

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



Mauro Maioli, MD,* Anna Toso, MD,* Mario Leoncini, MD,* Nicola Musilli, MD,*
Francesco Bellandi, MD,* Mitchell H. Rosner, MD,† Peter A. McCullough, MD, MPH,‡§
Claudio Ronco, MD||

Prato and Vicenza, Italy; Charlottesville, Virginia; and Dallas and Plano, Texas

- 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 ≥ 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 ± 71 Ohm/m vs. 352 ± 58 Ohm/m, $p = 0.001$ for women; 303 ± 59 Ohm/m vs. 279 ± 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

From the *Division of Cardiology, New Prato Hospital, Prato, Italy; †Division of Nephrology, University of Virginia Health System, Charlottesville, Virginia; ‡Baylor Healthcare System, Baylor Heart and Vascular Institute, Baylor Jack and Jane Hamilton Heart and Vascular Hospital, Baylor University Medical Center, Dallas, Texas; §Heart Hospital, Plano, Texas; and the ||Department of Nephrology, International Renal Research Institute, St. Bortolo Hospital, Vicenza, Italy. All authors have reported that they have no relationships relevant to the contents of this paper to disclose.

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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 pre-procedural 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 Cockcroft-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

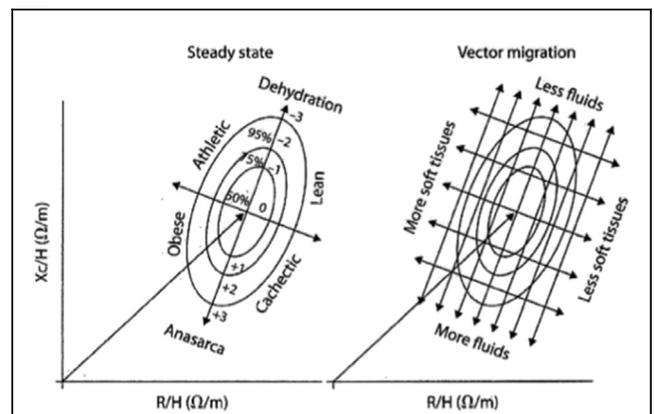


Figure 1 R/Xc Graph

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.

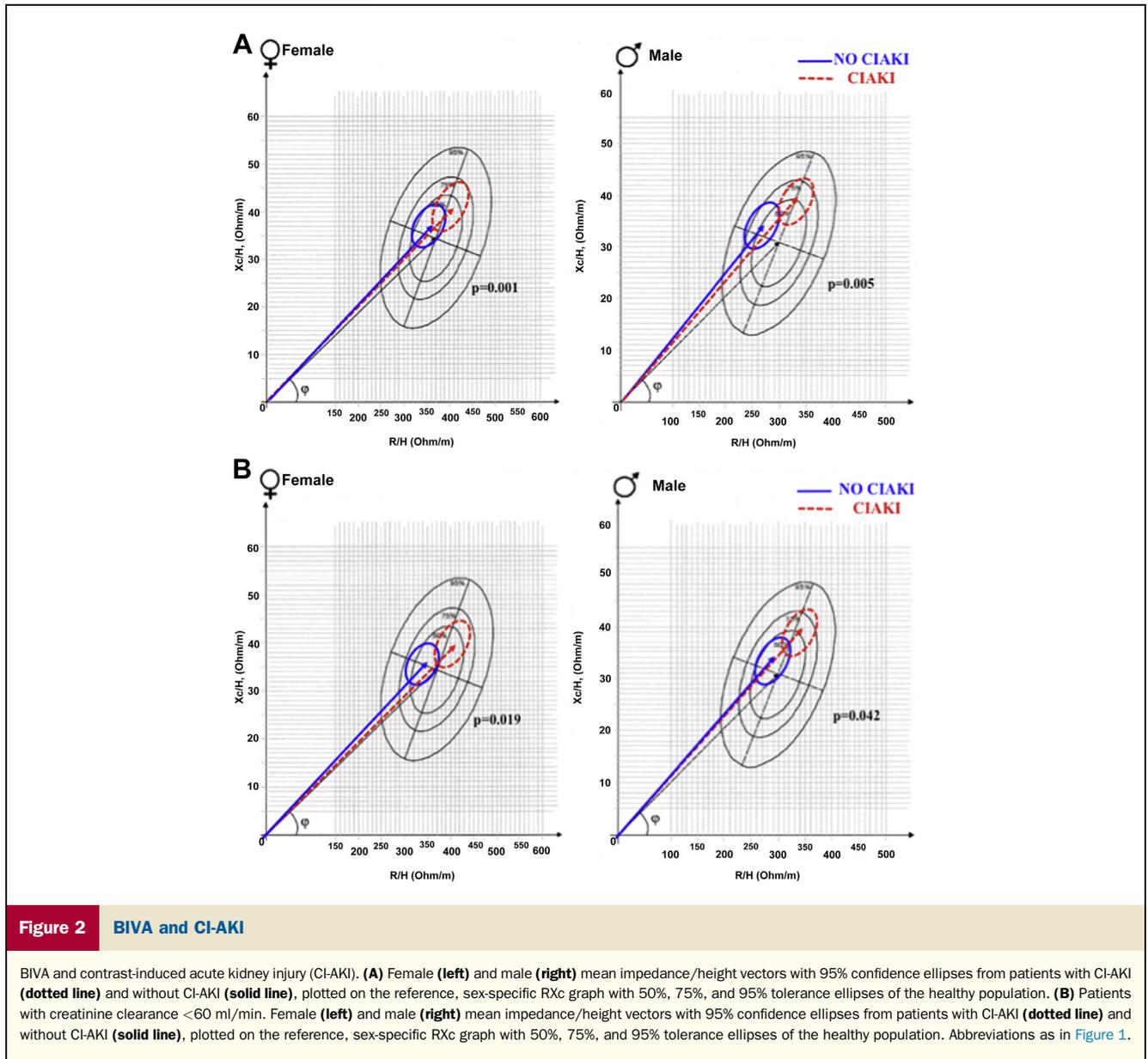


Figure 2 BIVA and CI-AKI

BIVA and contrast-induced acute kidney injury (CI-AKI). (A) Female (left) and male (right) mean impedance/height vectors with 95% confidence ellipses from patients with CI-AKI (dotted line) and without CI-AKI (solid line), plotted on the reference, sex-specific RXc graph with 50%, 75%, and 95% tolerance ellipses of the healthy population. (B) Patients with creatinine clearance <60 ml/min. Female (left) and male (right) mean impedance/height vectors with 95% confidence ellipses from patients with CI-AKI (dotted line) and without CI-AKI (solid line), plotted on the reference, sex-specific RXc graph with 50%, 75%, and 95% tolerance ellipses of the healthy population. Abbreviations as in Figure 1.

parameters of resistance and reactance were measured using an electric alternating current flux of 800 amperes and an operating frequency of 50 kHz. Whole-body impedance measurements were taken by using a standard position of outer and inner electrodes on the right hand and foot. After the patient had remained in a supine position with arms separated from trunk by about 30° and legs separated by about 45° for at least 5 min and the skin was cleaned to ensure good contact, electrodes were attached to the right hand and foot, according to the standard protocol of the National Institutes of Health technology assessment conference statements (29). The R/H ratio and impedance/height (Z/H) vector were calculated and used to define the global fluid volume (19,20). In the present study, all patients underwent BIVA evaluation in the catheterization laboratory immediately before contrast administration and after the completion of standard intravenous

infusion of saline solution. The possible error of bioimpedance measurement was evaluated in 50 patients: the mean coefficients of variation of Z/H ratio were 0.5% intrapatient and 1.6% interoperator.

Definitions. CI-AKI was defined as an increase in serum creatinine ≥ 0.5 mg/dl above baseline within 3 days after contrast medium administration (6). Baseline kidney function was categorized according to the National Kidney Foundation (U.S.) staging system, with estimated glomerular filtration rate (eGFR) ≥ 90 ml/min considered normal, 60 to 89 ml/min mildly impaired, 30 to 59 ml/min moderately impaired, and <30 ml/min severely impaired (30). Advanced congestive heart failure was defined according to New York Heart Association functional classes III and IV. Anemia was defined using World Health Organization criteria: baseline hematocrit value $<39\%$ for men

Table 1 Clinical, Procedural, and Bioimpedance Data of Study Population

Age, yrs	68 ± 11
Age ≥75 yrs	298 (22.3)
Female	316 (35.1)
Body mass index, kg/m ²	27 ± 4
Diabetes mellitus	201 (22.3)
Hypertension	562 (62.4)
Anemia	184 (20.4)
Advanced congestive heart failure	21 (2.3)
Diuretic therapy	126 (14.0)
Percutaneous coronary intervention	456 (50.7)
Left ventricular ejection fraction, %	55 (40–60)
Left ventricular ejection fraction ≤30%	96 (10.7)
Periprocedural hypotension	10 (1.1)
Serum creatinine, mg/dl	1.00 ± 0.32
Serum creatinine ≥2.0 mg/dl	9 (1.0)
Mean estimated creatinine clearance, ml/min	68 (54–87)
Estimated creatinine clearance <60 ml/min	314 (34.9)
Estimated creatinine clearance <30 ml/min	20 (2.2)
Contrast volume	120 (70–190)
<100 ml	379 (42.2)
101–200 ml	310 (34.4)
201–300 ml	147 (16.3)
>300 ml	64 (7.1)
Contrast volume-to-creatinine clearance ratio	1.7 (0.9–3.0)
Contrast nephropathy risk score	4.0 (2.0–7.0)
≤5	587 (65.3)
6–10	253 (28.1)
11–16	58 (6.4)
≥17	2 (0.2)
BIVA parameters—women	
Resistance/height ratio, Ohm/m	356 ± 61
Reactance/height ratio, Ohm/m	40 ± 15
Impedance/height vector, Ohm/m	358 ± 61
Phase angle, °	7.0 ± 2.3
BIVA parameters—men	
Resistance/height ratio, Ohm/m	280 ± 46
Reactance/height ratio, Ohm/m	36 ± 10
Impedance/height vector, Ohm/m	282 ± 46
Phase angle, °	7.1 ± 2.2

Normally distributed values are mean ± SD, categorical values are n (%), and non-normally distributed values are median (interquartile range). Advanced congestive heart failure was defined according to New York Heart Association functional classes III and IV.

BIVA = bioimpedance vectorial analysis.

and <36% for women (31). The risk score for development of CI-AKI was defined as specified by Mehran et al. (2). The contrast medium volume-to-creatinine clearance ratio was calculated according to Laskey et al. (32).

The terms “hydration” and “dehydration” refer to changes in total body water that affect only the osmolality of body fluids (i.e., serum sodium level). The terms “extracellular fluid volume expansion” and “contraction” refer to changes in intravascular volume that are caused by changes in both salt and water content (33).

Statistical analysis. Categorical variables were summarized as frequencies with percentages and were compared

by Pearson chi-square analysis or Fisher exact test. Normal distribution of continuous data was tested using a Kolmogorov-Smirnov test. Continuous variables were compared by Student *t* test for normally distributed values; otherwise, the Mann-Whitney *U* test was used. Bioimpedance variables (resistance and impedance) are standardized by height (19). As per Piccoli et al. (19), assuming the bivariate normal distribution of R/H and Xc/H, we calculated the bivariate 95% confidence ellipses of mean Z/H vector; the results are plotted on the 75% and 95% reference tolerance ellipses for the healthy population (Fig. 2).

Patients were stratified into 4 groups according to quartiles of R/H ratio values. Rates of CI-AKI were compared between quartiles by the Mantel-Haenszel linear-by-linear association chi-square test for trend. Receiver-operating characteristic (ROC) curve analysis was performed to establish the threshold values (Youden index) of bioimpedance variables (R/H ratio and Z/H vector) most predictive of CI-AKI, and C-statistic was used to describe the discriminatory ability of CI-AKI risk score and R/H ratio for predicting CI-AKI incidence.

Univariate odds ratios (ORs) were calculated for CI-AKI risk score and BIVA variables for development of CI-AKI. To avoid multicollinearity, only 1 significant BIVA parameter (R/H ratio or Z/H vector) and the CI-AKI risk score were entered into a multiple logistic regression model to identify independent predictors of CI-AKI and to estimate ORs. The goodness-of-fit assumption was assessed using the Hosmer-Lemeshow statistic and was satisfied when *p* > 0.05. All analyses were performed with SPSS statistical software, version 17.0 (SPSS Inc., Chicago, Illinois). All tests were 2 tailed, and statistical significance was defined as *p* < 0.05.

Results

Clinical and procedural characteristics. Baseline clinical, angiographic, and BIVA data of the study group are shown in Table 1. Mean age was 68 years, 35.1% were women, 22.3% of patients had diabetes, and 34.4% presented with impaired baseline kidney function. The enrolled population had a low overall risk for CI-AKI, and 65.3% of the patients presented with a CI-AKI risk score ≤5. All patients presented for all scheduled creatinine measurements even after discharge.

CI-AKI incidence. CI-AKI occurred in 54 of 900 patients (6.0%); 40 of these patients (74.1%) had a baseline eGFR <60 ml/min. The incidence of CI-AKI is 2.3% in patients with eGFR ≥60 ml/min and 12.7% in patients with eGFR <60 ml/min. Table 2 reports clinical, procedural, and BIVA data for the patients with and without CI-AKI. Patients with CI-AKI were generally older and presented with more hypertension, diabetes, and advanced stages of renal and heart failure, and more than one-half were women. There was no significant difference between the patients with and without CI-AKI in the amount of contrast medium administered, whereas the ratio between

contrast infusion volume and renal function and the CI-AKI risk score were both significantly greater in the patients who developed CI-AKI.

Pre-procedural fluid status and incidence of CI-AKI.

Pre-procedural BIVA parameters were significantly different in patients with and without CI-AKI, with higher R/H ratio and longer Z/H vector values indicating a significantly lower fluid volume in the patients with CI-AKI (Table 2). R/H ratio and PA were similar in patients with and without CI-AKI. The mean Z/H vector and 95% confidence ellipses with their relative PA, normalized for sex, is shown in Figure 2. Panel A includes all patients and panel B only patients with lower eGFR (<60/ml/min).

The nomograms clearly show that patients who developed CI-AKI presented a significantly lower pre-procedural fluid volume than patients without CI-AKI. We note that there was no significant correlation between Z/H vector and baseline creatinine clearance ($r = 0.31$; $p = 0.348$).

Quartiles analysis. With the study population stratified into quartiles according to the R/H ratio, the incidence of CI-AKI progressively increased from the lower R/H ratio first quartile (higher total body water) to the higher fourth quartile (fluid depleted), with an almost 3-fold higher risk of CI-AKI in the fourth quartile (OR: 2.9; 95% confidence interval [CI]: 1.5 to 5.5; $p = 0.002$) (Fig. 3).

Table 2 Clinical, Biochemical, Procedural, and Bioimpedance Characteristics in Association With CI-AKI Occurrence

	No CI-AKI (n = 846)	CI-AKI (n = 54)	p Value
Age, yrs	68 ± 11	76 ± 10	0.0001
Age ≥75 yrs	265 (31.3)	33 (61.1)	0.0001
Female	287 (33.9)	29 (53.7)	0.003
Body mass index, kg/m ²	27 ± 4	26 ± 5	0.39
Diabetes mellitus	182 (21.5)	19 (35.2)	0.019
Hypertension	520 (61.5)	42 (77.8)	0.016
Anemia	163 (19.3)	21 (38.9)	0.001
Advanced congestive heart failure	15 (1.8)	6 (11.1)	0.001
Diuretic therapy	113 (13.4)	13 (24.1)	0.028
Percutaneous coronary intervention	429 (50.7)	27 (50.0)	0.91
Left ventricular ejection fraction, %	55 (40-60)	40 (30-50)	0.074
Left ventricular ejection fraction ≤30%	78 (12.6)	18 (41.9)	0.0001
Serum creatinine, mg/dl	0.98 ± 0.30	1.17 ± 0.52	0.009
Serum creatinine ≥2.0 mg/dl	7 (0.8)	2 (3.7)	0.097
Mean creatinine clearance, ml/min	69 (55-88)	51 (41-69)	0.0001
Creatinine clearance <60 ml/min	274 (32.4)	40 (74.1)	0.0001
Creatinine clearance <30 ml/min	15 (1.8)	5 (9.3)	0.005
Contrast volume, ml	120 (67-190)	127 (75-217)	0.81
<100 ml	360 (42.6)	19 (35.2)	0.21
101-200 ml	292 (34.5)	18 (33.3)	
201-300 ml	134 (15.8)	13 (24.1)	
>300 ml	60 (7.1)	4 (7.4)	
Contrast volume-to-creatinine clearance ratio	1.7 (0.9-2.9)	2.6 (1.1-5.3)	0.123
Contrast nephropathy risk score	4.0 (2.0-6.0)	7.0 (5.0-10)	
≤5	565 (66.8)	22 (40.7)	0.001
6-10	232 (27.4)	21 (38.9)	0.0001
11-16	47 (5.6)	11 (20.4)	
≥17	2 (0.2)	0 (0.0)	
BIVA parameters—women			
Resistance/height ratio, Ohm/m	352 ± 58	395 ± 71	0.001
Reactance/height ratio, Ohm/m	40 ± 16	40 ± 10	0.88
Impedance/height vector, Ohm/m	354 ± 58	397 ± 71	0.001
Phase angle, °	6.6 ± 2.9	5.6 ± 1.2	0.08
BIVA parameters—men			
Resistance/height ratio, Ohm/m	279 ± 45	303 ± 59	0.009
Reactance/height ratio, Ohm/m	38 ± 10	40 ± 8	0.66
Impedance/height vector, Ohm/m	281 ± 45	307 ± 59	0.005
Phase angle, °	7.3 ± 1.8	6.6 ± 4.2	0.24

Values are mean ± SD, n (%), or median (interquartile range). The values were compared using the unpaired Student t test, Mann-Whitney U test, and chi-square or Fisher exact test, respectively.

BIVA = bioimpedance vectorial analysis; CI-AKI = contrast induced acute kidney injury.

ROC curve analysis. We also investigated the association between fluid status and CI-AKI occurrence using the optimal threshold values of R/H ratio and Z/H vector identified by ROC analysis (R/H ratio 380 Ohm/m in women and 315 Ohm/m in men; Z/H vector 382 Ohm/m in women and 320 Ohm/m in men) (Table 3). The incidence of CI-AKI was significantly higher in those patients with a lower fluid volume who presented with pre-angiographic R/H ratio and Z/H vector values above the ROC cutoffs (Fig. 4). Above these thresholds, there was an almost 3-fold increase in CI-AKI occurrence (R/H ratio OR: 3.1, 95% CI: 1.8 to 5.5, $p = 0.001$; Z/H vector OR: 3.3, 95% CI: 2.0 to 6.0, $p = 0.001$). The C-statistic in the model that included only the currently most used Mehran CI-AKI risk score was 0.69; when R/H ratio was added to the model, the C-statistic increased to 0.75, thus improving the predictive capacity of the model.

Multivariate analysis. In the multivariate analysis, the R/H ratio (included in the models as either a continuous or categorical variable) was a significant and independent predictor of development of CI-AKI (Table 4). An analogous significant result was obtained even with the Z/H vector.

Discussion

The present study showed that patients with stable CAD with lower pre-procedural BIVA-estimated fluid status presented with a statistically significant high risk of developing CI-AKI.

Contrast-induced nephropathy is the most common complication of the use of iodinated contrast media. In recent years, there has been growing attention paid to this adverse event, and a cause-and-effect relationship between CI-AKI and long-term cardiovascular outcome has been

identified (1,34-36). Given the ever-expanding use and complexity of contrast medium-based procedures, CI-AKI remains a serious concern for interventional and clinical cardiologists. Contrast-induced nephropathy occurs in 2% to 30% of patients undergoing diagnostic and therapeutic procedures (1,2). This wide range depends on the patient cohorts studied, definition criteria used to identify kidney injury, and preventive measures adopted (4).

CI-AKI is a multifactorial process, but intrarenal hemodynamic alterations and direct renal tubular toxic effects play a crucial role in its development (4). Fluid depletion and/or reduction of effective intravascular volume (due to congestive heart failure, liver cirrhosis, or abnormal fluid loss) have been reported to contribute to reduced renal perfusion, thus enhancing the toxic effect of contrast medium (4).

Intravascular volume expansion with intravenous saline is considered standard care in the prevention of CI-AKI (6). Periprocedural volume expansion represents an important protective strategy against both the intrarenal hemodynamic alterations and the direct renal tubular toxic effects that lead to the development of CI-AKI (4,37,38).

In the absence of an objective evaluation of adequate patient fluid status, it is difficult to establish optimal infusion volume. Most protocols rely on a “one size fits all” approach with fixed volume and times of infusion without monitoring of fluid status changes. The result is a high risk of suboptimal extracellular volume expansion of patients undergoing angiographic procedures.

To date, there is a lack of prospective studies analyzing effective fluid volume at the time of contrast medium injection. Only recently, Brar et al. (39) presented a graded relationship between the level of estimated intravascular volume status based on left ventricular end-diastolic pressure (LVEDP) and the development of CI-AKI. The incidence was 11.6% in patients with LVEDP >20 mm Hg, 14.6% in those with LVEDP of 10 to 20 mm Hg, and 16% in those with LVEDP <10 mm Hg (p for trend = 0.42).

The present study prospectively evaluated the association between pre-procedural fluid status assessed by BIVA and the occurrence of CI-AKI. Patients who presented with poor BIVA-estimated fluid volume had a 3 times higher incidence of CI-AKI. The BIVA parameters that best identify higher CI-AKI risk are the R/H ratio and the Z/H ratio. The cutoff values for the prediction of higher CI-AKI

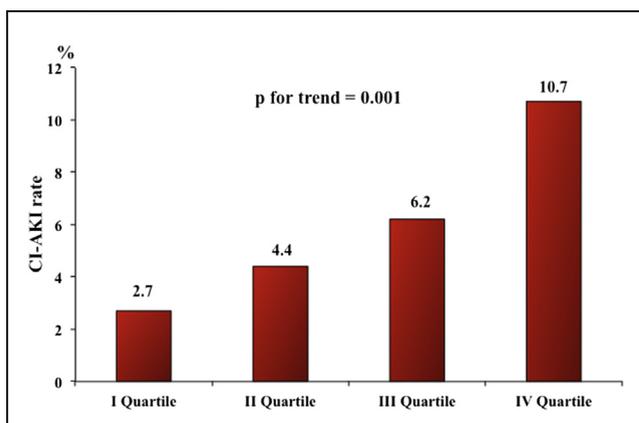


Figure 3 CI-AKI Rate According to Pre-Angiographic R/H Ratio Quartiles

The incidence of CI-AKI increased significantly (p for trend = 0.001) from the first (more fluid volume) to the fourth quartile (less fluid volume). CI-AKI = contrast induced acute kidney injury; R/H = resistance/height.

Table 3 ROC Curve BIVA Threshold Values Predictive of CI-AKI

	Cutoff Level	AUC ROC	p Value
Female resistance/height ratio	380	0.70	0.003
Female impedance/height vector	382	0.70	0.003
Male resistance/height ratio	315	0.72	0.003
Male impedance/height vector	320	0.72	0.002

Values are Ohm/m.
 AUC = area under the curve; ROC = receiver-operating characteristic; other abbreviations as in Tables 1 and 2.

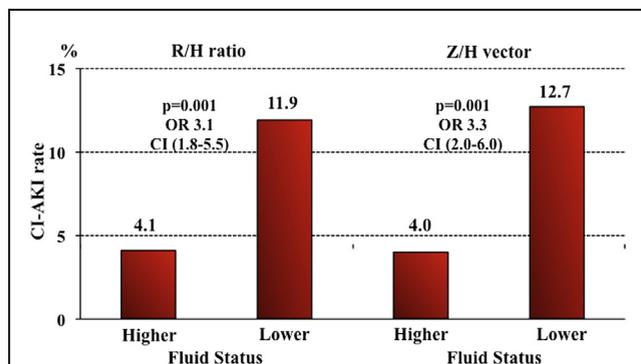


Figure 4 CI-AKI Rate and Pre-Angiographic BIVA Hydration Status

CI-AKI incidence in relation to pre-angiographic fluid status (higher or lower) as established by R/H ratio (left) and Z/H vector (right). Threshold values of R/H ratio (women ≥ 380 Ohm/m and men ≥ 315 Ohm/m) and Z/H vector (women ≥ 382 Ohm/m and men ≥ 320 Ohm/m) were established by receiver-operating characteristic analysis. CI = confidence interval; OR = odds ratio; other abbreviations as in Figures 1 and 2.

risk were 380 Ohm/m in women and 315 Ohm/m in men for R/H ratio and 382 Ohm/m in women and 320 Ohm/m in men for Z/H ratio. The addition of pre-procedural BIVA-estimated fluid status to the classic Mehran risk score moderately enhanced the ability to define CI-AKI risk.

Point-of-care BIVA is a user-friendly, rapid, simple tool for assessing peri-procedural fluid levels in patients with CAD undergoing contrast medium administration. It allows identification of patients at high risk for developing CI-AKI.

BIVA-guided monitoring of fluid infusion could be advisable to ensure optimal patient fluid status.

Study limitations. The main limitation is that BIVA evaluates overall body fluid volume, which may include eventual compartmentalized fluids, although our patients were screened to exclude patients with clinically-overt fluid retention (pleural, pericardial, or peritoneal effusion) and congestive heart failure. Moreover, although this study

enrolled only elective patients with low risk of kidney damage not related to the contrast medium (i.e., sepsis, hypotension or shock, nephrotoxic drugs), we cannot exclude that other causes may have contributed to the development of AKI in some patients. Finally, incorrect body position or placement of electrodes can distort the results.

Conclusions

Lower fluid status evaluated by BIVA immediately before contrast medium administration was a significant and independent predictor of CI-AKI in patients with stable CAD. However, before clinical use of BIVA-guided monitoring can be recommended for routine use, additional studies will be needed to establish more precisely the worth of BIVA-guided monitoring in the prevention of CI-AKI.

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Reprint requests and correspondence: Dr. Mauro Maioli, Division of Cardiology, Prato Hospital, Via Ugo Foscolo, Prato PO 59100, Italy. E-mail: mauromaioli1956@gmail.com.

REFERENCES

- Rihal CS, Textor SC, Grill DE, et al. Incidence and prognostic importance of acute renal failure after percutaneous coronary intervention. *Circulation* 2002;105:2259-64.
- Mehran R, Aymong ED, Nikolsky E, et al. A simple risk score for prediction of contrast-induced nephropathy after percutaneous coronary intervention: development and initial validation. *J Am Coll Cardiol* 2004;44:1393-9.
- Tepel M, Aspelin P, Lameire N. Contrast-induced nephropathy. A clinical and evidence-based approach. *Circulation* 2006;113:1799-806.
- McCullough PA. Contrast-induced acute kidney injury. *J Am Coll Cardiol* 2008;51:1418-28.
- Barrett BJ, Parfrey PS. Preventing nephropathy induced by contrast medium. *N Engl J Med* 2006;354:379-86.
- Stacul F, van der Molen AJ, Reimer P, et al. Contrast induced nephropathy: updated ESUR Contrast Media Safety Committee guidelines. *Eur Radiol* 2011;21:2527-41.
- KDIGO Clinical Practice Guideline for Acute Kidney Injury. Section 4: contrast induced AKI. *Kidney Int* 2012; Suppl 2:80-6.
- Mueller C, Buerkle G, Buettner HJ, et al. Prevention of contrast-associated nephropathy. *Arch Intern Med* 2002;162:329-36.
- Brar SS, Hiremath S, Dangas G, Mehran R, Brar SK, Leon MB. Sodium bicarbonate for the prevention of contrast induced-acute kidney injury: a systematic review and meta-analysis. *Clin J Am Soc Nephrol* 2009;4:1584-92.
- Thiele H, Hildebrand L, Schirdewahn C, et al. Impact of high-dose N-acetylcysteine versus placebo on contrast-induced nephropathy and myocardial reperfusion injury in unselected patients with ST-segment elevation myocardial infarction undergoing primary percutaneous coronary intervention. *J Am Coll Cardiol* 2010;55:2201-9.
- ACT Investigators. Acetylcysteine for prevention of renal outcomes in patients undergoing coronary and peripheral vascular angiography: main results from the randomized Acetylcysteine for Contrast-Induced Nephropathy Trial (ACT). *Circulation* 2011;124:1250-9.

Table 4 Multivariable Logistic Regression Models of Predictors of CI-AKI

	Parameter Estimates	Odds Ratio	95% CI	p Value
Model A (continuous variables)				
Intercept	-7.316			
CI-AKI risk score	0.169	1.2	1.1-1.4	0.001
Resistance/height ratio	0.010	1.01	1.0-1.02	0.001
Model B (categorical variables)				
Intercept	-4.759			
CI-AKI risk score ≥ 11	1.436	4.2	2.0-8.8	0.001
Resistance/height ratio (women ≥ 380 Ohm/m and men ≥ 315 Ohm/m)	1.157	3.2	1.8-5.6	0.001

Model A (continuous variables): CI-AKI risk score and resistance/height ratio: odds ratio for every 1-point increase. Model B (categorical variables): CI-AKI risk score ≥ 11 : high to very high risk. CI = confidence interval; CI-AKI = contrast induced acute kidney injury.

12. Spargias K, Alexopoulos E, Kyrzopoulos S, et al. Ascorbic acid prevents contrast-mediated nephropathy in patients with renal dysfunction undergoing coronary angiography or intervention. *Circulation* 2004;110:2837-42.
13. Han Y, Zhu G, Han L, et al. Short-term rosuvastatin therapy for prevention of contrast-induced acute kidney injury in patients with diabetes and chronic kidney disease. *J Am Coll Cardiol* 2014;63:62-70.
14. Leoncini M, Toso A, Maioli M, Tropeano F, Villani S, Bellandi F. Early high-dose rosuvastatin for contrast-induced nephropathy prevention in acute coronary syndrome: results from the PRATO-ACS study (Protective Effect of Rosuvastatin and Antiplatelet Therapy on Contrast-Induced Acute Kidney Injury and Myocardial Damage in Patients With Acute Coronary Syndrome). *J Am Coll Cardiol* 2014;63:71-9.
15. McCullough PA, Bertrand ME, Brinker JA, Stacul F. A meta-analysis of the renal safety of isosmolar iodixanol compared with low-osmolar contrast media. *J Am Coll Cardiol* 2006;48:692-9.
16. McCullough PA, Brown JR. Effects of intra-arterial and intravenous iso-osmolar contrast medium (iodixanol) on the risk of contrast-induced acute kidney injury: a meta-analysis. *Cardiorenal Med* 2011;1:220-34.
17. Cruz DN, Goh CY, Marenzi G, Corradi V, Ronco C, Perazella MA. Renal replacement therapies for prevention of radiocontrast-induced nephropathy: a systematic review. *Am J Med* 2012;125:66-78.
18. Kushner RF. Bioelectrical impedance analysis: a review of principles and applications. *J Am Coll Nutr* 1992;11:199-209.
19. Piccoli A, Rossi B, Pillon L, Buccianto G. A new method for monitoring body fluid variation by bioimpedance analysis: the RXc graph. *Kidney Int* 1994;46:534-9.
20. Piccoli A, Nigrelli S, Caberlotto A, et al. Bivariate normal values of the bioelectrical impedance vector in adult and elderly populations. *Am J Clin Nutr* 1995;61:269-70.
21. Pillon L, Piccoli A, Lowrie EG, Lazarus JM, Chertow GM. Vector length as a proxy for the adequacy of ultrafiltration in hemodialysis. *Kidney Int* 2004;66:1266-71.
22. Di Iorio B, Scalfi L, Terracciano V, Bellizzi V. A systematic evaluation of bioelectrical impedance measurement after hemodialysis session. *Kidney Int* 2004;65:2435-40.
23. F Gnanaraj J, von Haehling S, Anker SD, Raj DS, Radhakrishnan J. The relevance of congestion in the cardio-renal syndrome. *Kidney Int* 2013;83:384-91.
24. Kalantari K, Chang JN, Ronco C, Rosner M. Assessment of intravascular volume status and volume responsiveness in critically ill patients. *Kidney Int* 2013;82:1017-28.
25. Paterna S, Di Pasquale P, Parrinello G, et al. Changes in brain natriuretic peptide levels and bioelectrical impedance measurements after treatment with high-dose furosemide and hypertonic saline solution versus high-dose furosemide alone in refractory congestive heart failure: a double-blind study. *J Am Coll Cardiol* 2005;45:1997-2003.
26. Di Somma S, De Bernardinis B, Bongiovanni C, Marino R, Ferri E, Alfei B. Use of BNP and bioimpedance to drive therapy in heart failure patients. *Congest Heart Fail* 2010;16 Suppl 1:S56-61.
27. Cockcroft DW, Gault MH. Prediction of creatinine clearance from serum creatinine. *Nephron* 1976;16:31-41.
28. Tepel M, van der Giet M, Schwarzfeld C, Laufer U, Liermann D, Zidek W. Prevention of radiographic-contrast-agent-induced reductions in renal function by acetylcysteine. *N Engl J Med* 2000;343:180-4.
29. Bioelectrical impedance analysis in body composition measurement. Proceedings of a National Institutes of Health Technology Assessment Conference. Bethesda, Maryland, December 12-14, 1994. *Am J Clin Nutr* 1996;64 Suppl:387S-532S.
30. National Kidney Foundation. K/DOQI. Clinical practice guidelines for chronic kidney disease: evaluation, classification, and stratification. *Am J Kidney Dis* 2002;39 Suppl 1:S1-266.
31. Nutritional Anemias: Report of a WHO Scientific Group. Geneva, Switzerland: World Health Organization, 1968.
32. Laskey WK, Jenkins C, Selzer F, et al. Volume-to-creatinine clearance ratio: a pharmacokinetically based risk factor for prediction of early creatinine increase after percutaneous coronary intervention. *J Am Coll Cardiol* 2007;50:584-90.
33. Mange K, Matsuura D, Cizman B, et al. Language guiding therapy: the case of dehydration versus volume depletion. *Ann Intern Med* 1997;127:848-53.
34. Solomon R, Mehran R, Natarajan MK, et al. Contrast-induced nephropathy and long-term adverse events: cause and effect? *Clin J Am Soc Nephrol* 2009;4:1162-9.
35. James MT, Ghali WA, Knudtson ML, et al. Associations between acute kidney injury and cardiovascular and renal outcomes after coronary angiography. *Circulation* 2011;123:409-16.
36. Maioli M, Toso A, Leoncini M, Gallopin M, Musilli N, Bellandi F. Persistent renal damage after contrast-induced acute kidney injury: incidence, evolution, risk factors, and prognosis. *Circulation* 2012;125:3099-107.
37. Weisbord SD, Palevsky PM. Prevention of contrast-induced nephropathy with volume expansion. *Clin J Am Soc Nephrol* 2008;3:273-80.
38. Persson PB, Hansell P, Liss P. Pathophysiology of contrast medium-induced nephropathy. *Kidney Int* 2005;68:14-22.
39. Brar SS, Shen AY, Jorgensen MB, et al. Sodium bicarbonate vs sodium chloride for the prevention of contrast medium-induced nephropathy in patients undergoing coronary angiography: a randomized trial. *JAMA* 2008;300:1038-46.

Key Words: angiography ■ contrast media ■ contrast-induced nephropathy ■ renal insufficiency.