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Pre-Procedural Bioimpedance Vectorial Analysis of Fluid Status and Prediction of Contrast-Induced Acute Kidney Injury

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Objectives The aim of this study was to evaluate the relationship between pre-procedural fluid status assessed by bioimpedance vector analysis (BIVA) and development of contrast-induced acute kidney injury (CI-AKI).

Background Accurate fluid management in patients undergoing angiographic procedures is of critical importance in limiting the risk of CI-AKI. Therefore, establishing peri-procedural fluid volume related to increased risk of CI-AKI development is essential.

Methods We evaluated the fluid status by BIVA of 900 consecutive patients with stable coronary artery disease (CAD) immediately before coronary angiography, measuring the resistance/height (R/H) ratio and impedance/height (Z/H) vector. CI-AKI was defined as an increase in serum creatinine $\geq$0.5 mg/dl above baseline within 3 days after contrast administration (iodixanol).

Results CI-AKI occurred in 54 patients (6.0%). Pre-procedural R/H ratios were significantly higher in patients with CI-AKI than without CI-AKI (395 $\pm$ 71 Ohm/m vs. 352 $\pm$ 58 Ohm/m, p = 0.001 for women; 303 $\pm$ 59 Ohm/m vs. 279 $\pm$ 45 Ohm/m, p = 0.009 for men), indicating lower fluid volume in the patients with CI-AKI. When patients were stratified according to R/H ratio, there was an almost 3-fold higher risk in patients with higher values (odds ratio [OR]: 2.9; 95% confidence interval [CI]: 1.5 to 5.5; p = 0.002). The optimal receiver-operating characteristic curve analysis threshold values of R/H ratio for predicting CI-AKI were 380 Ohm/m for women and 315 Ohm/m for men. R/H ratio above these thresholds was found to be a significant and independent predictor of CI-AKI (OR: 3.1; 95% CI: 1.8 to 5.5; p = 0.001).

Conclusions Lower fluid status evaluated by BIVA immediately before contrast medium administration resulted in a significant and independent predictor of CI-AKI in patients with stable CAD. This simple noninvasive analysis should be tested in guiding tailored volume repletion. (J Am Coll Cardiol 2014;63:1387–94) © 2014 by the American College of Cardiology Foundation

Iodinated contrast media are a well-recognized cause of iatrogenic acute kidney injury (CI-AKI) in patients undergoing diagnostic and/or therapeutic angiographic procedures. CI-AKI contributes to morbidity, prolonged hospitalization, mortality, and increased costs of health care; thus, strategies to decrease its incidence are of utmost importance (1–4).

Several protocols have been tested for the prevention of CI-AKI (5–7), including periprocedural intravenous volume repletion (8,9); administration of *N*-acetylcysteine, ascorbic acid, and statins (10–14); use of low- or iso-osmolar contrast agents (15,16); and hemofiltration or dialysis (17). To date, intravenous volume expansion is the cornerstone of prevention strategies (6). However, there is no easy, fast, accurate, and bedside method to evaluate whether optimal fluid status has been achieved with solution infusion; thus, patients are sometimes either underhydrated or overhydrated. In either state, periprocedural risk management may be compromised, and establishing the degree of extracellular volume expansion of each individual patient would be advantageous for proper treatment.

Bioimpedance vector analysis (BIVA) is a rapid, inexpensive, and accurate tool for evaluating patient fluid volume; it is performed by nursing staff at the bedside within minutes (18–20). BIVA does not indicate the effective

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Abbreviations and Acronyms

BIVA = bioimpedance vector analysis
CAD = coronary artery disease
CI-AKI = contrast-induced acute kidney injury
eGFR = estimated glomerular filtration rate
LVEDP = left ventricular end-diastolic pressure
R/H = resistance/height ratio
Z/H = impedance/height

intravascular fluid volume but rather, in most cases (with the exclusion of patients who may be "third spacing" fluids), the overall fluid volume (often called total body water) that is well correlated with the effective intravascular volume (19). This method is used regularly to monitor the body fluid component, particularly in patients on dialysis or with heart failure, but it has not been used to monitor patients scheduled for angiographic procedures (21–26).

The aim of this study was to evaluate the relationship between BIVA-assessed preprocedural fluid status and CI-AKI occurrence in patients undergoing elective coronary angiography.

Methods

Population and study protocol. All 1,989 consecutive patients with coronary artery disease (CAD) listed for coronary angiographic procedures from September 2009 to August 2011 at the Prato Hospital (Prato, Italy) were screened for eligibility. Exclusion criteria were: 1) patients requiring urgent or emergency procedures (n = 985); 2) BIVA machine unavailability (n = 27); 3) contrast medium administration in the previous 10 days (n = 24); 4) overt congestive heart failure with ascites or pleuropericardial effusion (n = 22); 5) end-stage renal failure requiring dialysis (n = 16); and 6) patient consent refusal (n = 15). Thus, a total of 900 patients with stable CAD were enrolled in this study.

Creatinine clearance was calculated by applying the Cockroft-Gault formula to the baseline serum creatinine (defined as the creatinine 1 day prior to the procedure) (27). All patients received standard intravenous saline hydration (0.9% sodium chloride, 1 ml/kg/h for 12 h before and after the procedure) (8). The rate of hydration was halved in patients with left ventricular ejection fraction <40% or with clinical signs of heart failure (New York Heart Association functional class III to IV). *N*-acetylcysteine was given orally at a dose of 600 mg twice daily, on the day before and the day after the procedure (28). In all cases, iodixanol (Visipaque, GE Healthcare Ltd., Chalfont St. Giles, United Kingdom), a nonionic, dimeric iso-osmolar contrast medium was used for angiographic procedures.

Serum creatinine concentration (isotope dilution mass spectrometry traceable method) was assessed the day before angiography (baseline), immediately pre-procedural (day 0), and on days 1, 2, and 3 after contrast medium administration. All creatinine measurements, even after discharge, were completed in a single hospital laboratory with consistent methodology.

Demographic, clinical, and procedural data were prospectively recorded for all patients. The institutional review board and ethics committee approved the protocol, and all patients gave informed consent.

Bioimpedance analysis. Bioimpedance is based on the principle that the body acts as a circuit with a given resistance (opposition of current flow through intracellular and extracellular solutions [R]) and reactance (the capacitance of cells to store energy [Xc]) (18). The volume of the body fluid component is largely reflected in the resistance, whereas reactance might represent cell membrane integrity. The impedance (Z) is composed of the sum of resistance and reactance ($\sqrt{[R^2 + Xc^2]}$) (16). Another parameter that can be derived is the phase angle (PA), which is the arc tangent of Xc/R. When a current passes through cells, a portion of the electrical current is stored and subsequently released in a different phase, termed "phase angle." The PA is related to the ability of cells to function as capacitors, which is dependent on the integrity of the cell membrane and cellular health.

BIVA results are normalized by sex and patient height (19,20) and are displayed graphically (RXc graph), integrating resistance/height (R/H) (in Ohm/m) to reactance/height (Xc/H) (in Ohm/m) (19,20) (Fig. 1) and generating an output that simultaneously reflects fluid status and alterations of cellular integrity. BIVA data can be compared with that of the normal population (20), represented on the graph by confidence ellipses, with data expected to fall within the reference 75% tolerance ellipse. When presented as a vector, shorter or longer lengths are associated with more or less overall fluid volume, respectively.

BIVA has been validated in different settings, including 1 in which critically ill patients are undergoing renal replacement therapy and/or ultrafiltration and patients have refractory congestive heart failure (21–26). BIVA data were obtained using a tetrapolar impedance plethysmography (EFG electrofluidgraph, Akern, Florence, Italy). The bioelectrical

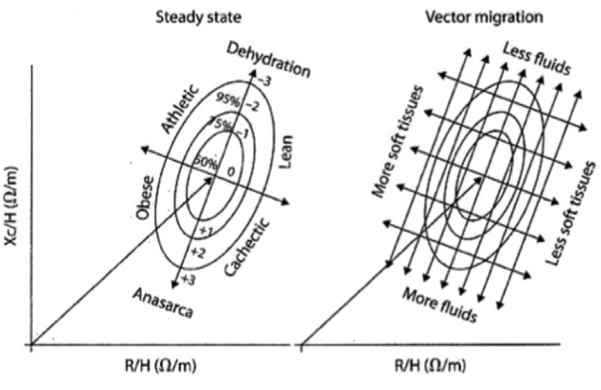

Figure 1 R/Xc Graph

Bioimpedance vector analysis (BIVA) results displayed graphically comparing resistance/height (R/H) with reactance/height (Xc/H). BIVA patterns: major axis → tissue hydration; minor axis → soft tissue mass.