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Chapter 3

Randomised trial of no hydration vs. sodium bicarbonate hydration in patients with chronic kidney disease undergoing acute computed tomography-pulmonary angiography

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ABSTRACT

Background
Hydration to prevent contrast induced-acute kidney injury (CI-AKI) induces a diagnostic delay when performing CT-pulmonary angiography (CTPA) in patients suspected of acute pulmonary embolism (PE).

Aim
To analyze whether withholding hydration is non-inferior to sodium bicarbonate hydration prior to CTPA in patients with chronic kidney disease (CKD).

Methods
We performed an open-label multicenter randomized trial between 2009 and 2013. 139 CKD patients were randomized of whom 138 were included in the intention-to-treat population; 67 randomized to withholding hydration and 71 to one-hour 250ml 1.4% sodium bicarbonate hydration prior to CTPA. Primary outcome was the increase in serum creatinine 48-96 hours post CTPA. Secondary outcomes were the incidence of CI-AKI (creatinine increase >25% >/=0.5mg/dl), recovery of renal function, and the need for dialysis within two months post CTPA. Withholding hydration was considered non-inferior if the mean relative creatinine increase was ≤15% compared with sodium bicarbonate.

Results
Mean relative creatinine increase was -0.14% (IQR-15.1 to 12.0%) for withholding hydration and -0.32%(IQR-9.7 to 10.1%) for sodium bicarbonate(mean difference 0.19%, 95%CI -5.88 to 6.25%, p-value non-inferiority <0.001). CI-AKI occurred in 11 patients (8.1%); 6 (9.2%) randomized to withholding hydration and 5 (7.1%) to sodium bicarbonate (relative risk 1.29, 95%CI 0.41-4.03). Renal function recovered in 80.0% of CI-AKI patients within each group (relative risk 1.00, 95%CI 0.54-1.86). None of the CI-AKI patients developed a need for dialysis.

Conclusion
Our results suggest that preventive hydration could be safely withheld in CKD patients undergoing CTPA for suspected acute PE. This will facilitate management of these patients and prevents delay in diagnosis as well as unnecessary start of anticoagulant treatment while receiving volume expansion.
INTRODUCTION

Diagnostic work-up of patients at high clinical suspicion of acute pulmonary embolism (PE) requires performance of computed tomography pulmonary angiography (CTPA) \[1,2\]. CTPA necessitates intravenous administration of iodinated contrast media, which imposes a 4-14% risk of contrast induced-acute kidney injury (CI-AKI)\[3-5\]. Utilization of CI-AKI preventative methods, such as peri-procedural hydration, are recommended for patients with pre-existing chronic kidney disease (CKD), who are at high risk to develop CI-AKI\[6-11\].

However, peri-procedural hydration regimes require one to twelve hours of hydration prior to contrast administration with an additional six to twelve hours afterwards\[10,12\]. CI-AKI preventive hydration therefore induces a significant diagnostic delay in CKD patients clinically suspected of acute PE undergoing CTPA. Notably, essential information regarding the need and type of CI-AKI preventative strategies in patients undergoing emergent contrast procedures is still missing in current literature. Additionally, at this time, it is unknown whether hydration after contrast administration has an additive effect over solely pre-procedural hydration in the prevention of CI-AKI. Consequently, guidelines make no recommendations for the use of CI-AKI preventative hydration regimes in CKD patients undergoing emergent contrast procedures\[6,12\], other than to start volume expansion as early as possible\[10\]. A novel one-hour 250 ml 1.4% sodium bicarbonate infusion prior to intravenous contrast enhanced-computed tomography can be used safely in patients with CKD without the need for hydration afterwards, as demonstrated by a previous randomized study\[13\]. The volume expansion of this short sodium bicarbonate regime prevents dehydration at time of contrast administration. Additionally, sodium bicarbonate alkalinizes urine, theoretically providing an additional protective effect\[14-16\]. Although this novel sodium bicarbonate regime already deals with some of the logistic difficulties associated with CI-AKI preventive hydration at an emergency department, it still induces a diagnostic delay. We therefore evaluated whether sodium bicarbonate hydration can be safely withheld in CKD patients clinically suspected of acute PE undergoing CTPA.

METHODS

We performed a randomized, non-inferiority trial in the Netherlands in one academic and three non-academic teaching hospitals. Patients were enrolled 24 hours a day, 7 days a week. In- and outpatients with high clinical suspicion of acute PE requiring CTPA were eligible for inclusion (i.e. Wells score $\geq 4$ or D-Dimer levels >500 ng/ml). All patients were at least 18 years old and had CKD (eGFR $< 60$ ml/min/1.73m$^2$ estimated by the Modifica-
tion of Diet in Renal Disease formula[17]). Exclusion criteria were pregnancy; previous contrast administration within the last seven days; documented allergy for iodinated contrast media; and hemodynamic instability (systolic blood pressure <100mmHg). Patients were only allowed to participate once in the trial. Study patients provided written informed consent before randomization. The trial protocol was approved by the Institutional Review Boards of each of the participating hospitals. An independent data and safety monitoring board periodically reviewed study outcomes. The trial complied with good clinical practice guidelines and the Declaration of Helsinki (2004), and was registered with the Netherlands Trial Register, NTR 1958.

**Randomization**

Patients were randomized using a computer-generated allocation sequence to either withholding hydration, or 250 ml intravenous 1.4% sodium bicarbonate one hour prior to CTPA without hydration post CTPA. Randomization was stratified by hospital of inclusion, and by renal function (eGFR 0-19, 20-39 or 40-59 ml/min/1.73m²), and diabetes mellitus, both major risk factors for CI-AKI[10,18]. The study had an open-label design.

**Procedures**

Contrast volumes used were registered and depended on CTPA protocol and body mass. The type of contrast media used for CTPA was according to hospital guidelines. Three hospitals used low-osmolar contrast media (Iopromide (Ultravist, Bayer Healthcare Pharmaceuticals, Leverkusen, Germany), Iobitridol (Xenetix, Guerbet, Aulnay-sous-Bois, France)) whereas the fourth center used an iso-osmolar contrast agent in all patients (Iodixanol (Visipaque, GE Healthcare, Chalfort St. Giles, United Kingdom)). No other CI-AKI preventive treatments were used, such as oral hydration or the administration of N-acetylcysteine. However, if a patient developed an indication for intravenous volume expansion other than the prevention of CI-AKI, the use of additional infusions were allowed and registered in a case report form. Serum and urine samples were collected prior to hydration and once between 48-96 hours post CTPA. Urine samples were also obtained at 2 hours post CTPA in order to determine whether sodium bicarbonate hydration had increased urinary pH levels compared with baseline[19]. Serum sampling was repeated two months post CTPA in patients diagnosed with CI-AKI (i.e. an increase in serum creatinine >25% or >44 µmol/L (0.5 mg/dL) at 48-96 hours post CTPA compared with baseline[10]). Samples were analyzed for serum creatinine values centrally in the laboratory of the Leiden University Medical Center using Roche Diagnostics analyzers (Mannheim, Germany) after trial completion. The presence of other risk factors of CI-AKI as stated by the European Society of Urogenital Radiology (ESUR) guideline was recorded for each patient (i.e. diabetes mellitus, congestive heart failure New York Heart Association grade 3-4, age over 70 years, gram of iodine dose over 3.7 times baseline...
eGFR value, anaemia, and the use of nephrotoxic medication e.g. non-steroid anti-inflammatory drugs)[10].

Outcomes
Primary outcome was the relative serum creatinine increase measured between 48-96 hours post CTPA compared with baseline. Secondary outcomes were the incidence of CI-AKI (defined as stated above); recovery of renal function in CI-AKI patients (recovery defined as an increase in serum creatinine < 25% or < 44µmol/L (0.5 mg/dL) measured at two months post CTPA compared with baseline)[20,21]; and the need for dialysis.

Statistical analyses
The trial was designed for non-inferiority. As a low relative serum creatinine increase in the sodium bicarbonate group was expected[22], withholding hydration prior to CTPA was considered non-inferior if the mean relative serum creatinine increase in this group was not more than 15% higher compared with the increase in the sodium bicarbonate group (in absolute terms). The power calculation was based on this criterion, and the assumption that the actual difference between both groups would be 5% with a standard deviation of 35%, based on a previous study on CI-AKI post CTPA[3]. This calculation indicated inclusion of 120 patients per treatment arm to be sufficient (β=0.2, α=0.05). However, inclusion rates were lower than expected and a report for the Data Safety Monitoring Board made in June 2009 demonstrated a standard deviation of 20.4% in our population, which was considerably lower than the expected 35%. The sample size for our study was therefore reduced to 64 patients per treatment arm, under the same assumptions but with the lower standard deviation. Assuming 10% of patients to be lost to follow-up, we calculated a total sample size of 140 patients.

The study was analyzed blinded on an intention-to-treat basis. Serum creatinine values of patients in whom CTPA was cancelled but in whom these variables were available were included in the study analysis. Differences in the mean relative serum creatinine increase and urinary pH levels between randomization groups were analyzed using an independent samples T-Test with corresponding 95% confidence intervals or p-values. For the primary outcome a one-sided p-value of non-inferiority was calculated under null hypothesis of equivalence. Cumulative incidences of CI-AKI, recovery of renal function, and the need for dialysis were reported and tested for statistical differences between both groups using relative risk ratios of the cumulative incidences (RR). Subgroup analyses were performed for the primary endpoint in high risk patients (i.e. eGFR < 30 ml/min/1.73m2, diabetes mellitus, age > 75 years). To test for differential treatment effects across subgroups, interaction terms between subgroup and treatment were added to the logistic and linear regressions. No corrections were made for multiple comparisons. Additionally, we performed a sensitivity analysis on the primary outcome and the risk
of CI-AKI comparing the two randomization arms restricted to patients with an eGFR < 45 ml/min/1.73m², as the ESUR guideline regards these patients as high risk of CI-AKI when undergoing intravenous contrast enhanced-computed tomography (Appendix 1). All calculations were performed using SPSS version 20.0 (IBM Corp, Armonk, New York).

RESULTS

Between November 2009 and June 2013, 139 patients provided written informed consent and were randomized. One patient withdrew consent after randomization, leaving 138 patients available for the intention-to-treat analysis: 67 patients randomized to withholding hydration and 71 to sodium bicarbonate hydration prior to CTPA (Figure 1). Protocol violation occurred in nine patients within the intention-to-treat population of whom three were randomized to the withholding hydration group. Two of them received 0.9% saline hydration prior to CTPA (1300 and 1000 ml, respectively) and the other patient randomized to withholding hydration received 1.4% sodium bicarbonate hydration 500 ml prior to and 250 ml after CTPA. Four of the six patients in the sodium bicarbonate arm in whom protocol violation occurred received 0.9% saline hydration prior to CTPA (volumes of 250, 500, 1000 and 2000 ml, respectively). The fifth patient received 500 instead of 250 ml bicarbonate hydration prior to CTPA and the last patient in whom protocol violation occurred received bicarbonate hydration also post CTPA.

Figure 1. Flow chart
All other patients received the study mandated randomized treatment. Two patients developed an indication for the use of intravenous volume expansion other than the prevention of CI-AKI; one in each randomization arm. Both patients received 0.9% saline with volumes of 200 and 3300 ml, respectively.

Patient and procedure characteristics at baseline were well balanced between the treatment groups (Table 1). In total, 52 (37.7%) patients within the intention-to-treat population had a baseline eGFR < 45 ml/min/1.73m2. Of the 86 patients with a baseline eGFR > 45 ml/min/1.73m2, 28 (32.6%) had two or more other risk factor for CI-AKI.

Table 1. Patient characteristics at baseline

<table>
<thead>
<tr>
<th></th>
<th>Withholding hydration (N=67)</th>
<th>Sodium bicarbonate (N=71)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, years</td>
<td>70.0 (12.4)</td>
<td>71.1 (13.3)</td>
</tr>
<tr>
<td>Sex, male</td>
<td>35 (52.2)</td>
<td>34 (47.9)</td>
</tr>
<tr>
<td>BMI, kg/m2</td>
<td>27.8 (6.8)</td>
<td>30.4 (18.8)</td>
</tr>
<tr>
<td>Outpatients</td>
<td>53 (79.1)</td>
<td>56 (78.9)</td>
</tr>
<tr>
<td>eGFR</td>
<td>50.2 (15.5)</td>
<td>48.2 (15.4)</td>
</tr>
<tr>
<td>eGFR &gt; 45 ml/min</td>
<td>45 (64.2)</td>
<td>43 (60.6)</td>
</tr>
<tr>
<td>eGFR 30-45 ml/min</td>
<td>16 (23.9)</td>
<td>20 (28.2)</td>
</tr>
<tr>
<td>eGFR 15-30 ml/min</td>
<td>8 (11.9)</td>
<td>6 (8.5)</td>
</tr>
<tr>
<td>eGFR &lt; 15 ml/min</td>
<td>0 (0.0)</td>
<td>2 (2.8)</td>
</tr>
<tr>
<td>Systolic blood pressure (mmHg)</td>
<td>142.6 (22.6)</td>
<td>139.7 (18.4)</td>
</tr>
<tr>
<td>Diastolic blood pressure (mmHg)</td>
<td>78.4 (14.8)</td>
<td>79.5 (14.7)</td>
</tr>
<tr>
<td>Diabetes mellitus</td>
<td>10 (14.9)</td>
<td>13 (18.3)</td>
</tr>
<tr>
<td>Peripheral arterial disease</td>
<td>7 (10.9)</td>
<td>7 (10.3)</td>
</tr>
<tr>
<td>Coronary artery disease</td>
<td>16 (25.0)</td>
<td>13 (19.1)</td>
</tr>
<tr>
<td>Congestive heart failure</td>
<td>6 (9.0)</td>
<td>5 (7.0)</td>
</tr>
<tr>
<td>Primary renal or urological disease</td>
<td>23 (35.9)</td>
<td>24 (35.3)</td>
</tr>
<tr>
<td>Anaemia*</td>
<td>27 (40.3)</td>
<td>31 (43.7)</td>
</tr>
<tr>
<td>Medication</td>
<td></td>
<td></td>
</tr>
<tr>
<td>NSAIDS**</td>
<td>5 (7.8)</td>
<td>3 (4.4)</td>
</tr>
<tr>
<td>Diuretics</td>
<td>33 (51.6)</td>
<td>31 (45.6)</td>
</tr>
<tr>
<td>ACE-inhibitors</td>
<td>22 (34.4)</td>
<td>17 (25.0)</td>
</tr>
<tr>
<td>Angiotensin II receptor blockers</td>
<td>12 (18.8)</td>
<td>12 (17.6)</td>
</tr>
<tr>
<td>Contrast volume in mL</td>
<td>74.5 (10.3)</td>
<td>73.5 (8.1)</td>
</tr>
<tr>
<td>Iodine dose in grams</td>
<td>24.9 (3.8)</td>
<td>24.7 (3.1)</td>
</tr>
<tr>
<td>Median time in hours between CTPA and creatinine measurements (IQR)</td>
<td>72.0 (53.8-96.0)</td>
<td>72.0 (57.0-85.0)</td>
</tr>
</tbody>
</table>

Data are mean (SD), n (%) unless stated otherwise

eGFR = estimated glomerular filtration rate. BMI = body mass index. CKD = chronic kidney disease. CTPA = computed tomography pulmonary angiography. IQR = interquartile range.

* defined as Hb < 7.4 mmol/L if female and Hb < 8.1 mmol/L if male  ** Non-steroid anti-inflammatory drugs
Patient outcome
The primary outcome was assessed in 97.8% (135/138) of patients. One of three patients in whom the primary outcome was not assessed died, presumably of a cardiac origin, within 24 hours after CTPA. The two other patients were lost to follow-up. Mean relative serum creatinine increase 48-96 hours post CTPA compared with baseline was -0.14% (IQR-15.1 to 12.0%) in the withholding hydration versus -0.32% (IQR-9.7 to 10.1%) in the sodium bicarbonate group, for a mean difference of 0.19% (95%CI −5.88 to 6.25%, p-value for non-inferiority < 0.001). These results were consistent under the predefined subgroups, including severe renal failure, and no significant interactions between subgroups and treatment were found, except for patients with diabetes mellitus in whom the relative serum creatinine was lower in the withholding hydration group (Figure 2). The incidence of CI-AKI did not differ significantly between groups, i.e. 9.2% (6/65) in the withholding hydration and 7.1% (5/70) in the sodium bicarbonate group (RR 1.29, 95%CI

Figure 2. Subgroup analyses on the primary outcome of a relative increase in serum creatinine 48-96 hours post computed tomography pulmonary angiography. Effect size is calculated as the difference in the mean relative increase in serum creatinine between both randomization groups. The dashed line indicates the point estimate of the entire study population and the straight line indicates no effect.
Follow-up on recovery of renal function was complete in 10 of 11 (90.9%) CI-AKI patients. The other patient died within days after CTPA of a cause other than PE or CI-AKI. Renal function had recovered two months after CTPA in 4 of the 5 CI-AKI patients in each randomization group (RR 1.00, 95% CI 0.53-1.86). Renal function of the two CI-AKI patients in whom renal function had not recovered was 57 ml/min/1.73m² two months post CTPA in the patient randomized to withholding hydration and 8 ml/min/1.73m² in the patient randomized to sodium bicarbonate. This latter patient already had severe chronic kidney disease prior to randomization (baseline eGFR 11 ml/min/1.73m²). None of the CI-AKI patients developed a need for dialysis within two months post CTPA. Mean urinary pH was 6.0 (SD 0.8) at baseline and 5.8 (SD 1.2) at 2 hours post CTPA in the withholding hydration group. For sodium bicarbonate these values were 6.3 (SD 1.0) and 6.7 (SD 1.1), respectively, (with a mean pH difference at two hours post CTPA between both groups of -0.8, 95% CI -1.3 to -0.4, p <0.001).

**DISCUSSION**

Our study results demonstrate that withholding hydration is non-inferior to sodium bicarbonate hydration prior to CTPA in patients with pre-existing CKD. PE has an acute treatment indication, and a fast diagnostic work-up including CTPA is therefore of vital importance[23]. CI-AKI preventive hydration prior to CTPA induces a diagnostic delay, while evidence for its need is lacking. This information is, however, relevant as 10-25% of patients clinically suspected of acute PE have CKD[3-5,24]. Furthermore, according to the American College of Chest Physicians (ACCP) Guidelines, a high clinical suspicion of PE justifies treatment with low-molecular-weight-heparins prior to CTPA in case of a diagnostic delay[25], a drug that is known for high major bleeding rates in patients with CKD[26,27].

Our study is the first randomized trial that has compared withholding to administering hydration in CKD patients undergoing CTPA. Two previous studies have been performed comparing renal outcomes after withholding vs. administering hydration in patients undergoing non-emergent percutaneous coronary interventions or angiography, requiring intra-arterial contrast administrations and not intravenous as for CTPA. It was concluded that the risk of CI-AKI could be lowered by the use of hydration [11,28]. Importantly, these studies were performed in patient populations that differed from ours: more patients had co-morbidity potentially increasing the risk of CI-AKI, and much larger contrast volumes were used than for CTPA (range 187 to 387 ml, compared with 54-96 ml in our study)[11,28]. Future studies should therefore evaluate whether hydration could also be withheld in patients with CKD undergoing intravenous contrast enhanced-computed tomography for other indications, requiring larger volumes of iodinated contrast media.
The clinical relevance of CI-AKI post intravenous contrast administration has become subject of debate after publication of retrospective studies demonstrating that CI-AKI occurs as often in patients undergoing intravenous contrast enhanced-computed tomography as in a control group not receiving contrast media[29-34]. Unfortunately, these studies were prone for confounding by factors associated with the indication for contrast media use, and their results are therefore difficult to generalize into clinical practice[35]. Moreover, physicians are still reluctant to withhold CI-AKI preventive measures or even to perform computed tomography in patients with CKD[36]. It is therefore of importance to assess whether hydration can be safely withheld in CKD patients undergoing intravenous contrast enhanced-computed tomography, especially in those suspected of acute PE, in whom a diagnostic delay is undesirable.

We observed a small non-significant increase in the risk of CI-AKI in patients in whom hydration was withheld (RR 1.29). Nevertheless, renal function recovery rates were similar between both groups, i.e. 80%, and none of the patients developing CI-AKI had a need for dialysis. Furthermore, CI-AKI patients have a risk of 1% to develop a need for dialysis, according to the results of a meta-analysis on risks of CI-AKI and dialysis post intravenous contrast enhanced-computed tomography[37]. Based on these numbers and the CI-AKI incidences found in our study, withholding hydration would result in an estimated 0.02% absolute increase in the risk of dialysis post CTPA. Therefore, we do not consider the 1.3-fold increased CI-AKI risk observed in the withholding hydration arm of clinical importance with respect to long-term renal outcomes. Additionally, in patients with an eGFR < 45 ml/min/1.73m² (i.e. those at increased risk of CI-AKI according to the ESUR guidelines), the relative risk of CI-AKI comparing withholding hydration with sodium bicarbonate was 0.97 (Appendix 1).

Our study provides clinically relevant knowledge on the need for preventive hydration in CKD patients undergoing CTPA. As withholding hydration was non-inferior to sodium bicarbonate hydration throughout all subgroups, our results can be extrapolated to clinical practice of CKD patients undergoing CTPA. Furthermore, our study results stand back for future studies withholding hydration in CKD patients undergoing computed tomography for other indications, requiring larger contrast volumes. Additionally, we demonstrated the ability of 250 ml 1.4% bicarbonate to alkalinize urine, one of its hypothesized mechanisms of action in the prevention of CI-AKI.

Some aspects of our trial warrant comment. First, although subject of debate[6,38-40], CI-AKI is frequently defined by an increase in serum creatinine > 25% or > 44 µmol/L (0.5 mg/dl)[10]. This definition makes CI-AKI a relatively rare event, and as a result, requires a very large study sample size in a non-inferiority trial powered on that endpoint. We chose the relative increase in serum creatinine as our primary endpoint (and CI-AKI as a secondary endpoint), which resulted in a feasible sample size, and was used by several previous studies on CI-AKI prevention[13,41-47]. Moreover, we wanted to analyze expected small
differences in contrast media induced-nephrotoxicity between the two randomization arms, for which an increase in serum creatinine is an earlier and more sensitive marker. Second, we included CKD patients with a baseline eGFR < 60 ml/min/1.73m2. However, the updates of both the ESUR guideline and European Renal Best Practice recommend to use preventive hydration only in patients with an eGFR < 45 ml/min/1.73m2 when undergoing intravenous contrast enhanced-computed tomography[6,10]. Nonetheless, a sensitivity analysis of our study confirmed non-inferiority of withholding hydration to sodium bicarbonate in this specific subpopulation (Appendix 1). Third, we adjusted our power calculation to a maximum inclusion of 140 instead of 240 patients. However, our reduced sample size provided sufficient power to indicate that withholding hydration is non-inferior to sodium bicarbonate hydration in CKD patients undergoing CTPA, (p-value for non-inferiority <0.001). Fourth, we used a novel sodium bicarbonate regime as comparator for the withholding hydration arm. We acknowledge that the safety and efficacy of this regime has been studied by just one randomized trial. However, there is no standard hydration regime for emergent contrast procedures. Furthermore, although peri-procedural sodium bicarbonate hydration has been studied extensively[48,49], the six hours hydration post CTPA result in considerable logistic difficulties at emergency departments (especially in patient in whom PE is ruled out by CTPA) and would therefore be unfeasible.

In summary, our study findings suggest that CI-AKI preventive hydration could be safely withheld in CKD patients undergoing CTPA. This will greatly facilitate diagnostic management of these patients at the emergency department and prevents delay in diagnosis as well as unnecessary start of anticoagulant treatment in patients with CKD. Further research is needed to study whether hydration can also be withheld in CKD patients undergoing intravenous contrast enhanced-computed tomography for other indications, requiring larger contrast volumes.
REFERENCE LIST


36. Katzberg RW, Newhouse JH. Intravenous contrast medium-induced nephrotoxicity: is the medical risk really as great as we have come to believe? Radiology 2010; 256: 21-8.


## APPENDIX

**Appendix 1.** Sensitivity analysis on the primary endpoint and incidence of contrast induced-acute kidney injury restricted to patients with an estimated glomerular filtration rate < 45 ml/min/1.73m2

<table>
<thead>
<tr>
<th></th>
<th>Withholding hydration (N = 23)</th>
<th>Bicarbonate (N = 28)</th>
<th>Mean difference 2.1% (95% CI -10.0 to 14.3%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean serum creatinine increase, % (IQR)</td>
<td>2.9 (-9.4 to 10.6)</td>
<td>0.8 (-13.0 to 11.2)</td>
<td>RR 0.97 (95% CI 0.30 to 3.21)</td>
</tr>
<tr>
<td>Incidence of CI-AKI</td>
<td>4/23</td>
<td>5/28</td>
<td></td>
</tr>
</tbody>
</table>

Abbreviations: CI-AKI = contrast induced-acute kidney injury. RR = relative risk. CI = confidence interval.