Renal Perfusion Assessment by Renal Doppler During Fluid Challenge in Sepsis

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Objectives: To assess renal resistive index variations in response to fluid challenge.

Design: Prospective cohort study.

Setting: Three ICUs in French teaching hospitals.

Patients: Consecutive patients receiving mechanical ventilation and requiring a fluid challenge.

Intervention: Resistive index measurement before and after fluid challenge.

Measurements and Main Results: Renal Doppler was used to measure resistive index and esophageal Doppler to monitor aortic blood flow. Of the 35 included patients, 17 (49%) met our definition for fluid challenge responsiveness, that is, had at least a 10% increase in aortic blood flow. After fluid challenge, mean arterial pressure increased from 73 mm Hg (interquartile range 68–79) to 80 mm Hg (75–86; $p < 0.0001$) and stroke volume from 50 mL (30–77) to 55 mL (39–84; $p < 0.0001$). Stroke volume changes after fluid challenge were +28.6% (+18.8% to +38.8%) in fluid challenge responders and +3.1% (−1.6% to 7.4%) in fluid challenge nonresponders. Renal resistive index was unchanged after fluid challenge in both nonresponders (0.72 [0.67–0.75] before and 0.71 [0.67–0.75] after fluid challenge; $p = 0.62$) and responders (0.70 [0.65–0.75] before and 0.72 [0.68–0.74] after fluid challenge; $p = 0.11$). Stroke volume showed no correlations with resistive index changes after fluid challenge in the overall population ($r^2 = 0.04$, $p = 0.25$), in fluid challenge responders ($r^2 = -0.02$, $p = 0.61$), or in fluid challenge nonresponders ($r^2 = 0.08$, $p = 0.27$). Stroke volume did not correlate with resistive index changes after fluid challenge in the subgroups without acute kidney injury (AKIN definition), with transient acute kidney injury, or with persistent acute kidney injury.

Conclusion: Systemic hemodynamic changes induced by fluid challenge do not translate into resistive index variations in patients without acute kidney injury, with transient acute kidney injury, or with persistent acute kidney injury. (*Crit Care Med* 2013; 41:1214–1220)

Key Words: acute kidney injury; critically ill; Doppler ultrasonography; fluid responsiveness; renal resistive index

The diagnosis of acute kidney injury (AKI) is usually based on either serum creatinine elevation or oliguria (1, 2). These criteria have several limitations; however, oliguria is a nonspecific marker of AKI, and even mild serum creatinine elevation occurs only after several hours of a profound decrease in the glomerular filtration rate (3). Consequently, the identification of markers allowing the early detection of renal dysfunction or insult is a research priority (4).

Doppler-based renal resistive index (RI) measurement is rapid, noninvasive, and repeatable and may therefore hold promise for monitoring renal function or renal perfusion in critically ill patients (5). A growing body of evidence suggests that Doppler-based renal RI may be useful in critically ill patients. RI may predict AKI in patients admitted with severe sepsis (6) and may differentiate between transient and persistent AKI (7–10). In addition, repeated Doppler-based RI measurements may help in monitoring renal perfusion during gradual norepinephrine dose adjustment in patients receiving low-dose dopamine infusions or exhibiting hypoxemia (5, 11–13).

In most studies, RI was assumed to reliably reflect renal vascular resistance, based on earlier evidence (14). According to

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this assumption, higher RI is believed to correlate with higher renal resistances. However, experimental data suggest that the association between RI and pharmacologically induced changes in renal vascular resistance may be modest, even during supraphysiological increases in renal vascular resistance (15). In addition, both experimental and clinical studies have established that numerous factors in addition to vascular resistance can influence RI, including age, pulse pressure index, mean arterial pressure, arterial stiffness, renal interstitial pressure, and intra-abdominal pressure (16–18). Few studies have evaluated the influence of systemic hemodynamic variation on Doppler-based RI.

The main objective of this study was to assess the effects of a fluid challenge (FC) on Doppler-based renal RI in critically ill patients. Our secondary objective was to evaluate the influence of underlying renal dysfunction on RI changes after FC.

PATIENTS AND METHODS

Patients

The study was approved by the Institutional Review Board of the French Society for Intensive Care (SRLF, CE-SRLF 08-248), and the need for signed informed consent was waived according to French Law. A printed information sheet was, however, given to each patient's next of kin, none of whom refused participation.

We studied patients who were admitted to the three participating ICUs between January and August 2009 and who met our selection criteria. Patients receiving mechanical ventilation with real-time cardiac output monitoring were considered for inclusion if the physician in charge decided that an FC was in order. Noninclusion criteria were younger than 18 years; pregnancy; ongoing recovery from AKI; and conditions known to modify renal RI, namely suspected or confirmed obstructive renal failure, arrhythmia, and known renal artery stenosis. Another noninclusion criterion was severe chronic renal failure defined as a basal creatinine clearance value, as assessed according to Modification of Diet in Renal Disease equation (MDRD), lower than 30 $mL \cdot min^{-1}$. Patients were excluded if renal Doppler could not be performed without delaying the FC.

Study Protocol, Data Collection, and RI Measurement

Each patient under mechanical ventilation was assessed daily for inclusion and was included when FC was required. Renal sonography for RI measurement was performed before the FC (T0) and then after volemic expansion with 500 mL of normal saline (T1). The investigators who performed the RI measurements were not involved in patient care, and the physicians in charge of patient care were unaware of the RI measurement results.

FC was performed either on peripheral or on central venous access. The 500 mL of normal saline was perfused for 15–30 minutes using a pressure bag. Renal Doppler performed at T1 were performed 5–10 minutes following the end of FC.

Renal Doppler was performed by an intensivist (MD, LC, or DS) experienced in this technique. Measurements were obtained from the right kidney in most of the patients. After visualizing the kidney in gray scale and color Doppler modes, the absence of signs of chronic renal damage was checked. An interlobar or arcuate artery was then selected and measurements obtained using pulse-wave Doppler. The Doppler gain was set in order to obtain a clear outline of flow waves with minimal background noise. The Doppler spectrum was considered optimal when at least three similar consecutive waveforms were visualized. RI was calculated as (peak systolic velocity – end-diastolic velocity)/peak systolic velocity. Three to five measurements were performed and averaged to obtain the mean RI value.

The following clinical variables were collected before and after the FC: heart rate; systolic, diastolic, and mean blood pressures; respiratory variations in pulse pressure (19); urine output; respiratory rate; tidal volume; positive end-expiratory pressure; inspired fraction of oxygen; plateau pressure; Ramsay sedation score (20); and type and dose of sedative and vasoactive drugs infused. Aortic blood flow is routinely monitored in our ICU using an esophageal Doppler probe (CardioQ, Deltex Medical Ltd, Chichester, UK). For each study patient, aortic blood flow variations in response to FC were collected.

Definitions

For each patient, the presence of AKI was evaluated at the time of inclusion, that is, at the time of the first RI measurement (T0). AKI was defined according to the Acute Kidney Injury Network classification scheme (2) either as an increase in serum creatinine by greater than or equal to 26.4 μmol/L (0.3 mg/dL) or by greater than or equal to 150% from baseline or as urine output less than 0.5 mL/kg/hr for 6 hours or more. The lowest serum creatinine value in the 3 months preceding inclusion was taken as the baseline value. If no plasma creatinine was available, the lowest serum creatinine value during ICU stay (i.e., after renal recovery) was used to assess underlying renal function. When no such value was available, the baseline value was estimated using the MDRD formula (1). Transient AKI was defined as AKI with a cause of renal hypoperfusion and recovery within the first 3 days following inclusion. Recovery was defined as urine output normalization (in the absence of diuretic treatment) and/or an at least 50% serum creatinine decrease and/or serum creatinine normalization (7, 21). Persistent AKI was defined as persistent oliguria and/or serum creatinine elevation after 3 days.

FC responsiveness was evaluated after volume expansion with 500 mL of normal saline (22). Patients were classified as FC responders if their aortic blood flow was at least 10% higher at T1 compared with T0 (23).

The Sequential Organ Failure Assessment score (24) was calculated at study inclusion and the Knaus scale score at ICU admission (25). Sepsis was diagnosed using the criteria developed at the American College of Chest Physicians/Society of Critical Care Medicine consensus conferences (26).

Statistical Analysis

Results are reported as medians and interquartile range (IQR) or numbers and percentages (%). Categorical variables were compared using Fisher exact test and continuous variables

using the nonparametric Wilcoxon test or the Mann-Whitney test for pairwise comparisons or the Friedman test for comparisons across the three groups.

Precision of the RI measurements was evaluated by evaluating the more different RI measurements of three to five performed and averaged to obtain the mean RI value at T0 and T1. Differences between RI measurements were compared with Bland and Altman plots to evaluate the mean difference ± 2 SDs between the two measures with the greatest differences (*Y* axis) relative to the average of the measurements (*X* axis). Finally, the coefficient of variation was computed.

Based on previous findings (7), sample size was estimated as follows. Assuming an RI of 0.77 in the overall patient population and a standard deviation of 0.07, and using a two-sided test with 0.05 type I error and 0.2 type II error, we needed 15 patients per group to detect a 10% absolute difference in RI between FC responders and FC nonresponders.

All tests were two-sided, and p values less than 0.05 were considered statistically significant. Statistical tests were performed using the SAS 6.12 software package (SAS Institute, Cary, NC).

RESULTS

Study Population

During the study period, 35 mechanically ventilated patients were included and underwent Doppler sonography. **Table 1** reports their main characteristics. All 35 patients were receiving continuous intravenous sedation with midazolam and fentanyl and were under assisted controlled ventilation. Main settings of MV are reported in Table 1. Median Ramsay score was 5 (4–6). Most patients (94%) were admitted for medical conditions, among which the most common was severe sepsis or septic shock (n = 30, 86%). None of the included patients had suspected intra-abdominal hypertension.

According to our definitions, 17 (49%) patients were FC responders; 9 (26%) patients had no AKI, 13 (37%) had transient AKI, and 13 (37%) had persistent AKI. At the time of the study, no patient was receiving renal replacement therapy. During the ICU stay, renal replacement therapy was eventually required for 10 of the 13 patients with persistent AKI and four of the 13 patients with transient AKI.

Thirty patients were receiving vasopressors (norepinephrine in every of them) at study inclusion.

Response to FC

Table 1 reports the main characteristics of FC responders and nonresponders. In the FC responder group, need for vasoactive agents was more common than in the FC nonresponder group. Respiratory variability of pulse pressure was greater in FC responders (20% [15–27] vs. 10 [7–15]; $p = 0.001$).

Overall, after FC, mean arterial pressure increased from 73 mm Hg (68–79) to 80 mm Hg (75–86; $p < 0.0001$), stroke volume increased from 50 mL (30–77) to 55 mL (39–84; $p < 0.0001$), and heart rate decreased from 115 bpm (95–128) to 112 bpm (92–122; $p = 0.01$).

Stroke volume changes after FC were +28.6% (+18.8 to +38.8%) in FC responders and +3.1% (–1.6% to 7.4%) in FC nonresponders.

In FC nonresponders, FC was not followed by significant changes in heart rate (114 bpm [95–128] vs. 115 bpm [100–127]; $p = 0.14$) or stroke volume (55 mL [30–81] vs. 47 mL [28–83]; $p = 0.16$). However, mean arterial pressure increased significantly in FC nonresponders from 74 mm Hg (68–79) to 80 mm Hg (76–87; $p = 0.01$).

Precision of RI Measurement

RI was obtained from every patient as the mean of three consecutive measures. When comparing the most different RI values at each time, these values were strongly correlated ($r^2 = 0.91$; $p < 0.0001$). When comparing these values, bias, as illustrated by the mean difference in the Bland and Altman analysis, was negligible (–0.002). The 95% confidence interval of these differences in the Bland–Altman graphs were +0.078 and –0.082. Finally, coefficient of variation of the more different RI measurements was 7.6%.

Influence of Vasopressors on RI

In this study, RI was similar in patients with and without vasopressors at study inclusion (T0 RI 0.70 [0.66–0.75] vs. 0.720 [0.71–0.82], respectively; $p = 0.16$). In addition, no correlation was found between vasopressors dose and T0 RI ($r^2 = 0.11$; $p = 0.34$).

Changes in Doppler-Based Renal RI After FC

Doppler-based renal RI was not significantly different between FC nonresponders and FC responders (0.72 [0.67–0.75] and 0.70 [0.65–0.75], respectively; $p = 0.35$).

Doppler-based renal RI was not significantly changed by FC in nonresponders (0.72 [0.67–0.75] before and 0.71 [0.67–0.75] after FC; $p = 0.62$] or responders (0.70 [0.65–0.75] before and 0.72 [0.68–0.74] after FC; $p = 0.11$; **Fig. 1**). In addition, changes in Doppler-based RI were not different between these two patient groups (–4.4% [–6.4 to +7.1] in nonresponders vs. +2.2 [–0.9 to +4.9]; $p = 0.08$). Stroke volume was not correlated with RI changes after FC (**Fig. 2**) in the overall population ($r^2 = 0.04$, $p = 0.25$), FC responders ($r^2 = –0.02$, $p = 0.61$), or FC nonresponders ($r^2 = 0.08$, $p = 0.27$).

Doppler-based RI before FC was higher in patients with AKI at inclusion (0.72 [0.69–0.76] vs. 0.66 [0.65–0.70]; $p = 0.05$; **Fig. 3**). **Table 2** reports the hemodynamic and RI changes after FC in the groups with no AKI, transient AKI, and persistent AKI. No significant RI changes were observed after FC in any of these three groups. Stroke volume changes were not correlated with RI changes in patients with or without AKI (**Fig. 4**). Neither did changes in mean arterial pressure correlate with changes in RI ($r^2 = –0.01$; $p = 0.47$).

Finally, in this study, RI was similar in patients with and without vasopressors at study inclusion (T0 RI 0.70 [0.66–0.75] vs. 0.720 [0.71–0.82], respectively; $p = 0.16$). In addition, no correlation was found between vasopressor dose and T0 RI ($r^2 = 0.11$; $p = 0.34$).

TABLE 1. Characteristics of Patients According to Their Response to Fluid Challenge

	All patients, *n* = 35	Nonresponders to FC, *n* = 17	Responders to FC, *n* = 18	*p*
Male gender	18 (51%)	10 (55%)	8 (47%)	0.61
Age (y)	59 (43–73)	64 (52–73)	52 (42–73)	0.31
Body mass index (kg/m²)	26 (22–27)	26 (20–30)	25 (24-26)	0.76
Knaus C or D (24)	17 (49%)	11 (61%)	6 (33%)	0.23
Simplified Acute Physiology Score II score at ICU admission (27)	55 (41–72)	67 (49–72)	45 (34–69)	0.06
Sequential Organ Failure Assessment score at ICU admission (24)	11 (7–14)	14 (10–17)	7 (7–12)	0.07
Risk factors for AKI				
Moderate chronic kidney disease[a]	3 (9%)	2 (11%)	1 (6%)	0.58
Sepsis at ICU admission	30 (86%)	17 (94%)	13 (76%)	0.13
History of hypertension	13 (37%)	6 (33%)	7 (41%)	0.20
Diabetes	21 (60%)	14 (77%)	7 (41%)	0.47
Characteristics at inclusion				
Sao_2 (%)	100 (99–100)	100 (100–100)	100 (98–100)	0.84
Body temperature (°C)	37.8 (37.0–39.0)	37.9 (36.9–39.1)	37.3 (37.0–38.8)	0.73
Pulse pressure variation (%)	15 (10–20)	10 (7–15)	20 (15–27)	0.001
AKI	25 (71%)	14 (79%)	11 (64%)	0.73
Treatments at inclusion				
Need for vasopressors	30 (86%)	13 (72%)	17 (100%)	0.01
Vasopressors dose ($mg \cdot h^{-1}$)	1.7 (0.7–3.4)	1.8 (1.8–9)	5.0 (3.0–7.0)	0.64
Tidal volume (mL/kg predicted body weight)	6.6 (5.9–7.1)	6.3 (5.4–7.3)	6.9 (6.3–7.3)	0.32
Positive end-expiratory pressure level (cm H_2O)	5.0 (3.0–8)	5.0 (5.0–8.0)	5.5 (3.0–7.0)	0.13
Fio_2	0.5 (0.4–0.6)	0.5 (0.4–0.7)	0.5 (0.4–0.6)	0.18
Characteristics before FC (T0)				
Mean arterial pressure (mm Hg)	73 (68–79)	74 (68–79)	73 (67–78)	0.56
Heart rate (bpm)	115 (95–128)	115 (100–127)	120 (95–134)	0.94
Stroke volume (mL)	50 (30–77)	47 (28–83)	50 (32–66)	0.35
Resistive index	0.71 (0.66–0.75)	0.72 (0.67–0.75)	0.70 (0.65–0.75)	0.35
Characteristics after FC (T1)				
Mean arterial pressure (mm Hg)	80 (75–86)	80 (76–87)	80 (74–86)	0.84
Heart rate (bpm)	112 (92–122)	114 (95–128)	110 (89–120)	0.08
Stroke volume (mL)	55 (39–84)	55 (30–81)	70 (40–85)	0.97
Resistive index	0.71 (0.67–0.75)	0.71 (0.67–0.75)	0.72 (0.68–0.74)	0.81
Resistive index changes (%)	−0.5 (−5.4 to +6.2)	−4.4 (−6.4 to +7.1)	+2.2 (−0.9 to +4.9)	0.08
Stroke volume changes (%)	12.7 (3.1–28.6)	3.1 (-1.6 - +7.4)	28.6 (18.8–38.8)	<0.0001

AKI = acute kidney injury; FC = fluid challenge; Fio_2, fraction of inspired oxygen.

[a]Chronic kidney disease was defined as creatinine clearance before ICU admission of 30–60 $mL \cdot min^{-1}$.

Data are median (interquartile range). Resistive index was calculated as ([peak systolic velocity – end-diastolic velocity]/peak systolic velocity).

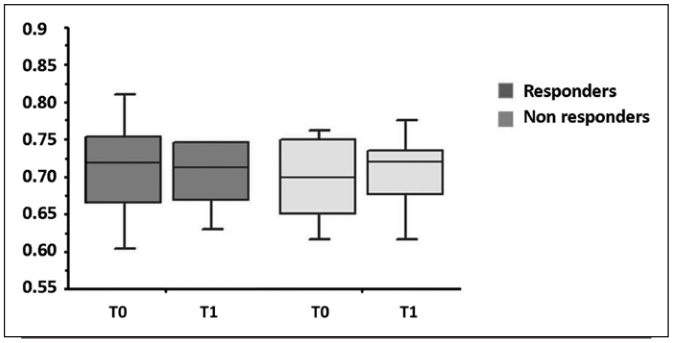

Figure 1. Boxplot showing the resistive index (RI) before and after fluid challenge (FC) in FC responders (*dark gray*) and nonresponders (*light gray*). The Doppler-based renal RI was not modified by the FC in nonresponders (0.72 [0.67–0.75] before and 0.71 [0.67–0.75] after FC, $p = 0.62$) or responders (0.70 [0.65–0.75] before and 0.72 [0.68–0.74] after FC, $p = 0.11$).

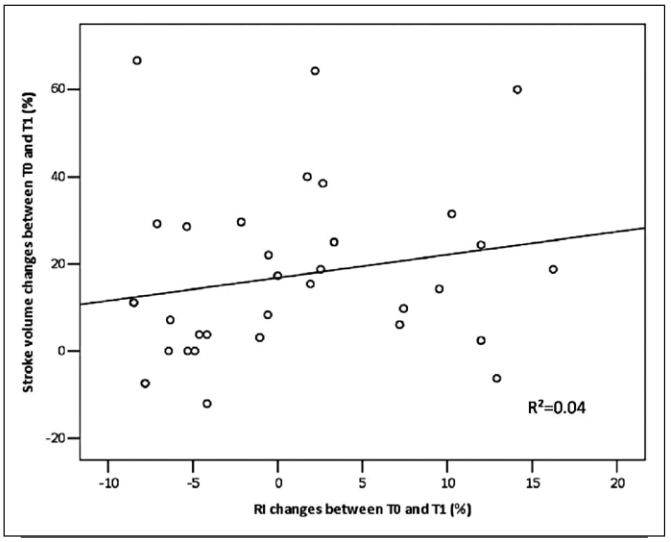

Figure 2. Scatterplot of the relationship between changes in stroke volume before (T0) and after (T1) fluid challenge (FC) and changes in renal resistive index (RI). Stroke volume was not correlated with RI changes after FC ($r^2 = 0.04$, $p = 0.25$).

DISCUSSION

Our study demonstrates that significant changes in stroke volume, mean arterial pressure, or heart rate do not translate into significant changes in Doppler-based renal RI. Although RI was higher in patients with AKI, the impact of systemic hemodynamic changes on RI was similar in patients with no AKI, transient AKI, or persistent AKI. Finally, in keeping with previous findings, RI was not modified in our study by norepinephrine use or dose in our study.

The main finding from our study was that significant hemodynamic variations induced by FC did not translate into significant changes in renal RI as measured using Doppler sonography. This finding reflects the ability of numerous confounding factors to influence RI, thereby limiting potential RI variations in response to systemic hemodynamic changes. Doppler-based renal RI measurement has been proposed for evaluating renal

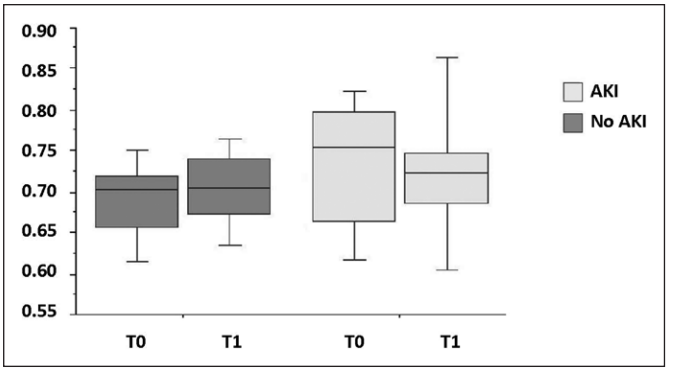

Figure 3. Boxplot of the renal resistive index (RI) before and after fluid challenge (FC) according to renal function. The *light gray boxplots* represent patients with acute kidney injury (AKI) and the *dark gray boxplots* patients without AKI. After FC, the Doppler-based renal RI was modified neither in the nonresponders (0.72 [0.67–0.75] before and 0.71 [0.67–0.75] after FC; $p = 0.62$) nor in the responders (0.70 [0.65–0.75] before and 0.72 [0.68–0.74] after FC; $p = 0.11$).

perfusion in critically ill patients (5, 11, 12). Two recent ICU studies evaluated the effect of low-dose dopamine on renal perfusion (12) and the influence of gradual changes in mean arterial pressure on RI in patients receiving norepinephrine (11), respectively. These studies gave important information regarding influence of dopamine and norepinephrine on renal perfusion assessed by RI. Indeed, according to these studies, norepinephrine was not associated with deleterious effects conversely to renal-dose dopamine in patients with AKI (11, 12). In keeping with these findings, we were unable to detect any deleterious effect of norepinephrine or norepinephrine use on Doppler-based RI in this study. In these studies, RI was assumed to faithfully reflect renal vascular resistance (15, 17). In experimental studies, however, the association between Doppler-based RI and renal vascular resistance was weak. Thus, large, nonphysiological, pharmacologically induced changes in renal vascular resistance translated into only small RI changes (0.047 IU ± 0.008 per logarithmic increase in renal vascular resistance) (15). In addition, several intrarenal or systemic hemodynamic factors have been demonstrated to influence both RI and the association between RI and renal vascular resistance. Thus, in several studies, arterial stiffness (vascular compliance) was a major determinant of RI (15–17). In addition, the relationship between vascular resistance and RI became weaker as arterial stiffness increased (17). Additionally, increases in interstitial or intra-abdominal pressure reduce the transmural pressure of renal arterioles, thereby diminishing arterial distension, decreasing vascular compliance, and ultimately increasing RI (16). Finally, several hemodynamic factors including pulse pressure index, mean arterial pressure, and heart rate have direct and dramatic effects on RI values (6, 7, 13, 15, 17). Each of these factors may act as a confounder. Our study further underlines that these factors must be taken into account if RI is to be adequately interpreted in clinical setting.

Conversely to our findings, previous studies demonstrated that hemodynamic changes induced by norepinephrine dose variations or by renal-dose dopamine therapy significantly influenced RI (11, 12). In a recent study, changes in norepinephrine doses that induced large variations in mean

TABLE 2. Response to Fluid Challenge and Resistance Index Variations According to Renal Status

	No AKI, *n* = 9	Transient AKI, *n* = 13	Persistent AKI, *n* = 13	*p*
Characteristics before FC (T0)				
Mean arterial pressure (mm Hg)	77 (73–81)	77 (73–81)	68 (64–78)	0.09
Heart rate (bpm)	115 (95–122)	113 (92–133)	120 (99–127)	0.89
Stroke volume (mL)	54 (41–69)	39 (27–64)	41 (27–102)	0.51
Resistive index	0.66 (0.65–0.70)	0.71 (0.70–0.73)	0.76 (0.67–0.80)	0.06
Characteristics after FC (T1)				
Mean arterial pressure (mm Hg)	80 (80–84)	81 (77–87)	76 (70–83)	0.24
Heart rate (bpm)	112 (90–122)	110 (90–130)	120 (94–122)	0.94
Stroke volume (mL)	70 (50–87)	45 (30–72)	45 (28–104)	0.39
Resistive index	0.69 (0.67–0.75)	0.71 (0.66–0.73)	0.72 (0.69–0.75)	0.72
Resistive index changes (%)	+3.3 (−2.7 to +12.0)	0.0 (−4.2 to +2.3)	−5.3 (−6.8 to +7.2)	0.15
Stroke volume changes (%)	24.4 (15.0–29.3)	15.3 (+7.2 – +28.3)	6.1 (0.0–17.9)	0.19
Responders to FC	7 (78%)	7 (54%)	3 (23%)	0.29

FC = fluid challenge; AKI = acute kidney injury.

arterial pressure (65–75 mm Hg) translated into RI variations (0.75 ± 0.07 vs. 0.71 ± 0.06) (11). Similarly, a randomized, cross-over study showed that renal-dose dopamine, although not associated with systemic hemodynamic changes, induced significant RI decreases in patients without AKI (0.70 vs. 0.65) or increases in patients with AKI (0.77–0.81) (12). These RI changes, although statistically significant, were within the limits of agreement of Doppler-based renal RI (13). In addition, there was no clear link between renal function improvement and lower RI in these studies (11, 12). Another factor that may have limited the influence of hemodynamic changes on RI in our study pertains to the study population. As demonstrated in a previous study, higher norepinephrine doses designed to increase the mean arterial pressure above 75 mm Hg may induce a renal RI increase that may indicate a deleterious effect of norepinephrine on renal perfusion (11). In our population, most of the patients received vasopressors, and half of the patients had mean arterial pressure values higher than 73 mm Hg. The effect of high-dose vasopressors on renal perfusion regulation is unknown but may explain the absence of associations between hemodynamic changes and RI.

Despite the large body of evidence demonstrating that established AKI is associated with impaired renal perfusion regulation, RI variations in our patients with AKI were not significantly different from those in the patients without AKI. This may indicate that the absence of RI changes in our study was unrelated to effects of AKI on renal perfusion regulation. In accordance with previous studies, RI was higher in our patients with AKI and more specifically in those with persistent AKI (7–10). Our study was not designed to assess the performance of RI for diagnosing persistent AKI. However, in contrast to previous studies in this field (7–10), there was marked overlap in RI values among the persistent AKI, transient AKI, and no AKI groups. The previously cited studies were performed, however, in selected patient populations, and differences in study populations between previous studies (7–10) and our study may explain this overlap. Additional studies are needed to evaluate the performance of Doppler-based renal RI in distinguishing between persistent AKI and transient AKI.

Our study has several limitations. First, true blinding to the clinical condition of the patient at the time of RI measurement was almost impossible. However, to minimize possible bias, the investigator who performed the Doppler measurements had no role in patient care or in recording the hemodynamic variables. Second, our sample size was small, which may have limited our ability to detect statistically significant changes in RI produced by hemodynamic changes. However, our study was powered to detect clinically significant changes in RI (i.e., changes greater than the range of uncertainty with Doppler RI measurement). Finally, our study was not designed to evaluate the influence of confounding factors, such as age or abnormal arterial stiffness, which may have affected RI. Larger studies are therefore needed to allow adjustment for these confounding factors.

In summary, we found that systemic hemodynamic changes induced by FC did not translate into RI variations. This finding may reflect either abnormal renal perfusion regulation in critically ill patients or an inability of renal Doppler to detect changes in renal perfusion after a single FC bolus. Further studies are needed to evaluate factors that may influence RI, with the goal of adequately interpreting RI changes in critically ill patients.

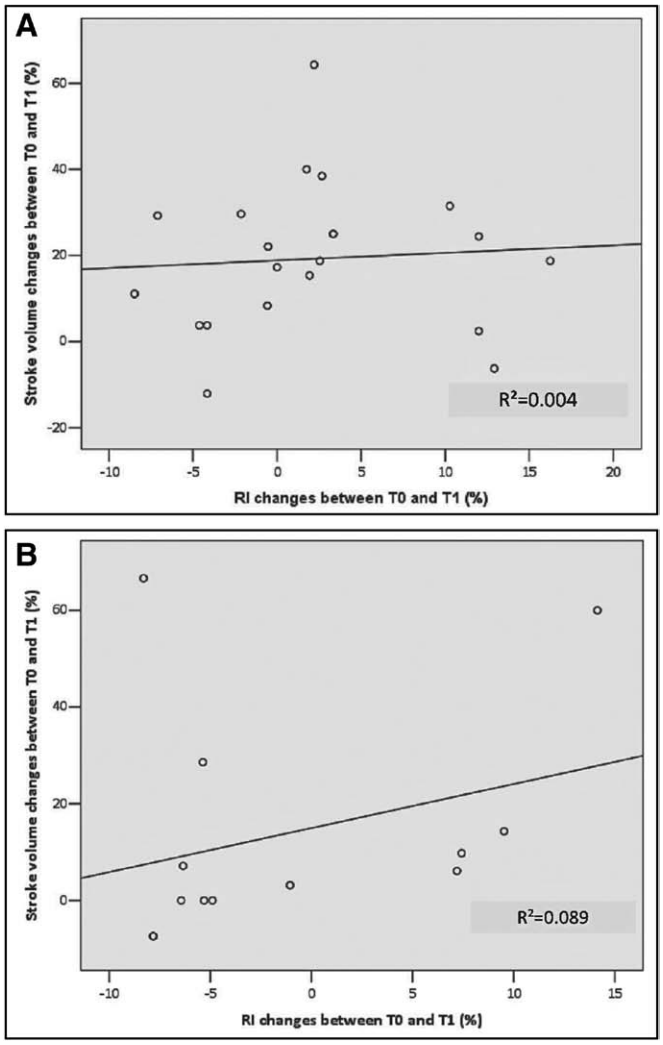

Figure 4. **A**, Scatterplot of the relationship between stroke volume changes before (T0) and after (T1) fluid challenge (FC) and resistive index (RI) changes in patients without acute kidney injury (AKI). Stroke volume was not correlated with RI changes after FC ($r^2 = 0.005$, $p = 0.95$). **B**, Scatterplot of the relationship between stroke volume changes before (T0) and after (T1) FC and RI changes in patients with AKI. Again stroke volume was not correlated with RI changes after FC ($r^2 = 0.09$, $p = 0.44$).

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