3rd International Fluid Academy Days

Abstracts of the oral presentations

Serum urea/creatinine ratio predicts successful loop diuretic therapy in congestive heart failure

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Introduction In congestive heart failure (CHF), a correlation between the prescribed dose of loop diuretics and all cause mortality as well as heart failure readmissions has been demonstrated [1, 2]. However, it remains unclear whether this correlation is causal or represents only the fact that sicker patients are treated with higher dosages. Importantly, the risk associated with high dose loop diuretics depends on blood urea nitrogen levels, which are a crude marker of neurohumoral stimulation [3]. ***Aim*** To assess the serum urea/creatinine ratio (UCR) as a prognostic marker for successful therapy with loop diuretics in CHF. ***Material and methods*** We included consecutive patients, admitted with a primary diagnosis of CHF in Ziekenhuis Oost Limburg (Genk, Belgium) between January, 2009 and March, 2011. A venous blood sample was obtained at the moment of hospital admission for serum urea and creatinine measurements. UCR was calculated as serum urea [mg/dL] over serum creatinine [mg/dL]. Patients with versus without loop diuretic dose increase at hospital discharge compared to admission were compared. Mortality and heart failure readmission data were prospectively collected. ***Results*** Three hundred eighteen patients (70±11 years; 71% male; ejection fraction 34±14%) were included. During follow up of 22±10 months, 54 patients died (17%), 91 were readmitted for worsening CHF symptoms (29%), while 194 (61%) had an event free survival. Admission UCR was 46±13, with higher values significantly associated with worse freedom from all cause mortality or heart failure readmission (p=0.001; Fig. 1). In 32% of patients, the maintenance dose of loop diuretics was increased at hospital discharge compared to baseline. Those patients had a non significantly higher risk of all cause mortality or heart failure readmission [HR (95% CI)=1.34 (0.92—1.95)]. When stratified according to UCR, patients with UCR≥46 had significantly worse outcome if they received a higher dose of loop diuretics (p=0.041), while patients with UCR<46 had not (p=0.559; Fig. 2). ***Discussion*** The clearance of urea is determined both by the glomerular filtration rate and tubular reabsorption of urea. Neurohumoral stimulation leads to increased tubular reabsorption of urea in addition to a decreased glomerular filtration rate in CHF [4]. Therefore, neurohumoral stimulation causes serum urea to increase more than serum creatinine in CHF, reflected by an increased UCR irrespectively of underlying renal function. We found that higher UCR levels at hospital admission are associated with worse clinical outcome in CHF patients. In addition, patients with a UCR larger than the mean responded particularly poor to an increase in loop diuretic dose. Conclusions The UCR may help to guide decongestive therapy with loop diuretics in patients admitted for CHF. ***Acknowledgement*** Oral presentation will take place in Room Belle Epoque on Friday November 29th at 14:40—14:50.

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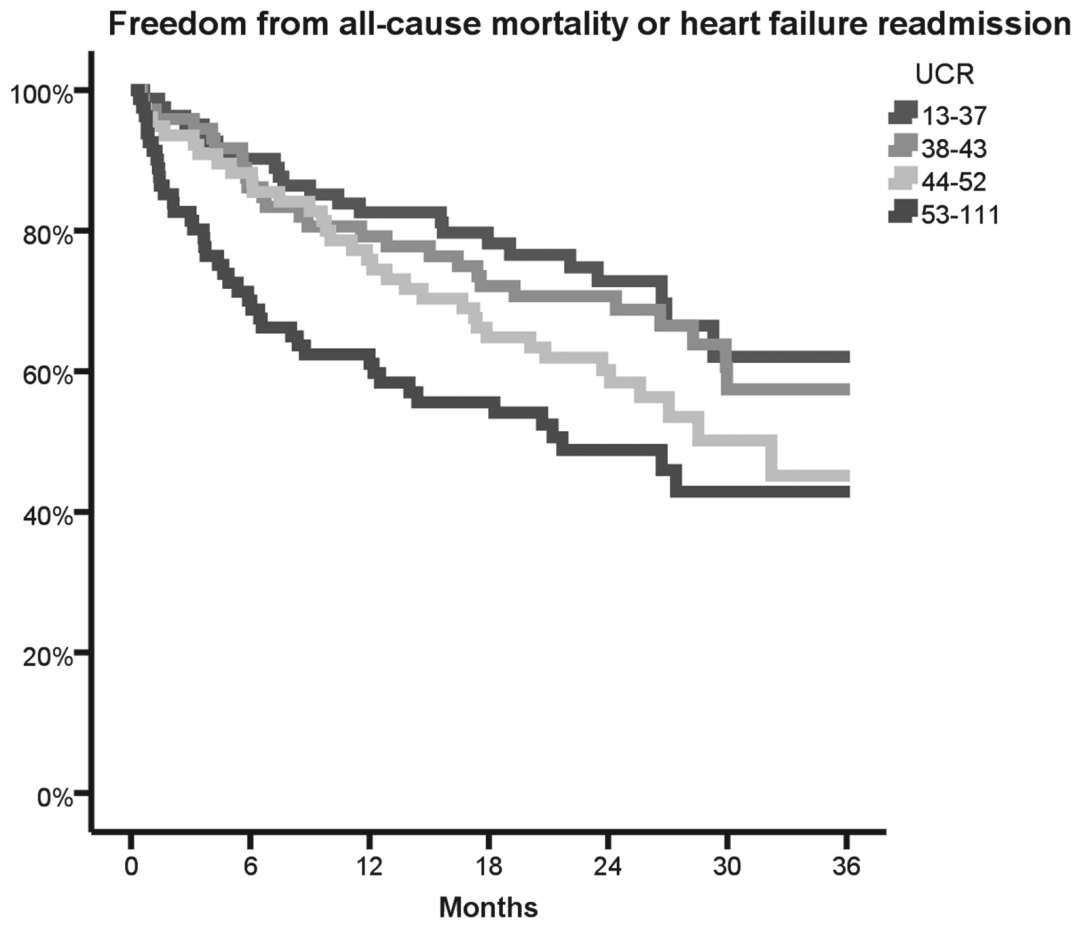

Fig. 1. Freedom from all-cause mortality or heart failure readmission in relation to admission serum urea/creatinine ratio (UCR)

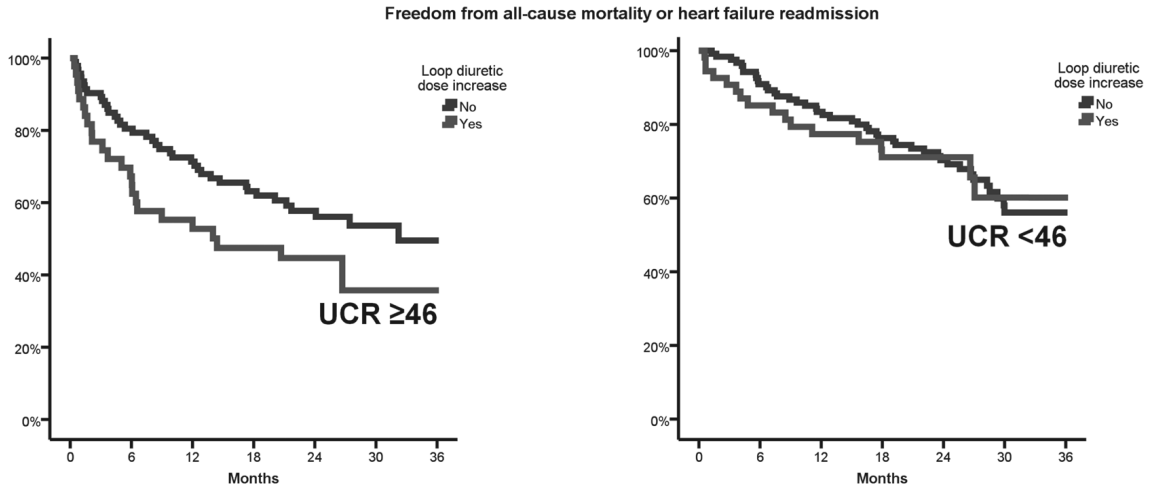

Fig. 2. Freedom from all-cause mortality or heart failure readmission in relation to use of loop diuretics and stratified according to admission serum urea/creatinine ratio (UCR)

Evaluation of CardioPAT autotransfusion system in elective cardiac surgery

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Introduction In order to reduce blood (RBC) transfusion and consequently its immunological complications, several strategies have been investigated. One of them is the use of cell saving devices and autologous

transfusion. With this intention the cardioPAT system (Haemonetics, Braintree, MA) was designed, which is more flexible than classical cell saving devices and thereby more easily to use in the postoperative period. ***Aim*** Observational non-randomized trial in 523 cardiac surgery cases. We evaluated perioperative blood loss, autologous transfusion rates and especially the use of allogeneic blood products. The transfusion trigger for RBC transfusion was 9 g/dL of hemoglobin. ***Material*** Observational non-randomized trial in 523 cardiac surgery cases. We evaluated perioperative blood loss, autologous transfusion rates and especially the use of allogeneic blood products. The transfusion trigger for RBC transfusion was 9 g/dL of hemoglobin. Results In 523 cardiac surgery cases (326 male *vs* 197 female) with a mean age of 70 (±12.7) years, the use of the cardioPAT system was evaluated. The most frequently performed operations were CABG, mitral valve plasty and double (or triple) valve operations. On average 1540 (±1151) mL of blood was drained. After processing, 376.5 (±320) mL of autologous blood was readministered to the patient (of which 192.2±154.7 ml intraoperatively and 184.57±165.68 mL postoperavely). Drainage and transfusion rates were higher in redo cases (1808.3 and 473.8 mL respectively) and patients that underwent reoperation in the postoperative phase (2232.5 and 526.3 mL respectively). In 50 patients (9.5 %) a classical cell saver was used intraoperatively and in 18 patients cardioPAT was started postoperatively. In 285 patients (54.4%), a total of 851 units of RBCs were administered (534 peroperatively and 317 postoperatively). In 79 of them, only 1 unit of PC was given. In total 374 units of fresh frozen plasma and 155 pools of platelets were administered (almost equally divided between the OR and the ICU). Eleven patients received platelets or plasma without transfusion of RBCs. Transfusion rates were higher in redo cases (88% of patients with average of 3.7 units of RBC) and revised patients (100% of patients with an average of 5 units of RBC). Nearly 29% of all blood products were given in the redo and revised cases (10.3% of all patients). Looking only at the postoperative period, approximately 20% (n=102) of patients received RBCs (on average 0.61/patient). On average 0.35 units of plasma and 0.14 pools of plasma were given per patient. During the observation period a reduction of overall transfusion rates was seen from 2.17 RBC/patient (after the first 100 patients) to 1.63 PC/patient (after 523 patients). A similar decline was seen for plasma and platelet transfusion rates. No device-related serious adverse events were noticed during the observation period. ***Discussion*** Several reports have shown that RBC transfusion was an independent risk factor for clinical complications after cardiac surgery, although there are only a few randomized trials [1]. Autotransfusion systems have been developed in order to reduce RBC transfusion. Around 30 well-designed trials studied the use of cell saving and a meta-analysis showed that the exposure to any allogeneic blood product was decreased [2]. Almost all studies however deal with intraoperative use of cell saving, and in a majority of them only cardiotomy suction blood is retransfused. Subanalyses suggest that a cell saver may be only beneficial when it is used for shed blood and / or residual blood or during the entire operative period [2]. The cardioPAT system, by its design, is also very convenient for prolonged use in the postoperative period. The end product reaches hematocrit levels of up to 70%. Only one randomized study with the cardioPAT system was published earlier, comparing intra-operative classical cell saving with intra- and postoperative use of the cardioPAT system [3]. In 512 patients the amount of retransfused blood was 370±250 and 350±370 mL in the intra- and postoperative phase respectively. Allogeneic RBC transfusion was reduced from 2.11±0.9 to 1.2±0.8 units per patient in comparison with the control group. Thirty-seven % of patient required allogeneic RBC's in the cardioPAT group versus 57.13% in the control group. From those, respectively 11.7% and 18.8% required only 1 unit of RBC. As we had no control group we took an historic control sample. More than 70% of cardiac surgery patients received packed cells in this sample. With the introduction of the cardioPAT system, this percentage was lowered to 54.4%. Excluding the patients receiving only 1 unit (with a hemoglobin trigger for transfusion of 9 g/dL at the time of observation), would further reduce the group of patients needing allogeneic RBC's to 39%. The decrease in RBC transfusion during the observation was probably biased by a changing transfusion trigger. Probably therefore the reduction is smaller than the ones published in earlier (randomized) series. Comparisons however are difficult for several reasons (redo cases excluded, only postoperative used evaluated). Anyhow, when evaluating only the postoperative phase, an average of 0.61 units of RBC per patient was administered, which is comparable with literature data. Conclusions Autologous transfusion in elective cardiac surgery can be done safely with the CardioPAT auto transfusion device. Due to the transfusion of autologous blood, allogeneic transfusion can be reduced especially in the postoperative period. ***Acknowledgement*** Oral presentation will take place in Room Belle Epoque on Friday November 29th at 14:50—15:00.

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Extravascular lung water, B-type natriuretic peptide and blood volume contraction enable diagnosis of weaning-induced pulmonary edema

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Introduction The gold standard for diagnosing weaning-induced pulmonary edema (PE) is the increase in pulmonary arterial occlusion pressure (PAOP) during a spontaneous breathing trial (SBT). Nevertheless, clinicians might be reluctant to use it because of invasiveness of pulmonary artery catheterization. ***Aim*** We tested whether the measurement of extravascular lung water indexed for ideal body weight (EVLWI) could detect weaning-induced pulmonary edema (PE). We also studied the diagnostic value of blood volume contraction indices and B-type natriuretic peptide (BNP) variations. ***Material and methods*** We performed a 60-minute T-tube spontaneous breathing trial (SBT) in patients who failed at a first SBT. Before and at the end of SBT, we recorded pulmonary artery occlusion pressure (PAOP), the EVLWI, plasma BNP level, hemoglobin and plasma protein concentrations. Weaning-induced PE was defined by the association of signs of clinical intolerance and a PAOP≥18 mmHg at the end of SBT. Because some patients performed several SBT, a primary analysis included all SBT and a secondary analysis included only the first SBT of each patient. ***Results*** In primary analysis, 36 SBT were analysed, 21 SBT with weaning-induced PE and 15 without. During SBT, EVLWI increased only in cases with weaning-induced PE (+25±23%). Plasma protein concentration, hemoglobin concentration and BNP also significantly increased only in cases with weaning-induced PE (+9±3%, +9±4%, +21±23%, respectively). The areas under the receiver operating characteristics curves to detect weaning-induced PE were 0.89 (95%CI: 0.78—0.99) for EVLWI, 0.97 (0.93—1.01) for SBT-induced changes in plasma protein concentration, 0.96 (0.90—1.01) for changes in hemoglobin concentration and 0.76 (0.60—0.93) for changes in BNP. An increase in EVLWI≥14% diagnosed weaning-induced PE with a sensitivity of 67% (95%CI: 43—85%) and a specificity of 100% (95%CI: 78—100%). The secondary analysis confirmed these results. ***Discussion*** This study showed that, if available at the time of weaning from mechanical ventilation, the SBT-induced variations in EVLWI are reliable in detecting weaning-induced PE. In addition, detection of SBT-induced blood volume contraction through increases in plasma protein concentration and hemoglobin supports the use of these tests as non-invasive tools for detecting weaning-induced PE. ***Conclusions*** SBT-induced increases in EVLWI, plasma protein concentrations, hemoglobin concentration and BNP are reliable alternatives to the pulmonary artery catheter for diagnosing weaning-induced PE. ***Acknowledgement*** Oral presentation will take place in Room Lijn on Friday November 29th at 14:40—14:50.

Raw impedance data analysis in severe ill patients with sepsis

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Introduction Critically ill patients especially with sepsis generally present change in body fluid distribution with migration of fluid from the intravascular to the extra vascular space. The systemic inflammatory response causes changes between the fat free mass and total body water distribution [1]. Oxidative stress and reactive oxygen species production observed in patients with sepsis are associated with cell membrane damage and related to the functional integrity [2]. Raw impedance data provide information on hydration and cell mass integrity [3]. Currently there are no clinical or laboratory parameters that can be commonly used to predict the outcomes of critically ill patients. Bioelectrical impedance analysis as a simple, non-invasive method is used in many clinical applications, but still little data exist about the raw bioelectrical impedance parameters in ICU patients. ***Aim*** The aim of this study was bioelectrical impedance vector and raw data analysis in severe ill patients with sepsis. ***Material and methods*** The sample comprised 68 patients (25 men and 43 women) aged 16 to 87 years, hospitalized in Intensive Care and Surgical Units. Exclusion criteria were: age >85 years, chemo- or radiotherapy, spread of cancer, chronic liver and kidney diseases, chronic steroid therapy, epilepsy, limb amputations, metallic prosthesis, pacemaker or implantable defibrillators. Healthy adults (n=65) were selected from our database to serve as a reference group. Patients were categorized as patients without sepsis – Group 1 (n=17) and with sepsis – Group 2 (n=51). Patients

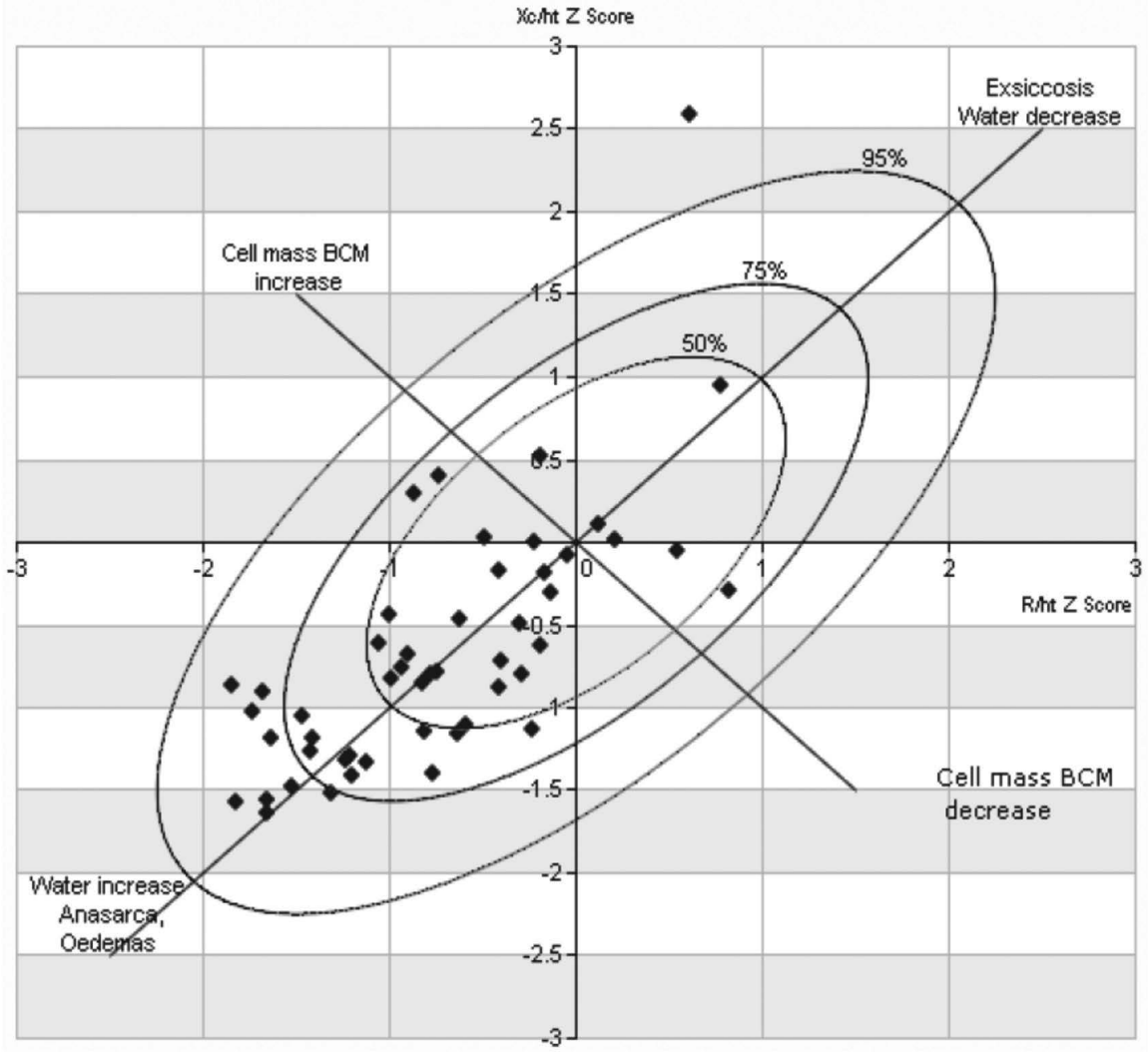

Fig. 1. The individual vectors of patients with sepsis (Group 2) plotted on the 3 tolerance ellipses (50%, 75% and 95%). Xc: reactance, R: resistance, Ht: height

were further allocated to subgroups Group 2a (n=22) – patients with sepsis and Group 2b (n=29) patients with severe sepsis. Severe sepsis criteria included: confirmed sepsis, ICU stay, sign of organ failure, respirator, APACHE II>20 points, SAPS II>14 points. Raw impedance data were obtained at multi-frequency bioimpedance analyzer model BioScan 920-2 (Maltron Int., UK). All measurements were performed at ICU admission. Individual bioelectrical vectors were analysed with tolerance ellipses (50%, 75% and 95% of individual points of the reference population) on BiaChart software (Maltron Int., UK). The reactance (Xc) and resistance (R) values were standardized by height. The results were also expressed as a mean and standard deviation ($\chi \pm SD$). Statistical significance was set at $p \leq 0.05$ for all tests which were performed with Statistica 10PL. The protocol of the study was approved by the Medical University Ethics Committee and conforms to the ethical guidelines of the World Medical Association Declaration of Helsinki. ***Results*** Patients without sepsis had significantly lower resistance values (401.1±129.56 Ω *vs* 490.4±142.06 Ω, $p=0.025$) and resistance normalized by height than patients with confirmed sepsis (241.16±80.3 Ω/m *vs* 293.05±89.35 Ω/m; $p=0.037$). The differences between phase angle (cellular biomarker), impedance and reactance in the groups (1 and 2) were not significant. Patients with sepsis showed significantly higher impedance (Group 2a 566±98.66 Ω *vs* Group 2b 423.86±149.7 Ω; -1491416348 $p=0.0003$) and resistance normalized by height (Group 2a 336.69±66.9 Ω/m *vs* Group 2b 259.94±90.9 Ω/m; $p=0.00165$) but lower percentage of extracellular water (Group 2a 45.95±2.97% 1192946737 *vs* Group 2b 49.2±6.11 %; $p=0.026$) and fat free mass hydration (Group 2a 70.65±3.61% *vs* 78.13±5.15%; $p=0.00000$) from those with severe sepsis. The distribution of individual impedance vectors in group patients with sepsis (Group 2) showed that 49% cases were located above 50 pc, lay above -1 Z (Xc); -1 Z (R) and within this group 9 cases were positioned above 75 pc. In the group 1 (without sepsis) only 3 cases were located above 75 pc (Fig. 1). However in both groups, there was a tendency toward a location mainly on the lower left side of the tolerance ellipses. After comparison patients laying above 50pc in both groups, we observed only significantly lower phase angle (cellular biomarker) in group with sepsis then in group without sepsis (Group 2 6.09°±2.46°) *vs* Group 1 8.29°±3.09°; $p=0.034$). ***Discussion*** Changes in tissues physiology produce changes in tissue electrical properties based on this especially the use of raw data from BIA has gained popularity. Raw data are not influenced by assumptions that can affect

body composition results. Bioimpedance vector analysis allows obtaining information about tissue hydration and body cell mass independent of regression equations, so raw data can be interpreted even if patients are overhydrated [4]. To our knowledge, there have been no applications of vector bioimpedance analysis to patients with sepsis. Our sepsis population was positioned mainly on the lower left side of the tolerance ellipses, characterized by fluid retention what is a comparable to chronic renal failure, obese hemodialysis patients [4]. In our sample, 49% cases with sepsis were located above 50th percentile what can indicate fluid accumulation. Piccoli et al. suggested that cardiac dyspnea patients lying on the lower pole of the 50% tolerance ellipse presented increasing fluid volume and central venous pressure [5]. In the present research, the lower mean phase angle of the patients with sepsis laying above 50th percentile could be related to a low body cell mass and high ECW/ICW ratio, as observed by other investigators [6]. ***Conclusions*** Severity level of sepsis has determined raw impedance and body composition data. Patient with severe sepsis were characterized by higher fluid disorders. Bioimpedance vector and raw data analysis are promising tools in routinely clinical practice especially for assessing hydration in critically ill patients with sepsis but more research is required. ***Acknowledgement*** This study was supported by grant No.1033/B/P01/2011/40. Oral presentation will take place in Room Lijn on Friday November 29th at 14:50—15:00.

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