition), but also in critically ill patients with burns, trauma or sepsis undergoing fluid resuscitation. This tool may offer a non-invasive, fast and reliable assessment of volume status and fluid distribution as well as evaluation of dynamic changes in fluid distribution. It measures total body water (TBW), extracellular water (ECW), and intracellular water (ICW). BIA can calculate absolute fluid overload (AFO), the difference between normal, expected ECW and the actual, measured ECW, expressed in liters, as well as relative fluid overload (RFO), AFO/ECW, expressed in percentages. BIA measurements may be performed easily at the bedside, do not require extensive training and have limited inter-observer variations [22]. Thereby, BIA sounds as a promising diagnostic tool in the ICU or operating room to assess fluid status. Recently, new BIA-devices have been introduced allowing not only calculation of TBW, ECW and ICW but also the intra- and extravascular fluids (IVF, EVF) and, in case of dialysis, Kt/V (Fig. 1).

3 Shedding new light

We read with great interest the work by Ciumanghel et al. [23]. Their study highlights an important clinical problem, fluid overload assessment, in a field that lacks clinical data. The study population was appropriate as abdominal surgery is among the most common elective surgical procedures [24]. The results confirm the potential role and usefulness of BIA monitoring to quantify body fluid composition and intercompartmental shifts in a major abdominal surgery perioperative setting. In this study 71 adult patients undergoing elective major abdominal surgery were included. Patients were then divided in two subgroups according to the presence of pre- and postoperative cumulative fluid overload (CFO): Normal Hydration (NH) subgroup with CFO < 5%, and Fluid Overload (FO) subgroup with CFO >= 5%. The authors found some differences between

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Table 1 Overview of recent studies published on the use of bio-electrical impedance analysis in critically ill patients

Author	Year	Type of study	Population	Number of patients	Protocol	Definition FO	Most important outcome
Bracco et al. [7]	1998	Prospective observational study	Adult patients undergoing open-heart surgery with cardiopulmonary bypass	26	To assess fluid accumulation after cardiac surgery by multiple frequency segmental BIA	No definition	Cardiac surgery produced a significant decrease in segmental trunk BIA, reflecting fluid accumulation at the trunk level
Piccoli et al. [15]	2000	Propective cross-sectional study	72% surgical patients, 28% craniocerebral trauma and bleeding	121	To determine relationships between CVP and tissue electrical conductivity measurements according to the BIVA, with also TBW predictions based both on anthropometry and conventional BIA regression equations	Short vectors out of the lower pole of the target 75% tolerance ellipse	(1) The agreement between BIVA and CVP indications was good in the high CVP group, moderate in the medium CVP group, and poor in low CVP group. (2) Direct impedance measurements were more highly correlated with CVP values than with TBW predictions from either conventional BIA equations or anthropometry
Lingwood et al. [20]	2000	Prospective study	NICU patients	24	To investigate the effects of factors like cardio-respiratory monitoring equipment, non-ideal electrode placement and inability to obtain accurate crown-heel measurements on impedance analysis and to develop a prediction equation for ECF volume in the neonate	NA	Despite many potential difficulties associated with impedance analysis in the NICU, reliable measurements of impedance can be obtained
House et al. [18]	2010	Prospective study	Adult ICU patients on mechanical ventilation	34	Relationships were assessed between CVP, BIVA, BNP, and oxygenation index (O2I) in a cross-sectional (baseline) and longitudinal fashion using both univariate and multivariable modeling	NA	No addition was found in BIVA measures to help in the fluid assessment of ICU patients

Table 1 (continued)

Author	Year	Type of study	Population	Number of patients	Protocol	Definition FO	Most important outcome
Basso et al. [1]	2013	Prospective observational study	Mixed ICU patients: post-surgery, sepsis, trauma, post-cardiac arrest	64	To investigate: (i) the hydration status of ICU patients, and how this varies during hospitalization following current fluid management practices; (ii) the hydration status of ICU patients in need of RRT, and how this varies during treatment, and (iii) the relationship between hydration and mortality with or without RRT	Body hydration percentage > 73.3%	(1) A marked tendency towards overhydration during the 1st day in ICU. (2) Significantly worse state of hyperhydration in patients on CRRT. (3) Non-survivors showed worse hyperhydration patterns in comparison to survivors. (4) Both the average and the maximum hydration represent a significant risk factor for mortality, both in the ICU and at 60 days
Dabrowski et al. [9]	2014	Prospective study	Septic shock complicated with acute kidney injury	30	Analysis of the effect and the time course of CVVH with UF on IAP and body fluid volumes in septic shock patients with AKI	No definition. Comparison of various fluid volumes between survivors and non-survivors	IAP correlated with fluid volume excess measured by BIA
Ismael et al. [16]	2014	Prospective experimental study	Hemodynamically stable patients requiring acute RRT for fluid overload	31	To quantify BCM, water compartments and FFM by methods usable at the bedside for evaluating the impact of sudden and massive fluid shifts on body composition in ICU patients	Ultrafiltration estimated ≥ 5% body weight before the hemodialysis session	BCM estimation is less driven by sudden massive fluid shifts than FMM. Assessment of BCM should be preferred to FFM when severe hydration disturbances are present in ICU patients
Jones et al. [8]	2015	Prospective, clinician-blinded, observational study	Mechanically ventilated patients in mixed ICU	61	To assess the feasibility and validity of BIVA as a measure of hydration in critically ill patients	NA	BIVA is feasible in critically ill patients. Directional changes in BIVA were consistent with directional changes in fluid balance. The sensitivity of repeated BIVA hydration measurements to detect fluid accumulation or fluid balance changes < 2 L was low

Table 1 (continued)

Author	Year	Type of study	Population	Number of patients	Protocol	Definition FO	Most important outcome
Chen et al. [10]	2015	Prospective observational study	Mixed (medical-surgical) ICU patients	89	To assess fluid status among patients on CRRT by using BIVA combined with serum NT-pro BNP and to identify correlations between outcome and fluid status, as determined by the combination of these two parameters	Point vector on the RXc point graph falling lower than the lower pole of the 75% tolerance ellipse	Different types of fluid status distinguished by BIVA combined with serum NT-pro BNP measurements corresponded to different clinical conditions and treatment outcomes. For patients receiving CRRT, real-time monitoring of fluid status by using BIVA and NT-pro BNP may be useful in fluid management by aiding in the identification of an optimal net ultrafiltration rate during CRRT
Rhee et al. [17]	2015	Retrospective study	Male ICU patients with AKI on CVVHDF	208	To analyze the effect of MF–BIA-defined volume status on the mortality of critically ill patients with AKI	No definition	MF–BIA-defined excess TBW/H^2 and ICW/H^2 are independently associated with higher in-hospital mortality in male patients with AKI undergoing CVVHDF
Mól and Kwinta [19]	2015	Prospective study	Extreme premature and full-term newborns	38	Evaluation of BIA values and body composition during early infancy in groups of preterm newborns and full term newborns	NA	The study confirms differences in body composition between preterm and full term newborns
Dewitte et al. [4]	2016	Prospective observational study	Mechanically ventilated patients in mixed ICU	25	To evaluate the feasibility and reproducibility of BIS to measure body-water composition in critically ill patients, and to compare fluid balance and daily changes in TBW measured by bioimpedance	No definition	Non-invasive determination of body-water composition using BIS is feasible in critically ill patients but requires knowledge of the patient's weight

Table 1 (continued)

Author	Year	Type of study	Population	Number of patients	Protocol	Definition FO	Most important outcome
Samoni et al. [11]	2016	Prospective, dual-center, clinician-blinded, observational study	Mixed (medical-surgical) ICU patients	125	To assess the impact of hyperhydration on ICU mortality in critically ill patients, comparing its measurement by BIVA and by CFB recording	Hydration > 74.3% of lean body mass (BIVA) or > 5% fluid overload (CFB)	The hydration status measured by BIVA seems to predict mortality risk in ICU patients better than the conventional method of fluid balance recording
Tierens et al. [21]	2017	Restrospective study	Mixed ICU patients	101	To assess the prognostic value of fluid overload in the first week of ICU-stay	5% increment in volume excess divided by initial body weight	Higher mortality rate in ICU patients with FO was observed. FO seems a new and independent prognostic factor
Hize and Gonzalez [6]	2018	Prospective study	Critically ill patients with AKI	224	Assessment of the hydration status measured using BIVA in critical patients in intensive care at the time of AKI diagnosis and its association with mortality	No definition	Greater hydration present at that time of AKI diagnosis was associated with lower survival
Kammar-Garcia et al. [12]	2018	Prospective observational study	Emergency Department (ED) patients	109	To investigate the association of fluid overload, measured by BIVA and also by accumulated fluid balance, with 30-day mortality rates in patients admitted to the emergency department	No definition	Fluid overload on admission evaluated by BIVA, but not by accumulated FB, was significantly related to mortality in patients admitted to an ED
Marino et al. [14]	2018	Prospective study	Children after cardiac surgery	50	To investigate the predictive value of a preoperative measures of BIS PA 200/5° in children admitted to pediatric ICU following cardiac surgery	NA	A statistically significant relationship between BIS PA 200/5° and PICU LOS and positive fluid balance the day following surgery was found
Slobod et al. [2]	2019	Prospective observational study	Mixed medical-surgical ICU patients on mechanical ventilation	36	To investigate the effect of BIA-measured volume status on duration of mechanical ventilation, 28-day mortality, and AKI requiring RRT in a population of medical/surgical patients admitted to the ICU	ECW/TBW ratio > 39%	A higher ECW/TBW ratio within 24 h of admission is associated with an increase in number of ventilator days in mechanically ventilated patients

Table 1 (continued)

Author	Year	Type of study	Population	Number of patients	Protocol	Definition FO	Most important outcome
Razzera et al. [13]	2019	Prospective cohort study	Mixed (medical-surgical) ICU patients	89	To evaluate the validity of BIA parameters as predictors of nutrition risk and clinical outcomes in critically ill patients	BIVA values above the 75th percentile in the tolerance ellipse	(1) PA < 5.5 showed an accuracy of 79% to identify patients at high nutrition risk. (2) Hyperhydration (BIVA > 70%) was a significant predictor of mortality

NA not applicable, *AKI* acute kidney injury, *BCM* body cell mass, *BIA* bio-electrical impedance analysis, *BIS* bioimpedance spectroscopy, *BIVA* bio-electrical impedance vector analysis, *CFB* cumulative fluid balance, *CVVH* continuous venovenous hemofiltration, *CVP* central venous pressure, *FFM* fat free mass, *FO* fluid overload, *IAP* intra-abdominal pressure, *LOS* length of stay, *MF* multi frequency, *LOS* length of stay, *PA* phase angle, *RRT* renal replacement therapy

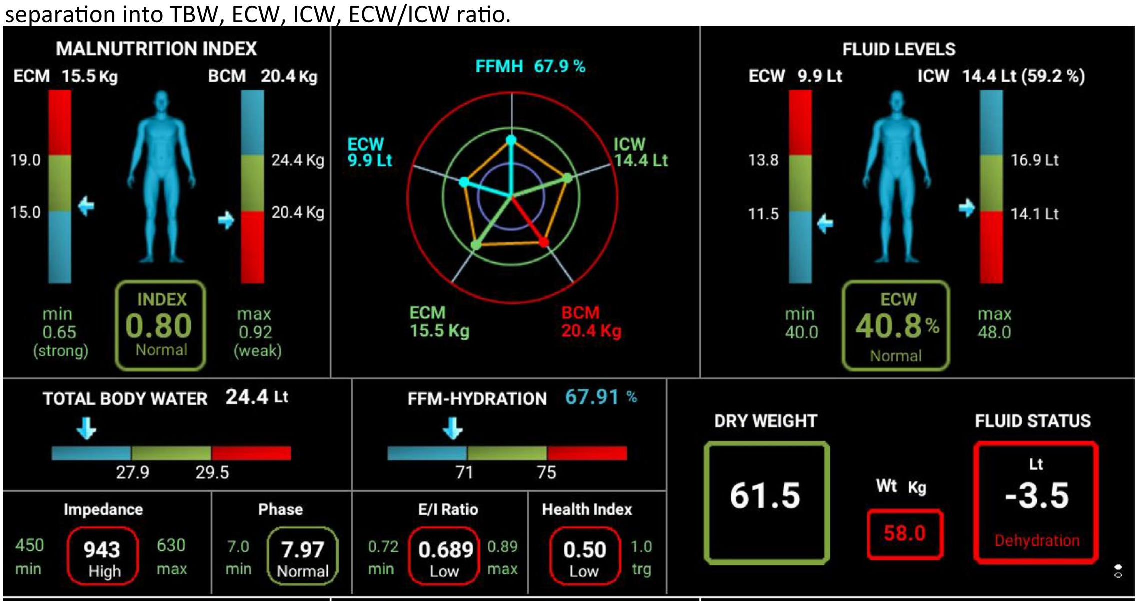
the subgroups regarding peroperative and postoperative parameters like median surgery duration and mean fluid infusion rate, amongst others. Positive intraoperative fluid balance (2.4 ± 1.0 L) resulted in a significant increase of TBW (1.4 ± 2.4 L) and of ECW (1.4 ± 1.2 L). Intraoperative fluid balance significantly correlated with TBW change ($r = 0.23$, $p = 0.04$) and with AFO change ($r = 0.31$, $p < 0.01$). A significant correlation was found between pre- and postoperative AFO and RFO on one hand, and ICU-LOS on the other. In addition, we would like to provide some additional comments as food for further thought.

First of all, before surgery, patients in the FO subgroup had significantly lower haemoglobin values and significantly lower diastolic blood pressure than patients in the NH subgroup. Furthermore, patients in the FO more frequently underwent duodeno-pancreatectomy, esophagectomy and aorto-femoral bypass. This was the case in around 72.7% (16 out of 22 patients) in the FO subgroup. This form of extensive surgery usually concerns patients presenting with a serious illness like cancer or peripheral vessel disease, also having more comorbidities.

Second, postoperative serum albumin levels dropped dramatically in FO patients, while in NH patients it decreased to a much lesser extent. A drop of serum albumin levels in the early postoperative period is known to be multifactorial: altered metabolism, blood loss/dilution and capillary leakage-related redistribution into the third space [25–29]. The latter being probably the most important mechanism [25], which may account for > 75% of albumin decrease in the early postoperative phase. This significant parameter also appears to be related to the magnitude of postsurgical systemic inflammatory response [26, 27], which, in turn, is directly related to the extent of surgery [25] and is believed to contribute to the risk of developing postoperative complications [28, 29]. Labgaa et al. [25] identified a serum albumin decrease ≥ 10 g/L on postoperative day 1 after elective abdominal surgery to be independently associated with a threefold increased risk for postoperative complications. Therefore, we believe that serum albumin drop in FO subgroup not only mirrors a higher intraoperative fluid regimen but may also indicates a more pronounced postsurgical systemic inflammatory response in those patients.

Altogether, those points led us to the feeling that preoperatively, FO subgroup patients may have been already more ill and therefore may have required increased fluid infusion during surgery. Indeed, even if blood loss was the same in both subgroups, FO patients received significantly more colloid infusion. Data on the inotropic and vasoactive medication use were collected but are not presented in the paper. One could expect more vasopressors in the FO subgroup. However, in order to maintain patient's blood pressure peroperatively, one can give intravenous fluid infusion or choose vasopressor drugs. Both strategies being widely

Panel A. The new touch i8 BIA device (Maltron, UK) allows to calculate fluid excess (fluid overload, hypervolemia, hyperhydration) but also fluid underload (hypovolemia, dehydration) and body fluid separation into TBW, ECW, ICW, ECW/ICW ratio.



Panel B. The new software allows not only to calculate body fluid separation into TBW, ECW, ICW, ECW/ICW ratio but also IVF and EVF.

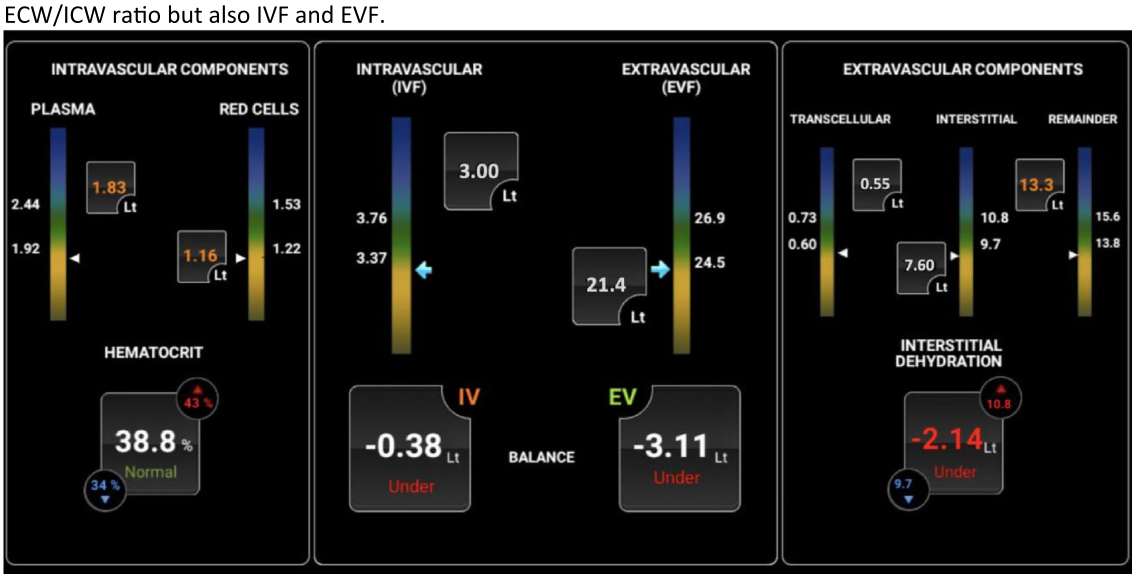


Fig. 1 The future of bio-electrical impedance analysis (BIA)

accepted in clinical practice. Unfortunately, little is known about the fluid management protocol, or whether it recommends early or late use of vasopressors? Even if fluid overload is known to impair the patient's clinical course in view of aforementioned comments, the greater rate of postoperative respiratory dysfunction and longer ICU stay in FO patients [30–32] seen in the work of Ciumanghel et al., may not be explained only by the presence of fluid overload [23].

Third, concerning BIA parameters, a comparison of pre- and postoperative BIA parameters was done for the whole group, and then in FO and NH subgroups separately. All these analyses consistently showed a significant increase in TBW, ECW, ECW/ICW ratio, AFO and RFO. We would also suggest a comparative analysis between FO and NH subgroup, as we believe that the increase in BIA-parameters in the FO subgroup would be more pronounced, due both to longer surgery and more severe illness, as partially discussed above. Moreover, the preoperative AFO and RFO values (more refined BIA parameters not related to body weight or height) were significantly

Panel C. Evolution of BIA parameters in a male patient of 44 years with polytrauma and cumulative fluid balance of +5L on day 5, a P/F ratio 98 and EVLWI 16 ml/kg PBW. The BIA-measurement showed a volume excess of 4.9L. Initially treated with diuretics but put on CVVH with ultrafiltration afterwards. The health plot shows return to normal conditions.

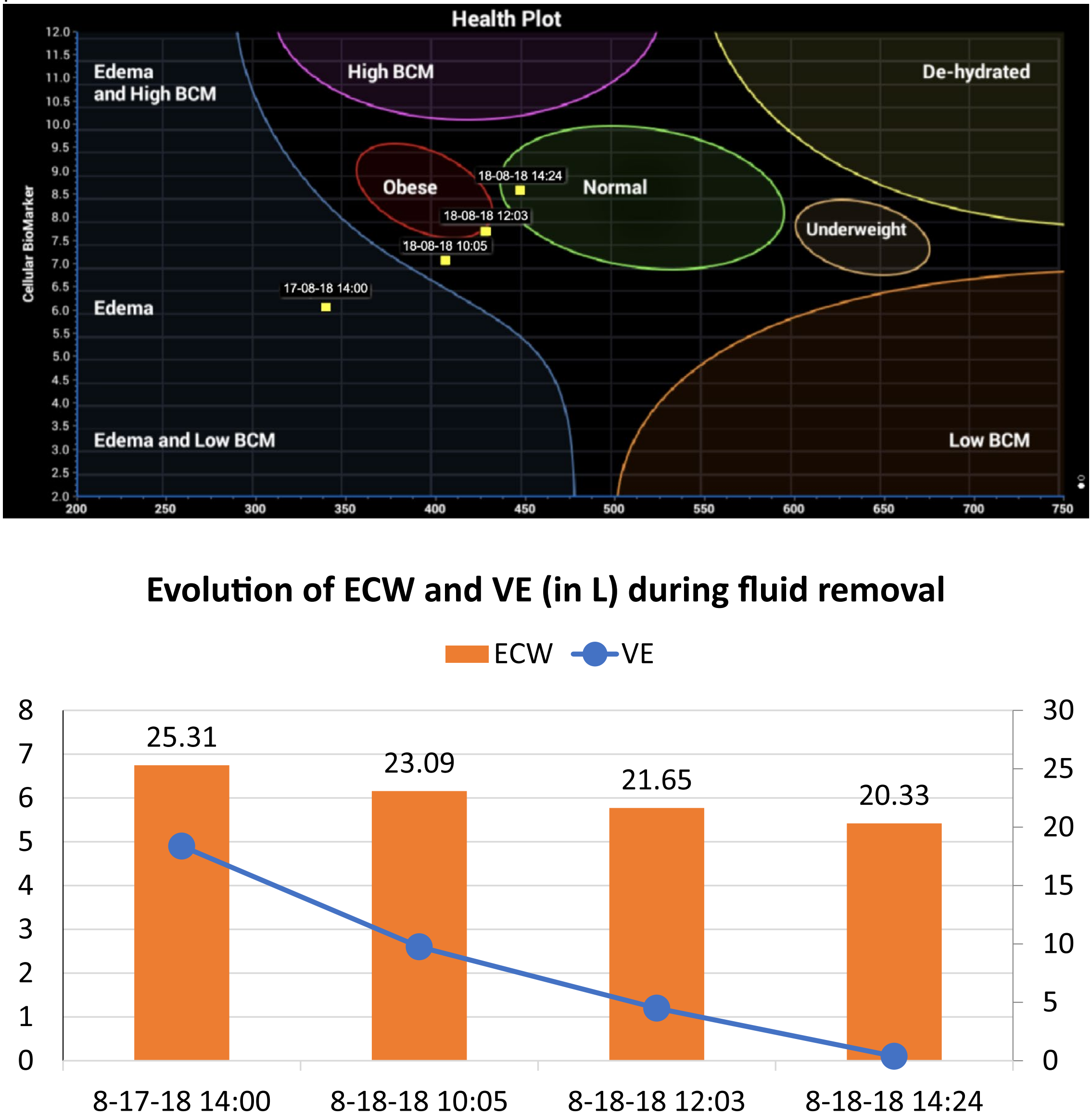


Fig. 1 (continued)

higher in FO group. This could, therefore, additionally indicate that NH and FO patients did not present with the same baseline parameters before surgery.

Fourth, regarding AFO and RFO differences between FO and NH patients, we were surprised to observe that FO patients had lower TBW and ECW values preoperatively compared to NH patients. This might be explained by significantly higher BMI values in NH patient's subgroup. Hence, it would seem appropriate to present BIA data as litre/kg body weight, as it would give a more appropriate estimation of patient's true fluid composition.

Fifth, as the authors stated themselves, having only one postoperative BIA measurement is a limitation for a broader understanding of dynamic changes in body fluid composition. More prolonged changes in the fluid balance and or distribution could probably have been revealed if later measurements would have been performed. For instance, a BIA measurement 12 and 24 h after ICU admission would

Panel D. Calculation of dialysis efficiency as K.t/V after 4 hours of CVVH with ultrafiltration.

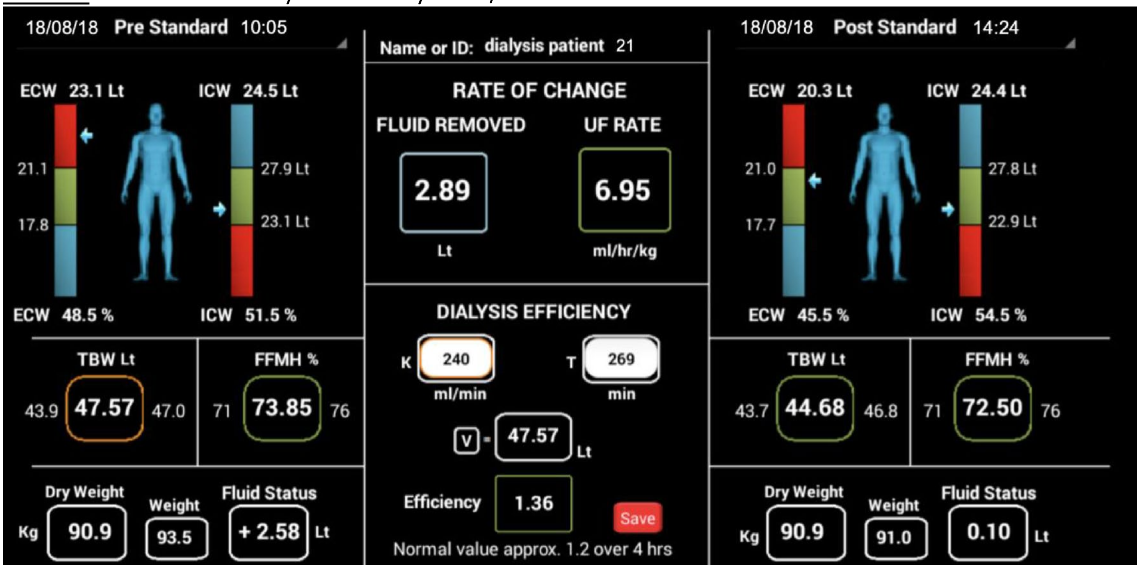


Fig. 1 (continued)

have been of great interest. Nevertheless, we recognise that this was probably challenging in the particular setting of this study, as the patients in the NH subgroup (i.e., 2/3 of included patients) had a median ICU stay of 5 h. This could be an interesting topic for further studies in the field.

4 Take home message

In conclusion, the study of Ciumanghel et al. addresses an important clinical problem and proposes a non-invasive, feasible, easy to perform bedside BIA-technique to assess and monitor fluid status and fluid distribution in the perioperative period, which may be of great interest to help physicians to improve management, care and outcome in critically ill patients. In the future, newer techniques may become available that allow not only calculation of TBW, ICW, ECW but also IVF and EVF. This could be of interest to assess performance of dialysis (Kt/V) but also to assess pharmacokinetics and pharmacodynamics of drugs and the fluids they are diluted in. The use of BIA in critically ill patients sounds promising but is probably not ready yet for prime time.

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