ABSTRACT

Background. Guidelines recommend saline hydration for prophylaxis of contrast-induced acute kidney injury (CI-AKI) in patients with chronic kidney disease (CKD) undergoing intravenous contrast media-enhanced CT (CE-CT). The safety and efficacy of a brief hydration protocol using sodium bicarbonate in this population is unknown. We analysed whether 1-h sodium bicarbonate hydration prior to CE-CT is non-inferior to saline hydration prior to and after CE-CT in CKD patients.

Methods. We performed an open-label multicentre randomized trial. Patients were randomized to 250 mL of 1.4% sodium bicarbonate hydration prior to CE-CT or 1000 mL of 0.9% saline hydration prior to and, once again, after CE-CT. Primary outcome was the relative increase in serum creatinine 48–96 h post-CE-CT. Secondary outcomes were incidence of CI-AKI [serum creatinine increase >25%/>44 µmol/L (0.5 mg/dL)], recovery of renal function, the need for dialysis and 2-month hospital costs.

Results. Five hundred and seventy adult CKD patients undergoing CE-CT were randomized between 2010 and 2012, of whom 548 were included in the intention-to-treat population. Mean relative serum creatinine increase was 1.2% for sodium bicarbonate and 1.5% for saline (mean difference −0.3%; 95% confidence interval −2.7 to 2.1, P-value for non-inferiority <0.0001). CI-AKI occurred in 22 patients (4.1%); 8 (3.0%) randomized to sodium bicarbonate versus 14 (5.1%) to saline (P = 0.23). Renal function recovered in 75 and 69% of CI-AKI patients, respectively (P = 0.81). No patients developed a need for dialysis. Mean hydration costs per patient were €224 for the sodium bicarbonate and €683 for the saline regime (P < 0.001). Other healthcare costs were similar.

Conclusions. Short hydration with sodium bicarbonate prior to CE-CT was non-inferior to peri-procedural saline hydration with respect to renal safety and may result in healthcare
INTRODUCTION

Contrast media are commonly used in clinical practice with 45 million patients undergoing computed tomography in the USA per year. Contrast induced-acute kidney injury (CI-AKI) is a well-known complication associated with the use of contrast media [1]. Patients with chronic kidney disease (CKD), ~16% of the total CT population, are at a particularly high risk of CI-AKI [2–4], and minimization of contrast volume, use of low-and iso-osmolar instead of high-osmolar, or non-ionic contrast media, and adequate peri-procedural hydration are strategies that are effective in reducing the risk of CI-AKI [5–10].

The most commonly recommended regime for prevention in patients at high risk of CI-AKI is peri-procedural intravenous hydration with normal saline [5, 9]. This treatment requires on average 2 days of elective hospitalization, is burdensome to patients and increases healthcare costs [5]. Recently, multiple studies have demonstrated the utility of a shorter hydration protocol using 1.4% sodium bicarbonate administered for 1 h prior to and 6 h following contrast injection [11–20], with the largest trial including 502 patients [21]. It has been hypothesized that even shorter infusions of sodium bicarbonate may be associated with similar prophylactic efficacy while simplifying patient care [22]. The volume expansion would prevent patients from being in a hypovolemic state at the time of intravenous contrast media-enhanced CT (CE-CT), an important risk factor for CI-AKI [23]. In addition, sodium bicarbonate alkalinizes urine, theoretically providing an additional protective effect [24, 25]. We evaluated the comparative efficacy of a novel 1-h hydration regime with 250 mL of 1.4% sodium bicarbonate prior to CE-CT as the only preventive measure in patients with pre-existing CKD and compared it with peri-procedural saline hydration.

MATERIALS AND METHODS

We performed a randomized non-inferiority trial in one academic and three non-academic Dutch hospitals. In- and outpatient scheduled for CE-CT regardless of the indication were eligible for inclusion. All patients were at least 18 years of age, had CKD (eGFR < 60 mL/min/1.73 m² estimated by the Modification of Diet in Renal Disease formula [26]) and were eligible for the fluid challenge of saline hydration. Exclusion criteria were pregnancy, previous contrast administration within the last 7 days, documented allergy for iodinated contrast media, haemodynamic instability (systolic blood pressure <100 mmHg) and previous participation in the trial. All patients provided written informed consent prior to randomization. The trial protocol was approved by the Institutional Review Boards of each participating centre. 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). This trial was registered with the Netherlands Trial Register, NTR 2149.

Randomization

Patients were randomized using a computer-generated allocation sequence to either hydration with 250 mL intravenous 1.4% sodium bicarbonate 1 h prior to CE-CT without hydration post-CE-CT, or standard peri-procedural intravenous saline hydration. All patients randomized to saline received 2000 mL of 0.9% saline, 1000 mL prior to and 1000 mL post-CE-CT. Infusion rates were adjusted by the treating physician to a patient’s cardiac function, based on symptoms or a history of congestive heart failure, and varied between 83 and 250 mL/h. Randomization was stratified by hospital of inclusion and by renal function (eGFR 0–19, 20–39 or 40–59 mL/min/1.73 m²) and diabetes mellitus, both major risk factors for CI-AKI [9, 23]. The study had an open-label design.

Procedures

Patients were hospitalized to undergo CE-CT and to receive their randomized CI-AKI-preventing treatment. Patients randomized to sodium bicarbonate were admitted at a day care department for study purposes. Contrast volumes used were registered and dependent on CE-CT protocol and body mass. CE-CT was performed with low-osmolar contrast media in all hospitals [Iomeprol (Iomeron, Bracco Imaging, Milan, Italy), Iobitrindol (Xenetix, Guerbet, Aulnay-sous-Bois, France) or Iodixanol (Visipaque, GE Healthcare, Chalfont St. Giles, UK]. No other CI-AKI preventive treatments were used, such as administration of N-acetylcysteine. Serum and urine samples were collected prior to hydration and once between 48 and 96 h post-CE-CT. Urine samples were also obtained at 4–6 h post-CE-CT, after which patients were discharged if they had been randomized to sodium bicarbonate. Patients randomized to saline were discharged after completion of hydration. Serum sampling was repeated 2 months post-CE-CT 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 h post-CE-CT compared with baseline]. Samples were analysed for serum creatinine values centrally in the laboratory of the Leiden University Medical Center using Roche Diagnostics analysers (Mannheim, Germany) after trial completion. Urinary pH levels were measured at baseline and 4–6 h post-CE-CT, to determine whether sodium bicarbonate hydration had increased urinary pH. 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, contrast volumes 3.7 times baseline eGFR value and use of nephrotoxic medication) [9].

Outcomes

Primary outcome was the relative increase in serum creatinine measured between 48 and 96 h post-CE-CT compared with baseline. Secondary outcomes were the incidence of
Cl-AKI (defined as stated above) recovery of renal function in Cl-AKI patients [recovery defined as an increase in serum creatinine <25% or <44 μmol/L (0.5 mg/dL) measured at 2 months post-CE-CT compared with baseline] [27, 28], the need for dialysis, acute heart failure due to volume expansion, and rehospitalization or outpatient visits. Patients were assumed to not have developed Cl-AKI if CE-CT was cancelled or performed without contrast enhancement and serum creatinine values were therefore not obtained. Serum creatinine values of patients who did not receive contrast media but in whom these variables were available were included in the study analysis.

**Economic evaluation**

Costs were estimated from a hospital perspective, with a 2-month time horizon, at the price level of 2012. Costs included the hydration itself, hospital days and specialist consultations (excluding visits for study purposes). Volumes of healthcare were estimated from hospital information systems. Direct costs per hydration treatment included the costs of the infusions (€3 for sodium bicarbonate and €2 for saline), mostly short day care for the sodium bicarbonate regime (€194) and normal day care or an inpatient hospital day for the saline regime (€382 and €602, respectively). Other hospitalizations and outpatient visits were valued using standard prices, designed to reflect societal costs and to standardize economic evaluations [29]. Cost-effectiveness acceptability curves were used to relate the difference in costs to the difference in the incidence of Cl-AKI (according to intention-to-treat with multiple imputation for missing values on the occurrence of Cl-AKI and one-sided unequal-variance t-tests). Acceptability curves show the probability that one strategy has a better net benefit (NB = WTP × incidence − Costs) than the other strategy, depending on the willingness to pay (WTP) to avoid one case of Cl-AKI [30].

**Statistical analyses**

The trial was designed for non-inferiority. As a low relative serum creatinine increase in the saline group was expected [31], 1-h sodium bicarbonate hydration prior to CE-CT 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 saline hydration 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 40%. This calculation included inclusion of 250 patients per treatment arm to be sufficient (β = 0.2, α = 0.05). Assuming 15% of patients to be lost to follow-up, we calculated a total sample size of 574 patients.

The study was analysed blinded on an intention-to-treat basis. Differences in the mean relative serum creatinine increase, absolute urinary pH levels and healthcare costs between randomization groups were analysed using an independent samples t-test with corresponding 95% confidence intervals (CIs) or P-values. For the primary outcome, a one-sided P-value of non-inferiority was calculated under null hypothesis of equivalence. Incidences of Cl-AKI, reversibility of Cl-AKI, acute heart failure and the need for dialysis were reported and tested for statistical differences between both groups using relative risks (RRs). Subgroup analyses were performed for the primary end point and the incidence of Cl-AKI in high-risk patients (i.e. eGFR < 30 mL/min/1.73 m², diabetes mellitus, age >75 years). No corrections were made for multiple comparisons. Incidences of Cl-AKI according to the acute kidney injury network (AKIN) criteria were compared between both groups in a post hoc analysis [32].

All calculations were performed using SPSS version 20.0 (IBM Corp, Armonk, New York, USA).

**RESULTS**

Between January 2010 and June 2012, 570 patients provided written informed consent and were randomized. Twenty-two withdrew consent after randomization, leaving 548 patients available for the intention-to-treat analysis: 267 patients randomized to sodium bicarbonate hydration prior to CE-CT and 281 to saline prior to and after CE-CT (Figure 1).

Protocol violation occurred in 10 patients within the intention-to-treat population of whom six were randomized to saline hydration. Four patients randomized to saline had pre-existing severe chronic congestive heart failure and were therefore hydrated with sodium bicarbonate. Another patient in the saline group received a total volume of 1000 instead of 2000 mL by mistake, and in one patient the saline infusion was stopped prematurely (due to acute dyspnoea). Of the four patients in the sodium bicarbonate arm in whom protocol violation occurred, one patient received 500 instead of 250 mL of sodium bicarbonate. Another patient received saline hydration. Two other patients received an additional 25 and 400 mL of saline, respectively. All other patients received the study mandated randomized treatment.

Patient and procedure characteristics at baseline were well-balanced between the treatment groups (Table 1). In total, 171 patients within the intention-to-treat population had a baseline eGFR < 45 mL/min/1.73 m². Of those with a baseline eGFR > 45 mL/min/1.73 m², 231 (74%) had two or more other risk factor for Cl-AKI. Eight of 548 patients (1.5%) received combination treatment of angiotensin-converting enzyme (ACE) inhibitors and angiotensin receptor blockers prior to CE-CT. Infused volumes of sodium bicarbonate and saline per kilogram bodyweight are presented in the Supplementary data, Appendix 1.

**Patient outcome**

The primary outcome was assessed in 93.6% (513/548) of patients. In 24 of the 35 patients in whom the primary outcome was not assessed, CE-CT was cancelled or performed without intravenous contrast enhancement. Mean relative serum creatinine increase 48–96 h post-CE-CT compared with baseline was 1.2% (SD 13.3%) in the sodium bicarbonate versus 1.5% (SD 14.2%) in the saline group, for a mean difference of −0.3% (95% CI −2.7 to 2.1%, P-value for non-inferiority <0.0001). Follow-up on the end point of Cl-AKI was complete in 98.2% (538/548). The incidence of Cl-AKI did not differ significantly between groups, i.e. 3.0% (8/264) in the sodium...
bicarbonate and 5.1% (14/274) in the saline group (RR 0.59, 95% CI 0.25–1.39). Risks of CI-AKI were similar for patients in whom diuretics were withheld prior to CE-CT (4/83, 4.9%) and those in whom diuretic therapy was continued (8/173, 4.6%). Incidences of CI-AKI defined by the AKIN criteria are presented in Table 2. The results on the primary end point and the risk of CI-AKI comparing sodium bicarbonate with saline hydration were consistent under the predefined subgroups (Figure 2A and B). No significant interactions between subgroups and treatment were found. Follow-up on recovery of renal function was complete in 95% (21/22) of CI-AKI patients. Renal function had recovered 2 months after CE-CT in 75% (6/8) of CI-AKI patients randomized to sodium bicarbonate versus 69% (9/13) randomized to saline (RR 1.08, 95% CI 0.63–1.86). eGFRs 2 months post-CE-CT of CI-AKI patients in whom renal function had not recovered were 32 and 51 mL/min/1.73 m² in patients randomized to sodium bicarbonate and 22, 24, 27 and 47 mL/min/1.73 m² in those randomized to saline. None of the CI-AKI patients developed a need for dialysis.

Acute heart failure due to volume expansion (based on the treating physician’s clinical judgement) occurred in none of the patients in the sodium bicarbonate group versus 6 of 281 patients in the saline group (P = 0.03). Consequently, saline hydration was prematurely stopped in 1 of 281 patients. Four other patients received intravenous furosemide. One of them was admitted to the Intensive Care Unit for 2 days and underwent emergency percutaneous transluminal coronary angioplasty. Another patient had to be rehospitalized. Saline volumes per kilogram bodyweight were similar for patients who did and did not develop acute heart failure, with mean volumes of 29.7 (SD 3.3) and 26.6 mL (SD 5.4), respectively (95% CI –1.3 to 7.4, P = 0.16). Three of six patients developing acute heart failure were on diuretic treatment prior to CE-CT, yet none of them used NSAIDs. Four of these six patients had a history of congestive heart failure.

Mean urinary pH was 6.1 (SD 0.9) at baseline and 6.6 (SD 1.0) at 4–6 h post-CE-CT in the sodium bicarbonate group. For saline these values were 5.8 (SD 0.8) and 6.1 (SD 0.8), respectively (P < 0.001 for difference in mean pH at 4–6 h post-CE-CT between both groups).

**Economic evaluation**

Of the outpatients treated with sodium bicarbonate, 96% underwent CE-CT in mostly short day care, and 4% were admitted for a median duration of 2.0 (2.5–97.5 percentile 2.0–5.0) days because of other imaging or interventional procedures. Of the outpatients treated with sodium bicarbonate, 58% were treated in day care setting, whereas the other 42% of patients were hospitalized for a median duration of 2 (2.5–97.5 percentile 2.0–3.0) days using a lower saline infusion rate of 1000 mL in 12 h prior to and post-CE-CT. The difference in hydration-related costs was €459 per patient in favour of the sodium bicarbonate group (95% CI €383–€535, Table 3), due to more extensive day care and more frequent inpatient hospitalization for the saline regime. Other categories of hospital costs during the 2 months of follow-up were comparable (P ≥ 0.16).

Whether a hydration strategy is cost-effective, depends on how much one is willing to pay (WTP) to avoid one case of CI-AKI. Figure 3 shows the probability that 1-h hydration prior to CE-CT with sodium bicarbonate is cost-effective compared with saline hydration prior to and after CE-CT. Taking all hospital costs into account, hydration with sodium bicarbonate is at least 92% likely to be cost-effective, regardless the WTP. For example, if one is WTP €10 000 to prevent one case of CI-AKI, then it is 96% certain that hydration with sodium bicarbonate is cost-effective. Restricting to only the hydration-related costs (i.e. including the required hospitalization, but

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**FIGURE 1:** Trial profile. CT, computed tomography; eGFR, estimated glomerular filtration rate; i.v., intravenous.
assuming non-inferiority on other costs), makes hydration with sodium bicarbonate almost 100% certain to be cost-effective for WTP up to €10 000 per case of CI-AKI.

**DISCUSSION**

Our study demonstrates that a novel 1-h hydration regime prior to CE-CT with 250 mL of sodium bicarbonate is non-inferior to standard peri-procedural saline hydration. Secondly, the short sodium bicarbonate treatment resulted in a substantial decrease in hydration costs by €459 per patient, without impact on clinical outcome. As a result, 1-h hydration with sodium bicarbonate prior to CE-CT is at least 90% likely to be more cost-effective.

<table>
<thead>
<tr>
<th>Table 1. Patient and procedure characteristics</th>
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<tr>
<td><strong>Sodium bicarbonate (n = 267)</strong></td>
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<tr>
<td><strong>Mean age, years</strong></td>
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<tr>
<td><strong>Sex, male</strong></td>
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<tr>
<td><strong>Outpatients</strong></td>
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<tr>
<td><strong>Mean eGFR</strong></td>
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<tr>
<td><strong>eGFR &gt;45 mL/min/1.73 m²</strong></td>
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<tr>
<td><strong>eGFR 30–45 mL/min/1.73 m²</strong></td>
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<tr>
<td><strong>eGFR 15–30 mL/min/1.73 m²</strong></td>
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<td><strong>eGFR &lt;15 mL/min/1.73 m²</strong></td>
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<td><strong>Mean systolic blood pressure</strong></td>
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<td><strong>Mean diastolic blood pressure</strong></td>
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<tr>
<td><strong>Diabetes mellitus</strong></td>
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<td><strong>Peripheral arterial disease</strong></td>
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<td><strong>Coronary artery disease</strong></td>
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<td><strong>Congestive heart failure</strong></td>
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<tr>
<td><strong>Primary renal or urological disease</strong></td>
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<tr>
<td><strong>Microalbuminuria</strong></td>
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<tr>
<td><strong>Macroalbuminuria</strong></td>
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<tr>
<td><strong>Anemia</strong></td>
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<tr>
<td><strong>Medication</strong></td>
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<tr>
<td><strong>NSAIDS</strong></td>
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<tr>
<td><strong>Diuretics</strong></td>
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<tr>
<td><strong>ACE-inhibitors</strong></td>
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<td><strong>Angiotensin II receptor blockers</strong></td>
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<tr>
<td><strong>Chemotherapy</strong></td>
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<tr>
<td><strong>Pre-procedural stop of medication</strong></td>
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<table>
<thead>
<tr>
<th>Type of CT-scan</th>
<th>Sodium bicarbonate (n = 267)</th>
<th>Saline (n = 281)</th>
</tr>
</thead>
<tbody>
<tr>
<td>CT abdomen</td>
<td>96 (36.0)</td>
<td>81 (28.8)</td>
</tr>
<tr>
<td>CT thorax</td>
<td>26 (9.7)</td>
<td>31 (11.0)</td>
</tr>
<tr>
<td>CT angiography</td>
<td>88 (33.0)</td>
<td>110 (39.1)</td>
</tr>
<tr>
<td>Other</td>
<td>57 (21.3)</td>
<td>59 (21.0)</td>
</tr>
<tr>
<td>Mean contrast volume in mL</td>
<td>105.7 (21.0)</td>
<td>104.7 (21.6)</td>
</tr>
<tr>
<td>Mean iodine dose in grams</td>
<td>36.6 (8.3)</td>
<td>35.5 (10.5)</td>
</tr>
<tr>
<td>Median time in hours between CT and creatinine measurements (IQR)</td>
<td>70 (56–86)</td>
<td>70 (51–94)</td>
</tr>
</tbody>
</table>

Data are mean (SD), n (%).

eGFR, estimated glomerular filtration rate; CKD, chronic kidney disease.

*Microalbuminuria was defined as albumin-creatinine ratio 30–300 mg/g; macroalbuminuria as albumin-creatinine ratio >300 mg/g.

Defined as Hb <7.4 mmol/L if female and Hb <8.1 mmol/L if male.

*Non-steroid anti-inflammatory drugs.

<table>
<thead>
<tr>
<th>Table 2. Incidence of CI-AKI according to the AKI criteria</th>
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<tr>
<td><strong>AKIN stage</strong></td>
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<td>----------------</td>
</tr>
<tr>
<td>I (increase &gt;26.5 µmol/L or 150–200% from baseline)</td>
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<tr>
<td>II (increase 200–300% from baseline)</td>
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<tr>
<td>III (increase &gt;300% from baseline, or ≥354 µmol/L, or on RRT)</td>
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AKIN, acute kidney injury network.
This first randomized trial that has compared head-to-head a 1-h hydration scheme of 250 mL of sodium bicarbonate prior to CE-CT with peri-procedural saline hydration to prevent CI-AKI. Prior studies have evaluated different hydrating regimes with the goal of simplifying the hydration strategy. One earlier study among patients undergoing either CE-CT or intra-arterial contrast administrations demonstrated saline hydration to be more effective for CI-AKI prevention than sodium bicarbonate infusion before contrast administration in combination with both oral sodium bicarbonate and water administration [33]. As the sample size of this study was small, and the patient population heterogeneous, it is difficult to compare these results to the current study. Additionally, there is a large body of data demonstrating the efficacy of a 7 h infusion of sodium bicarbonate compared with normal saline with most studies and meta-analyses concluding either non-inferiority or a slight benefit of sodium bicarbonate among patients undergoing invasive cardiac and peripheral vascular procedures [11–20, 34]. However, there has been a paucity of data on the ideal prophylactic strategy for patients undergoing CT-CE, a very common procedure worldwide. We evaluated a relatively simple protocol that is likely to be more practical and has the feasibility of easy adoption and improving patient satisfaction. Moreover, the risk of hospital acquired infections might decrease by the use of the short sodium bicarbonate regime that can be implemented in an out-patient setting. This is especially of importance for CKD patients, who are at increased risk of developing infections [35].

Further, in our study, there was a slight excess of complications associated with saline hydration. Four patients randomized to saline did not receive it because of pre-existing severe chronic congestive heart failure and six of the patients receiving saline hydration developed symptoms of acute heart failure due to volume expansion. In two patients, this required even temporary (ICU) readmission. Finally, in the absence of clinically important differences between the two strategies, cost implications must be considered [36–38]. In our study, the clinical efficacy of a short infusion with sodium bicarbonate in preventing CI-AKI was comparable with the saline hydration scheme, whereas the costs were only a third. Therefore, from a value-based care perspective, the use of sodium bicarbonate hydration prior to CE-CT should be preferred over saline hydration.

This study extends prior work in the field. It had a robust trial design, with few drop-outs or missing data. A short hydration has been assessed, which is easy to apply in clinical practice and has strong potential for drastically decreasing healthcare costs for preventive hydration, and at the same time reducing the inconvenience for the patient. The results of our study were homogenous throughout the population, and can therefore be extrapolated to clinical practice of CKD patients undergoing CE-CT. In addition,
we used standardized hydration volumes instead of volumes adjusted to bodyweight to ease the clinical use of the infusions. At the same time, these standardized volumes corresponded well with the volumes that would have been achieved using a bodyweight adjusted approach (data not shown).

Some aspects of our trial warrant comment. First, CI-AKI is frequently defined by an increase in serum creatinine >25% or >44 μmol/L (0.5 mg/dL) [5, 39–41], but this definition is often debated [9]. One of the most prominent disadvantages is that this definition leads to CI-AKI being a rare event, which as a consequence requires a very large study sample size in a non-inferiority study. We therefore chose the relative increase in serum creatinine as our primary end point (and CI-AKI as a secondary end point). This end point has been used in several previous studies on CI-AKI prevention [42–48]. It resulted in a feasible sample size, and importantly, it allowed us to analyse expected small differences in contrast media induced-nephrotoxicity between treatment arms, for which an increase in serum creatinine is an earlier and more sensitive marker. Secondly, our cost analysis is specific for the Dutch healthcare system. Nevertheless, we expect the reduction in hospital days for preventive hydration to be generalizable to other settings. Although the exact numbers may differ from country to country, the health economic impact of our results can be substantial worldwide. Thirdly, we included patients with a baseline eGFR < 60 mL/min/1.73 m² while the updates of both the ESUR guideline and European Renal Best Practice advise to use preventive hydration only in patients with an eGFR < 45 mL/min/1.73 m² when undergoing CE-CT [5, 9]. However, a sensitivity analysis of our study confirmed non-inferiority of sodium bicarbonate to saline in patients with an eGFR < 45 mL/min/1.73 m² (data not shown). Fourthly, based on our study design, we were unable to determine whether smaller volumes of saline (comparable with the sodium bicarbonate regime but not resulting in alkalinization of urine as seen in the sodium bicarbonate group) would also be non-inferior to peri-procedural saline hydration. Fifthly, although the vast majority of international guidelines recommends preventive hydration in CKD patients undergoing intravascular contrast administration (CE-CT or intra-arterial contrast injections) [5, 9], the American College of Radiology manual on contrast media does not endorse its routine use prior to CE-CT [49]. We therefore cannot exclude that the results of our study may have less clinical impact on hospitals adhering to that guideline.

In summary, in this trial we show that a simple pre-procedural regime with sodium bicarbonate is non-inferior to standard peri-procedural saline infusion in CKD patients undergoing CE-CT and results in considerable healthcare savings. Further research is needed to study whether 1-h sodium bicarbonate hydration is also non-inferior to peri-procedural saline hydration in patients undergoing invasive (cardiac) procedures requiring intra-arterial administration of iodinated contrast media.

**SUPPLEMENTARY DATA**

Supplementary data are available online at http://ndt.oxfordjournals.org.

**ACKNOWLEDGEMENTS**

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**CONFLICT OF INTEREST STATEMENT**

There are no conflicts of interest for any of the authors. The results presented in this paper have not been published previously in whole or part, except in abstract format.

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