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Title: Risk and prevention of contrast induced-acute kidney injury
Issue Date: 2015-12-10

Chapter 8

Randomized trial of one-hour sodium bicarbonate vs standard periprocedural saline hydration in patients with chronic kidney disease undergoing cardiovascular diagnostic or interventional contrast procedures

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ABSTRACT

Background
Guidelines advise periprocedural saline hydration for prevention of contrast induced-acute kidney injury (CI-AKI). We analysed whether 1-hour sodium bicarbonate hydration administered solely prior to contrast exposure is non-inferior to standard saline hydration in chronic kidney disease (CKD) patients undergoing elective cardiovascular diagnostic or interventional contrast procedures.

Methods and Results
We performed an open-label multicentre trial between 2011 and 2014. Patients were randomized to 250 ml 1.4% sodium bicarbonate hydration prior to contrast exposure (N= 168) or 1000 ml 0.9% saline hydration (N= 165) prior to and following contrast administration. Primary outcome was the relative serum creatinine increase 48-96 hours post contrast exposure. Secondary outcomes were: incidence of CI-AKI (serum creatinine increase >25%/ > 44μmol/L), recovery of renal function, the need for dialysis, and 2-month hospital costs. Mean creatinine increase was 3.1% (SD 13.6%) in the bicarbonate and 1.1% (SD 15.0%) in the saline arm, mean difference 1.9% (95%CI -1.2 to 5.1%, p-non-inferiority <0.001). CI-AKI occurred in 23 patients; 11 (6.7%) patients randomized to sodium bicarbonate and 12 (7.5%) to saline (p-value 0.79). Renal function did not fully recover in 40.0% and 44.4% of CI-AKI patients, respectively (p=0.84). No patient developed a need for dialysis. Mean costs for preventive hydration and clinical preparation for the contrast procedure were $1309 for sodium bicarbonate vs. $1921 for saline (p-value < 0.001). Other healthcare costs were similar.

Conclusion
Short hydration with sodium bicarbonate prior to cardiovascular diagnostic or interventional contrast procedures is non-inferior to standard periprocedural saline hydration in CKD patients with respect to renal safety and resulted in considerable healthcare savings.

INTRODUCTION

Contrast induced-acute kidney injury (CI-AKI) is a common complication among patients undergoing cardiovascular diagnostic or interventional contrast procedures (1). The development of CI-AKI is associated with morbidity, mortality, and a longer duration of hospital stay (2-4). Guidelines on the prevention of CI-AKI recommend the use of periprocedural intravenous saline (12 hours prior to and following contrast exposure) or sodium bicarbonate (1 hour prior to and 6 hours following contrast exposure) hydration in patients with chronic kidney disease (CKD), who are at particularly high risk of developing CI-AKI (5-7). However, the use of CI-AKI preventive hydration is burdensome to patients and increases healthcare costs.

A previous randomized trial on the prevention of CI-AKI performed by our research group demonstrated the efficacy and safety of a 1-hour sodium bicarbonate regime administered solely prior to intravenous contrast enhanced-CT in patients with CKD (8). The use of this sodium bicarbonate regime resulted in considerable healthcare cost savings. Yet, it is unclear whether these results are generalizable to CKD patients undergoing elective cardiovascular diagnostic or interventional procedures requiring intra-arterial contrast administration. Hence, the aim of this study was to assess whether 1-hour sodium bicarbonate hydration prior to contrast exposure is non-inferior to standard periprocedural saline hydration in this specific setting.

METHODS

We performed a multicenter randomized non-inferiority trial in one academic hospital, and seven non-academic teaching hospitals. Consecutive in- and outpatients undergoing elective intravascular interventional or diagnostic radiology or cardiology procedures (i.e. percutaneous transluminal angiography, percutaneous coronary intervention, coronary angiography, endovascular aneurysms repair, angiography, or digital subtraction angiography) were screened for inclusion. We included patients 18 years or older with an estimated glomerular filtration rate (eGFR, calculated using the Modification of Diet in Renal Disease formula (9)) < 45 ml/min, or an eGFR 45-60 ml/min in combination with diabetes mellitus or at least two other risk factors for the development of CI-AKI (i.e. peripheral artery disease, congestive heart failure, age > 75 years, anemia, use of diuretics or non-steroidal anti-inflammatory drugs) (10). Patients were excluded if they were on dialysis treatment, received iodinated contrast media in the preceding seven days, currently had acute kidney injury, were pregnant, or had a documented allergy for iodinated contrast media.

The trial was approved by the Institutional Review Boards of the participating centers and performed according to the declaration of Helsinki. All patients provided written informed consent. Study outcomes were periodically reviewed by an independent data and safety monitoring board. The trial was registered at the Nederlands Trial Register (www.trialregister.nl), under number NTR2149.

Randomization

Randomization was performed in a 1: 1 ratio using a computer generated allocation sequence. The study had an open-label design. Patients were randomized to 1-hour pre-procedural intravenous hydration using 250 ml 1.4% sodium bicarbonate or periproce-dural intravenous hydration with 0.9% saline, 1000 ml in 4-12 hours prior to and 1000 ml in 4-12 hours following contrast administration (8). Infusion rates for saline hydration were adjusted to a patient's cardiac condition based on the clinical judgment (symptoms or a history of congestive heart failure) of the treating physician. Randomization was stratified for hospital of inclusion, renal function (i.e. eGFR 0-20, 20-40, 40-60 ml/min) at time of randomization and whether a patient had been diagnosed with diabetes mellitus, as both severe chronic kidney disease (eGFR < 30 ml/min) and diabetes mellitus are risk factors for the development of CI-AKI (1, 11).

Procedures

Contrast media use in the eight participating hospitals was according to clinical practice and included the use of Iobitridol (Xenetix, Guerbet, Aulnay-sous-Bois, France), Io-dixanol (Visipaque, GE Healthcare, Chalfort St. Giles, UK), and Iopromide (Ultravist, Bayer Schering Pharma, Berlin, Germany). Patients did not receive other CI-AKI preventive treatments besides their randomized hydration regimen.

Serum and urine samples were collected at baseline (prior to hydration and contrast exposure), 4-6 and 48-96 hours following the contrast procedure. All samples were shipped to the laboratory of the Leiden University Medical Center after trial completion for re-analysis of serum creatinine values (Roche Diagnostic analyzers, Mannheim, Germany) and assessment of urinary pH-values. Urinary pH-values were measured to determine whether the use of sodium bicarbonate had alkalinized urine.

Patients diagnosed with CI-AKI (defined as a serum creatinine increase > 25% or > 44 μmol/L compared with baseline (1)) based on serum creatinine values measured at the hospital of inclusion were asked to return to the outpatient clinic two months after contrast exposure to assess whether their renal function had recovered. Patients in whom the diagnosis of CI-AKI was not made based on the creatinine values measured at the hospital of inclusion but who did fulfill the criteria of CI-AKI grounded by the creatinine values quantified after trial completion were lost to follow-up for prospective assessment of the endpoint of recovery of renal function. For those patients, medical charts

were scrutinized retrospectively for serum creatinine values assessed in routine practice approximately two months following contrast administration.

Outcomes

Primary outcome of the study was the increase in serum creatinine measured (once) in the 48-96 hours following contrast exposure compared with baseline (8). Secondary outcomes were the incidence of CI-AKI, recovery of renal function (i.e. no longer fulfilling the criteria of CI-AKI compared with baseline), a need for dialysis, acute heart failure due to volume overload, re-hospitalization, and outpatient visits.

Economic evaluation

To analyze whether the use of sodium bicarbonate results in healthcare savings, costs were estimated from a hospital perspective, with a 2-month time horizon, at the price level of 2012. Costs for preventive hydration and clinical preparation prior to the contrast procedure were calculated separately. These costs were defined as costs for the randomized infusion fluids ($6 for sodium bicarbonate, $4 for saline), hospitalization on the day prior to the contrast procedure ($731), on the day of the procedure (either day care -$464- or inpatient hospital day), and the day following contrast exposure in those discharged on that particular day. Hospitalization days directly following the contrast procedure of patients admitted for a longer duration following contrast exposure were defined and calculated separately. Other admissions and visits to the outpatient clinic or emergence department were valued using standard prices, designed to reflect societal costs and to standardize economic evaluations. We used cost-effectiveness acceptability curves to relate the difference in healthcare costs to the difference in CI-AKI incidence (according to intention-to-treat and one-sided unequal-variance t-tests). Acceptability curves illustrate the probability that one strategy has a better net benefit (NB= WTP $\times$ incidence $-$ Costs) than the other strategy, depending on the willingness to pay (WTP) to prevent one case of CI-AKI (12).

Statistical analyses

Our study had a non-inferiority design. The use of sodium bicarbonate was considered non-inferior to saline hydration if the mean serum creatinine increase in the sodium bicarbonate group was not more than 15% higher compared with the increase in patients treated with saline (8). The sample size was set at 152 patients per study arm based on an expected difference in the mean serum creatinine increase of 5% with a standard deviation of 31% (α 0.025, β 0.800) (13). Taking into account a lost to follow-up of 15%, our total sample size comprised 346 patients.

Study outcomes were computed by an independent medical statistician blinded for randomization, using an intention-to-treat approach. The primary endpoint of an

Table 1. Patient and procedure characteristics

	Sodium bicarbonate (N=168)		Saline (N=165)	
Mean age, years	73.0	(9.2)	72.5	(8.8)
Sex, male	105	(62.5)	110	(66.7)
Outpatients	159	(94.6)	153	(92.7)
Mean BMI	29.0	(11.4)	29.5	(21.7)
Mean eGFR	50.0	(14.8)	51.1	(16.7)
eGFR > 45 ml/min/1.73m2	107	(63.7)	103	(62.4)
eGFR 30-45 ml/min/1.73m2	47	(28.0)	46	(27.9)
eGFR < 30 ml/min/1.73m2	14	(8.3)	16	(9.7)
Mean systolic blood pressure	145.7	(22.1)	139.2	(21.1)
Mean diastolic blood pressure	76.7	(13.3)	74.2	(14.1)
Diabetes mellitus	65	(35.7)	64	(38.8)
Peripheral arterial disease	109	(64.9)	119	(72.1)
Coronary artery disease	92	(54.8)	89	(53.9)
Congestive heart failure	33	(19.6)	22	(13.3)
Primary renal or urological disease	107	(63.7)	116	(70.3)
Microalbuminuria*	12	(7.1)	15	(9.1)
Macroalbuminuria*	63	(37.5)	67	(40.6)
Medication				
Diuretics	102	(60.7)	94	(57.0)
ACE-inhibitors	76	(45.2)	78	(47.3)
Angiotensin II receptor blockers	45	(26.8)	44	(26.7)
Preprocedural stop of medication	11	(6.5)	13	(7.9)
Type of contrast procedure				
Angiography	9	(5.4)	12	(7.3)
DSA	4	(2.4)	4	(2.4)
PTA	88	(52.4)	101	(61.2)
EVAR	22	(13.1)	7	(4.2)
CAG	33	(19.6)	30	(18.2)
PCI	5	(3.0)	3	(1.8)
Other	5	(3.0)	7	(4.2)
Mean contrast volume in mL**	112.9	(44.9)	112.6	(48.1)
Mean iodine dose in grams	35.2	(14.1)	34.9	(15.6)

Data are mean (SD), n (%)

eGFR = estimated glomerular filtration rate. CKD = chronic kidney disease. PTA = percutaneous coronary intervention. CAG = coronary angiography. PCI = percutaneous coronary intervention. DSA = digital subtraction angiography. EVAR = endovascular aneurysm repair.

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

** Missing in 34 and 40 patients, respectively.

increase in serum creatinine was tested using an independent samples *t*-test. Additionally, an one-sided p-value for non-inferiority was calculated under the null hypothesis of equivalence. Secondary outcomes were tested for statistical differences between randomization groups using relative risks with corresponding 95% confidence intervals (CI). Subgroup analyses were performed to test for interaction between randomization arms and patient groups at high risk of CI-AKI (i.e. those with eGFR < 30 ml/min, diabetes mellitus, or age > 75 years) on the primary endpoint and secondary endpoint of CI-AKI. The incidences of CI-AKI based on the AKI definitions of the AKI network (AKIN) criteria were calculated and reported in Appendix Table 1 (14). Calculations were performed using SPSS version 20.0 (IBM Corp, Armonk, New York, USA).
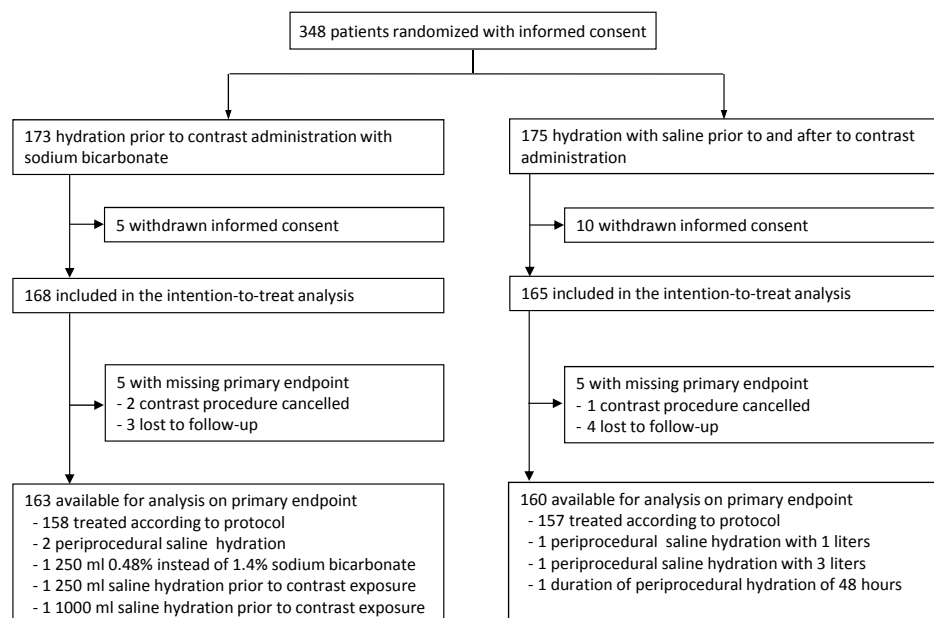
RESULTS

We included and randomized 348 patients between 2011 and 2014, of whom 15 (4.3%) withdrew consent after randomization. As a result, the intention-to-treat population consisted of 333 patients; 168 randomized to sodium bicarbonate and 165 to saline hydration. Patient characteristics at baseline were well balanced between randomization arms, except for an imbalance in type of contrast procedure. Patients in the sodium bicarbonate group were less likely to undergo percutaneous transluminal angiography, yet more frequently underwent endovascular aneurysms repair (Table 1). Protocol violation occurred in 8 (2.4%) patients (Figure 1). In addition, the contrast procedure, and consequently hydration, had been cancelled in 2 patients in the sodium bicarbonate and 1 patient in the saline group. All other patients received the study mandated treatment.

Study outcomes

The primary endpoint of an increase in serum creatinine 48-96 hours following contrast exposure compared with baseline and the secondary endpoint of CI-AKI were assessed in 323/333 (97.0%) patients. Mean increase in serum creatinine was 3.1% (SD 13.6%) in the sodium bicarbonate group and 1.1% (SD 15.0%) in patients treated with saline, for a mean difference of 1.9% (95% CI -1.2 to 5.1%, p-value for non-inferiority < 0.001). The risk of CI-AKI was comparable between randomization groups, 6.7% (11/163) in patients randomized to sodium bicarbonate and 7.5% (12/160) in patients randomized to saline hydration, relative risk 0.90 (95% CI 0.41-1.98). The results on the primary endpoint and incidence of CI-AKI were homogenous for predefined subgroups of patients at high risk of CI-AKI, including those with severe CKD (Figure 2A and 2B). No significant interaction between randomization arms and the predefined subgroups was observed.

One CI-AKI patient in the sodium bicarbonate group and two CI-AKI patients randomized to saline were lost to follow-up for the endpoint of recovery of renal function. The

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│        348 patients randomized with informed consent        │
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| 173 hydration prior to contrast administration with sodium bicarbonate | 175 hydration with saline prior to and after to contrast administration |
5 withdrawn informed consent	10 withdrawn informed consent
168 included in the intention-to-treat analysis	165 included in the intention-to-treat analysis
5 with missing primary endpoint - 2 contrast procedure cancelled - 3 lost to follow-up	5 with missing primary endpoint - 1 contrast procedure cancelled - 4 lost to follow-up
163 available for analysis on primary endpoint - 158 treated according to protocol - 2 periprocedural saline hydration - 1 250 ml 0.48% instead of 1.4% sodium bicarbonate - 1 250 ml saline hydration prior to contrast exposure - 1 1000 ml saline hydration prior to contrast exposure	160 available for analysis on primary endpoint - 157 treated according to protocol - 1 periprocedural saline hydration with 1 liters - 1 periprocedural saline hydration with 3 liters - 1 duration of periprocedural hydration of 48 hours

Figure 1. Trial profile

diagnosis of CI-AKI in those three patients was based on serum creatinine values as measured after trial completion and not during their active trial participation. In addition, one CI-AKI patient randomized to saline died within two weeks following contrast exposure of pneumonia. Renal function had not recovered to the pre procedure value within two months following the development of CI-AKI in 4/10 patients randomized to sodium bicarbonate vs. 4/9 patients in the saline arm with complete follow-up, relative risk 0.90 (95% CI 0.31-2.58). No patient had a need for dialysis.

No patient randomized to sodium bicarbonate vs. 3 patients (1.9%) in the saline group developed pulmonary oedema (p =0.19). Of the 3 patients developing pulmonary oedema, hydration was prematurely stopped in 1, 2 patients received furosemide treatment, and 1 patient was admitted to the intensive care unit after successful resuscitation of a cardiac arrest due to volume overload.

Mean urinary pH was 6.0 (SD 0.9) at baseline and 6.9 (SD 1.0) at 4-6 hours following contrast exposure in the sodium bicarbonate group. For patients randomized to saline, these values were 5.8 (SD 0.7) and 6.4 (SD 0.9), respectively, (p-value for difference in mean pH at 4-6 hours following contrast administration between randomization groups < 0.001).
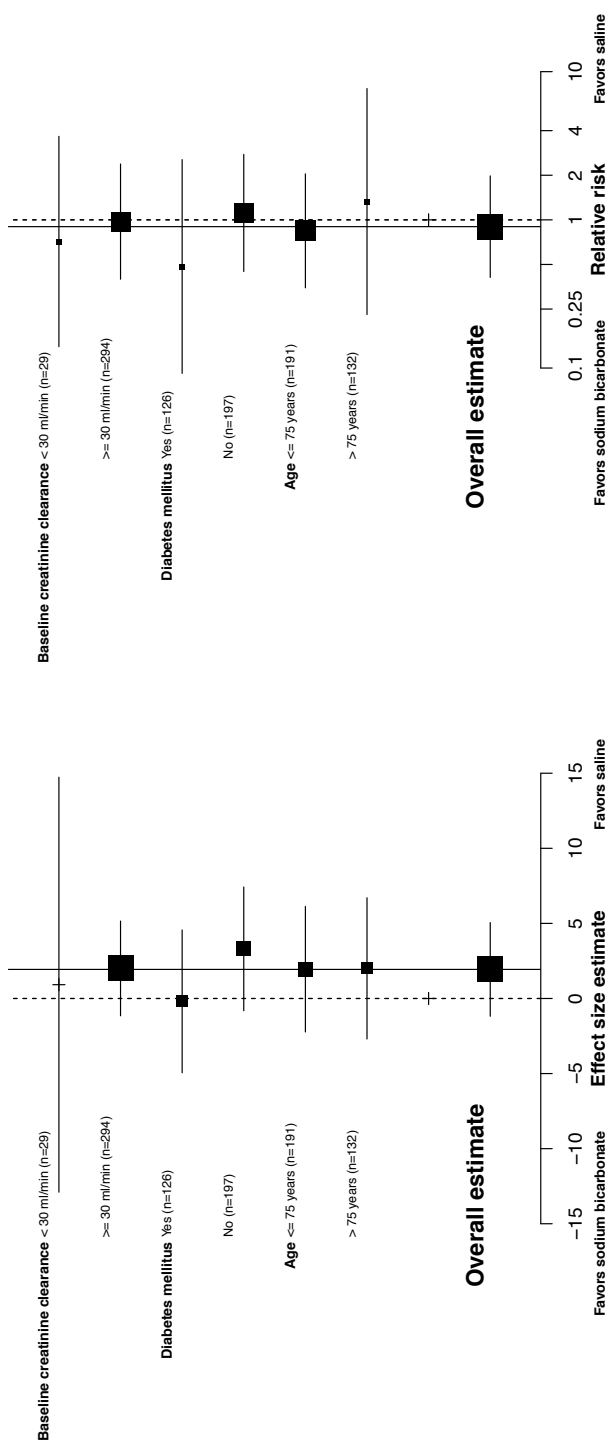
Figure 2a. Subgroup analyses on the primary outcome of a relative increase in serum creatinine 48-96 hours post intra-arterial contrast administration. Effect size is calculated as the difference in the mean relative increase in serum creatinine between both randomisation groups. The dashed line indicates the point estimate of the entire study population and the straight line indicates no effect.

Figure 2b. Subgroup analyses on the secondary outcome of risk of contrast-induced acute kidney injury, calculated as relative risk. The dashed line indicates the point estimate of the entire study population and the straight line indicates no effect.

Table 2. Estimated hospital costs per patient between randomisation and two months follow-up

	Sodium bicarbonate N = 168		Saline N = 163		P-value for difference in costs
	Volume*	Costs in $	Volume*	Costs in $	
Hospitalization related to the arterial interventional radiology/ cardiology procedure, including hydration and clinical preparation					
- N receiving hydration treatment		NA		NA	NA
- infusion fluids	0.96	6	0.96	4	< 0.001
- days prior to contrast exposure	0.52	382	0.93	677	< 0.001
- day of contrast exposure[1]	0.96	655	0.96	698	0.01
- day following contrast exposure[2]	0.36	266	0.57	417	<0.001
- ICU days due to hydration complications†	0.00	0	0.01	36	0.31
- non-ICU days due to hydration complications†	0.0	0	0.12	90	0.20
- total related to the preparation for arterial interventional radiology/cardiology procedure	*NA*	*1309*	*NA*	*1921*	*<0.001*
Other hospitalization					
- following contrast exposure[3]	2.21	1353	1.87	947	0.31
- day care	0.14	67	0.17	76	0.68
- non-ICU, AKI[4]	0.00	0	0.08	58	0.31
- non-ICU, non-AKI[4]	1.97	1441	2.11	1542	0.83
- ICU[4]	0.08	248	0.04	127	0.59
Outpatient visits					
- emergency department	0.09	21	0.10	23	0.80
- nephrology	0.32	42	0.25	33	0.38
- non-nephrology	2.84	379	3.29	439	0.22
Total costs	**NA**	**4860**	**NA**	**5295**	**0.66**

Abbreviations: ICU = intensive care unit, AKI = acute kidney injury
* Volumes represent percentage of patients or mean number of procedures, hospital days or visits
† i.e. acute heart failure due to volume overload
[1] Costs based on prices for either day-care or non-ICU days depending on duration of hospitalisation
[2] Only in those discharged on the day following the contrast procedure
[3] Excluding the day following contrast exposure in patients discharged on that following day
[4] Hospitalization not directly following contrast exposure

Healthcare cost perspective

Of the 159 outpatients randomized to sodium bicarbonate 31 (19.5%) were treated in day care compared with 4/153 (2.6%) outpatients randomized to saline hydration. Mean costs for preventive hydration and clinical preparation prior to the contrast procedure were $1309 for sodium bicarbonate vs. $1921 for saline, with a mean difference of $-612, (95% CI $-860 to -363, p-value < 0.001), Table 2. Other healthcare costs were comparable.
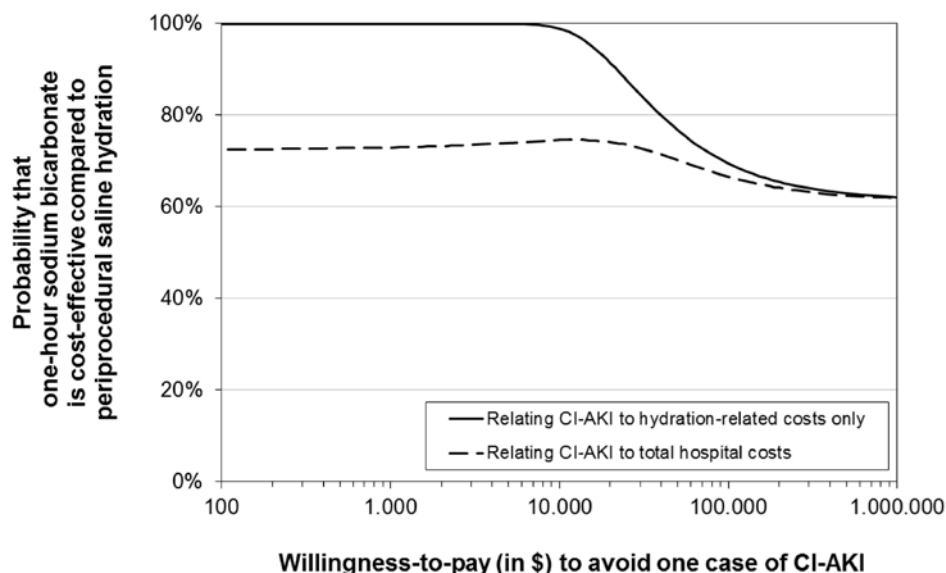
Figure 3. Whether a hydration strategy is cost-effective, depends on how much one is willing to pay (WTP) (in euro) to avoid one case of CI-AKI. This figure shows the probability that one-hour hydration with sodium bicarbonate prior to intra-arterial contrast administration is cost-effective compared with peri-procedural saline hydration.

How much one is willing to pay (WTP) to prevent one case of CI-AKI determines whether a hydration strategy is cost-effective. The probability that sodium bicarbonate hydration prior to contrast exposure is cost-effective compared with periprocedural saline hydration is shown in Figure 3. Costs and effectiveness in terms of incidences of CI-AKI are both non-significantly in favour of hydration with sodium bicarbonate. Regardless of the WTP to avoid CI-AKI and taking all hospital costs into account, hydration with sodium bicarbonate is at least 62% likely to be more cost-effective than standard saline hydration. Restricting to only the costs of hydration and clinical preparation for the contrast procedure, the estimated costs difference is larger and more certain. As a result, for a WTP of up to $10,000 to avoid one case of CI-AKI, the use of sodium bicarbonate is at least 99% likely to be more cost-effective.

DISCUSSION

Our study results show that the use of sodium bicarbonate hydration 1 hour prior to elective cardiovascular diagnostic or intervention procedures is non-inferior to periprocedural saline hydration in patients with CKD. Second, the use of sodium bicarbonate instead of saline hydration results in healthcare cost savings of $600 per patient. There-

fore, the use of this brief sodium bicarbonate regime is at least 62% likely to be more cost-effective.

Over the last decades, significant effort has focused on CI-AKI preventive measures in different patient settings (15-18). Using this large body of data, most guidelines advice the use of either periprocedural saline hydration, which often results in a patients admission for two to three days, or periprocedural sodium bicarbonate hydration administered 1 hour prior to and 6 hours following contrast administration (1, 19). Although the use of periprocedural sodium bicarbonate instead of saline hydration shortens the duration of hospitalisation, the six hours of hydration following the contrast procedure make it often unfeasible to treat patients in a day-care setting. Based on the findings of our study, the use of sodium bicarbonate can be reduced to a single bolus of 250 ml prior to contrast exposure, increasing the possibilities for day-care treatment.

With comparable efficacy of two hydration regimes, value-based care perspectives and patient convenience become of increased importance. In our study, the use of sodium bicarbonate was non-inferior to standard saline hydration, yet healthcare savings with the use of sodium bicarbonate were considerable (i.e. $600 per patient). Additionally, the proportion of patients that can be treated in day-care increased with the use of this brief sodium bicarbonate regime, improving patient convenience.

Another aspect that should be considered is safety. Although not statistically significant in our study, the use of periprocedural saline hydration was associated with pulmonary oedema, in one patient even leading to cardiac arrest and admission to the intensive care unit. This association between periprocedural saline hydration and acute heart failure has also been reported by other studies on the prevention of CI-AKI (8, 17, 20), while it has not been observed in patients treated with sodium bicarbonate, most likely due to the much smaller amount of volume expansion (8, 21).

This is the first trial to compare the use of a 1-hour pre-procedural sodium bicarbonate regime with periprocedural saline hydration in patients with CKD undergoing cardiovascular diagnostic or interventional procedures requiring intra-arterial contrast administration. A previous trial studied the efficacy of a single-bolus of sodium bicarbonate to prevent CI-AKI in patients undergoing elective coronary procedures. However, in that study, the use of the sodium bicarbonate bolus was additive to the use of periprocedural saline hydration, instead of the only preventive measure as was done in our study (22).

Our study extends prior work in the field. It had a robust design, with few drop outs on the primary outcome. The results of our study were homogenous among the predefined subgroups of patients at high risk of CI-AKI. Moreover, the 6% risk of CI-AKI found in our study corresponds well with the incidence of CI-AKI following elective cardiovascular interventional or diagnostic contrast procedures reported in literature, confirming the generalizability of our study cohort (23, 24). In addition, our results are consistent with the findings of an earlier randomized controlled trial performed by our research group

comparing the use of this short sodium bicarbonate regime to periprocedural saline hydration in patients with CKD undergoing intravenous contrast enhanced-computed tomography (8).

Some aspects of our study warrant comment. First, the majority of patients were randomized after the logistic arrangements for hospitalization planned for preventive hydration based on the use of standard saline hydration had been made. In those patients, the duration of hospitalization prior to the contrast procedure was not adjusted to the randomized treatment. As a result, healthcare cost savings associated with the use of sodium bicarbonate in our study might be underestimated. Second, our study was powered on an increase in serum creatinine and not on the risk of CI-AKI. We have chosen this primary endpoint for the following reasons: CI-AKI is a relatively rare event, which as a consequence requires a very large sample size in a trial with a non-inferiority design. Additionally, the definition of CI-AKI is often debated (1, 19). Moreover, the use of an increase in serum creatinine as a primary outcome allowed us to study small differences in contrast media induced-nephrotoxicity and has been used by several other studies (8, 21, 25-31). Third, 3/23 CI-AKI patients were lost for the endpoint of recovery of renal function. However, as the number of patients lost to follow-up was comparable for both randomization arms (1 in the sodium bicarbonate and 2 in the saline group), it is unlikely that this would have influenced the relative risk of renal function recovery comparing sodium bicarbonate with saline hydration. Fourth, our cost analysis was based on the Dutch healthcare system. Nonetheless, we expect the reduction in hospital days to be generalizable to other settings. Therefore, the health economic impact of our study results is likely to be also substantial in other countries. Fifth, there was some imbalance in the type of contrast procedure between randomization arms. However, results on the primary outcome were consistent in a sensitivity analysis correcting for kind of contrast procedure (mean difference in serum creatinine increase between study arms 2.0%, 95% -1.2 to 5.1%).

In summary, our study results show that a simple hydration regime using sodium bicarbonate administered 1 hour prior to elective cardiovascular diagnostic or interventional procedures requiring intra-arterial contrast administration is non-inferior to periprocedural saline hydration in patients with CKD. The use of this brief hydration protocol results in considerable healthcare cost savings. Further research is needed to study whether this short sodium bicarbonate regime can also be used in an emergency setting such as primary percutaneous coronary interventions, where the risk of (CI-) AKI is considered higher.

Acknowledgements

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APPENDIX

Appendix Table 1. Incidence of CI-AKI according to the AKI criteria

AKIN Stage	Sodium bicarbonate N = 163	Saline N=160	Relative risk (95% CI)
I : Increase > 26.5 µmol/L or 150% to 200% from baseline	16 (9.8)	15 (9.4)	1.0 (0.5-2.0)
II: Increase 200-300% from baseline	0 (0.0)	0 (0.0)	NA
III: Increase > 300% from baseline, or ≥ 354 µmol/L, or on RRT	0 (0.0)	0 (0.0)	NA

Abbreviation: RRT = renal replacement therapy

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