ONLINE-ONLY SUPPLEMENT

**Individual patient data meta-analysis of sodium bicarbonate versus sodium chloride for all-cause mortality hazard after coronary angiography or intervention**

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**Supplementary Statistical Methodology**

## Alternative Approaches to Outcome Analysis

We completed sensitivity analyses to assess the influence of the statistical method chosen to do the survival analysis, using several alternative approaches.

These were:

1. two-stage, log-rank test, where trial-specific estimates were pooled using the DerSimonian and Laird random-effects model[1](#_ENREF_1)
2. one-stage, non-stratified, Cox proportional hazard regression
3. one-stage, stratified-by-trial, Cox proportional hazard regression
4. one-stage, shared-frailty-by-trial, Cox proportional hazard regression.

For the secondary outcome, trial-specific treatment effect estimates were calculated as risk ratios (RRs) and 95% CIs. When the number of events in either arm (not both) equaled zero, 0·5 events were added to all four cells comprising the 2×2 contingency table. Likewise, meta-analysis for the secondary outcome was done by pooling trial-specific estimates into a combined-effect summary estimate using the Mantel–Haenszel fixed-effect model, and for sensitivity analysis, using the DerSimonian & Laird random-effects model.

To assess the influence of including each trial in the meta-analysis of both the primary and secondary outcome, we performed sensitivity analyses using the one-by-one removal method. For each summary estimate, the degree of statistical heterogeneity across trial-specific estimates was quantified by calculating the *I2* statistic.[2](#_ENREF_2)

To assess patient-level covariates of the primary outcome at each endpoint, HRs and 95% CIs were calculated for the interactions at each endpoint using a one-stage, stratified-by-trial, Cox proportional hazard regression. Whenever possible, characteristics included in interaction analyses were modeled as continuous, not categorical, variables. We applied intention-to-treat estimation throughout.

## Number Needed to Treat Calculation

Additionally, to quantify the effect of sodium bicarbonate vs. sodium chloride, we completed a number needed to treat calculation. Our calculations are listed here, where NNT = number needed to treat and ARR = absolute risk reduction.

Out of all patients administered sodium chloride, 65 of 967 patients died within one year. Therefore, the control event rate is calculated by dividing 967 by 65.

Out of all patients administered sodium bicarbonate, 36 of 987 patients died within one year. Therefore, the experimental event rate is calculated by dividing 987 by 36.

Therefore, in order to prevent one death within one year, only 32.5 patients would need to be treated with sodium bicarbonate rather than sodium chloride.

# Figure e1: Study flow diagram



10 Trials included in meta-analysis

7 Individual participant data provided

1 Meeting abstract

RCT=randomized, controlled trial.

# Figure e2: Forest plot comparing contrast-associated nephropathy

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CI=confidence interval. RR=risk ratio.

# Figure e3: Kaplan-Meier survival functions for all-cause mortality by contrast-associated nephropathy



# Figure e4: Funnel plot for publication bias



# Table e1: Electronic database search strategies

|  |  |
| --- | --- |
|  | **MEDLINE** |
| 1. | (contrast or radiocontrast OR contrast-induced).ti,ab |
| 2. | (bicarbonate or NaHCO\* OR sodium bicarbonate OR HCO\*).ti |
| 3. | 1 AND 2 |
| 4. | (kidney\* OR renal OR nephropathy).ti,ab |
| 5. | 3 AND 4 |
| 6. | (randomized OR randomised).ti,ab |
| 7. | 5 AND 6 |
| 8. | meta-analysis.ti |
| 9. | 7 NOT 8 |
|  | **Web of Science** |
| 1. | TS=((contrast) OR (radiocontrast) OR (contrast-induced)) |
| 2. | TI=((bicarbonate) OR (NaHCO\*) OR (sodium bicarbonate) OR (HCO\*)) |
| 3. | #2 AND #1 |
| 4. | TS=((kidney\*) OR (renal) OR (nephropathy)) |
| 5. | #4 AND #3 |
| 6. | TS=((randomized) OR (randomised)) |
| 7. | #6 AND #5 |
| 8. | TI=(meta-analysis) |
| 9. | #7 NOT #8 |
|  | **BIOSIS** |
| 1. | TS=((contrast) OR (radiocontrast) OR (contrast-induced)) |
| 2. | TI=((bicarbonate) OR (NaHCO\*) OR (sodium bicarbonate) OR (HCO\*)) |
| 3. | #2 AND #1 |
| 4. | TS=((kidney\*) OR (renal) OR (nephropathy)) |
| 5. | #4 AND #3 |
| 6. | TS=((randomized) OR (randomised)) |
| 7. | #6 AND #5 |
| 8. | TI=(meta-analysis) |
| 9. | #7 NOT #8 |

NaHCO3=sodium bicarbonate. ti,ab=title,abstract. TI=title. TS=topic search.

\*Wildcard search operator

# Table e2: Imputed time-to-event data for the 3 trials that did not provide individual patient datasets

|  |  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  | **Dead** | | **Censored** | | **Bicarbonate** | | **Chloride** | | **Participants** | | **Days imputed** | |
| **Brar 2008**[**3**](#_ENREF_3) | | ● | | ○ | | ● | | ○ | | 3 | | 30 \* | |
|  | | ● | | ○ | | ● | | ○ | | 1 | | 180 \* | |
|  | | ● | | ○ | | ○ | | ● | | 3 | | 30 \* | |
|  | | ● | | ○ | | ○ | | ● | | 4 | | 180 † | |
|  | | ○ | | ● | | ● | | ○ | | 171 | | 180 † | |
|  | | ○ | | ● | | ○ | | ● | | 171 | | 180 † | |
| **Masuda 2008**[**4**](#_ENREF_4) | | ● | | ○ | | ● | | ○ | | 1 | | 335 ‡ | |
|  | | ● | | ○ | | ○ | | ● | | 1 | | 30 ‡ | |
|  | | ● | | ○ | | ○ | | ● | | 1 | | 90 ‡ | |
|  | | ● | | ○ | | ○ | | ● | | 1 | | 150 ‡ | |
|  | | ○ | | ● | | ● | | ○ | | 28 | | 365 § | |
|  | | ○ | | ● | | ○ | | ● | | 27 | | 365 § | |
| **Ueda 2011**[**5**](#_ENREF_5) | | ● | | ○ | | ● | | ○ | | 2 | | 23 ¶ | |
|  | | ● | | ○ | | ○ | | ● | | 3 | | 21 ¶ | |
|  | | ○ | | ● | | ● | | ○ | | 28 | | 23 ¶ | |
|  | | ○ | | ● | | ○ | | ● | | 27 | | 21 ¶ | |

●=Yes. ○=No. Bicarbonate=Sodium bicarbonate. Chloride=Sodium chloride.

\*Based on the number of events (numerators) in each arm reported for 30-day and 6-month all-cause mortality.

†Based on the number of maximum follow-up period (6 months) described in the original report, calculated as the total number of participants randomized to each arm minus the number of participants that died within the first 30 days after randomization in each arm respectively.

‡Based on Figure 1 from the original report of Masuda et al. 2008 (see page 1612), which is a Kaplan-Meier plot where the y-axis was survival (as a proportion of 1·00, where 1·00=100% survival), and the x-axis was time from randomization (in months). By visually inspecting the survival functions for each study arm, we estimated the corresponding x-axis value for each death. We then derived the number of days each value corresponded to by multiplying by the conversion factor of 30·42 days per month, and then rounded this value to the nearest number of days. Based on this approach, the estimated x-axis values for deceased participants (going down from the first row for this trial in the above table) were 11 months (or 335 days), 1 month (or 30 days), 3 months (or 90 days), and 5 months (or 150 days).

§Based on Figure 1 from the original report of Masuda et al. 2008 (see page 1612), which is a Kaplan-Meier plot where the y-axis was survival (as a proportion of 1·00, where 1·00=100% survival), and the x-axis was time from randomization (in months). By visually inspecting the plot, as well as the corresponding text from the methods and results sections of the report, we determined the maximum follow-up was 1 year (365 days). We derived the number of participants censored at 365 days for each arm by calculating the total number of participants randomized less the number the died in each arm respectively.

¶Based on the values for each arm for the mean hospital stay (in days), (sodium bicarbonate: 22·8 ± 17·9 days; sodium chloride: 21‚4 ± 19·6 days) rounded to the nearest day, as reported in Table 2 (see page 1166) of the original report. It was determined that the value provided was the mean ± standard deviation from the description provided in the methods section of the text, which states that "Continuous data are expressed as the mean ± SD." In addition, the results section states that all 5 deaths in this trial occurred "in-hospital."

# Table e3: Sensitivity analysis for primary outcome, all-cause mortality hazard

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
| **1 year** | | **Hazard ratio** | **(95% CI)** | | **p value** | **I2** |
| Total, 2-stage, stratified-by-trial, log-rank test, fixed effect[3-12](#_ENREF_3) | | 0·61 | | (0·41–0·89) | 0·011 | 0% |
|  | Excluding BOSS 2014[6](#_ENREF_6) | 0·71 | | (0·46–1·08) | 0·11 | 0% |
|  | Excluding Brar 2008[3](#_ENREF_3) | 0·61 | | (0·41–0·92) | 0·02 | 4% |
|  | Excluding Gomes 2012[7](#_ENREF_7) | 0·58 | | (0·38–0·87) | 0·009 | 0% |
|  | Excluding Klima 2012[12](#_ENREF_12) | 0·61 | | (0·41–0·90) | 0·01 | 4% |
|  | Excluding Maioli 2008[8](#_ENREF_8) | 0·55 | | (0·36–0·84) | 0·005 | 0% |
|  | Excluding Maioli 2011[9](#_ENREF_9) | 0·61 | | (0·40–0·92) | 0·02 | 4% |
|  | Excluding Masuda 2008[4](#_ENREF_4) | 0·62 | | (0·42–0·92) | 0·02 | 1% |
|  | Excluding Recio-Mayoral 2007[10](#_ENREF_10) | 0·63 | | (0·43–0·94) | 0·02 | 0% |
|  | Excluding Thayssen 2014[11](#_ENREF_11) | 0·54 | | (0·36–0·82) | 0·003 | 0% |
|  | Excluding Ueda 2011[5](#_ENREF_5) | 0·64 | | (0·43–0·94) | 0·02 | 0% |
|  | Excluding confounded comparisons[9](#_ENREF_9),[10](#_ENREF_10) | 0·64 | | (0·42–0·98) | 0·04 | 8% |
|  | Excluding non individual-patient data trials[3-5](#_ENREF_3) | 0·66 | | (0·43–1·01) | 0·05 | 2% |
| Total, 2-stage, stratified-by-trial, log-rank test, random effect[3-12](#_ENREF_3) | | 0·61 | | (0·41–0·89) | 0·011 | 0% |
| Total, 1-stage, non-stratified, Cox proportional hazard model[3-11](#_ENREF_3) | | 0·65 | | (0·44–0·95) | 0·027 | .. |
| Total, 1-stage, stratified-by-trial, Cox proportional hazard model[3-11](#_ENREF_3) | | 0·60 | | (0·41–0·90) | 0·012 | .. |
| Total, 1-stage, shared frailty by trial, Cox proportional hazard model[3-11](#_ENREF_3) | | 0·64 | | (0·44–0·95) | 0·026 | .. |

CI=confidence interval.

# Table e4: Sensitivity analysis for the secondary outcome, contrast-associated nephropathy risk

|  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  | | **Sodium bicarbonate** | | |  | **Sodium chloride** | | | | **Risk ratio** | **(95% CI)** | | **p value** | **I2** |
|  | | Events | (%) | Total |  | Events | | (%) | Total |  |  | |  |  |
| Total, 2-stage, fixed-effect model[3-12](#_ENREF_3) | | 155 | (11) | 1381 |  | 207 | (15) | | 1383 | 0·75 | | (0·62–0·91) | 0·003 | 44% |
|  | Excluding BOSS 2014[6](#_ENREF_6) | 152 | (12) | 1235 |  | 204 | (16) | | 1238 | 0·75 | | (0·62–0·91) | 0·003 | 50% |
|  | Excluding Brar 2008[3](#_ENREF_3) | 134 | (11) | 1206 |  | 183 | (15) | | 1205 | 0·73 | | (0·60–0·90) | 0·003 | 50% |
|  | Excluding Gomes 2012[7](#_ENREF_7) | 146 | (12) | 1231 |  | 198 | (16) | | 1232 | 0·74 | | (0·61–0·90) | 0·003 | 49% |
|  | Excluding Klima 2012[12](#_ENREF_12) | 151 | (11) | 1344 |  | 205 | (15) | | 1348 | 0·74 | | (0·61–0·90) | 0·002 | 46% |
|  | Excluding Maioli 2008[8](#_ENREF_8) | 130 | (11) | 1131 |  | 178 | (14) | | 1131 | 0·73 | | (0·59–0·89) | 0·003 | 49% |
|  | Excluding Maioli 2011[9](#_ENREF_9) | 137 | (11) | 1231 |  | 173 | (15) | | 1233 | 0·79 | | (0·65–0·98) | 0·03 | 40% |
|  | Excluding Masuda 2008[4](#_ENREF_4) | 153 | (11) | 1352 |  | 197 | (15) | | 1353 | 0·78 | | (0·64–0·94) | 0·01 | 36% |
|  | Excluding Recio-Mayoral 2007[10](#_ENREF_10) | 154 | (12) | 1325 |  | 195 | (15) | | 1328 | 0·79 | | (0·65–0·96) | 0·02 | 26% |
|  | Excluding Thayssen 2014[11](#_ENREF_11) | 85 | (8) | 1023 |  | 131 | (13) | | 1026 | 0·65 | | (0·50–0·84) | 0·001 | 43% |
|  | Excluding Ueda 2011[5](#_ENREF_5) | 153 | (11) | 1351 |  | 199 | (15) | | 1353 | 0·77 | | (0·63–0·94) | 0·008 | 41% |
|  | Excluding confounded comparisons[9](#_ENREF_9),[10](#_ENREF_10) | 136 | (12) | 1175 |  | 161 | (14) | | 1178 | 0·85 | | (0·69–1·05) | 0·12 | 11% |
|  | Excluding non-IPD trials[3-5](#_ENREF_3) | 130 | (11) | 1147 |  | 165 | (14) | | 1145 | 0·79 | | (0·64–0·97) | 0·03 | 39% |
| Total, 2-stage, random effects model[3-12](#_ENREF_3) | | 155 | (11) | 1381 |  | 207 | (15) | | 1383 | 0·72 | | (0·52–0·99) | 0·046 | 44% |

CI=confidence interval. IPD=individual patient data.

# Table e5: Deceased participant characteristics

|  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  | | Sodium bicarbonate (№=73) | | |  | Sodium chloride (№=94) | | |
|  | | Events or mean | | Total |  | Events or mean | | Total |
| **Follow-up (days)** | |  |  |  |  |  |  |  |
|  | Mean (SD) | 501 | (597) | 73 |  | 431 | (598) | 94 |
|  | Median (IQR) | 289 | (23–739) | 73 |  | 120 | (21–755) | 94 |
| **All-cause mortality (№)** | |  |  |  |  |  |  |  |
|  | 0 to 30 days | 23 | (32%) | 73 |  | 36 | (38%) | 94 |
|  | 30 days to 6 months | 11 | (15%) | 73 |  | 22 | (23%) | 94 |
|  | 6 months to 1 year | 8 | (11%) | 73 |  | 7 | (7%) | 94 |
| **Cause-of-death (№)** | |  |  |  |  |  |  |  |
|  | Renal failure | 0 | (0%) | 73 |  | 3 | (3%) | 94 |
|  | Cardiovascular | 32 | (44%) | 73 |  | 32 | (36%) | 94 |
|  | Cerebrovascular | 2 | (3%) | 73 |  | 4 | (4%) | 94 |
|  | Unknown | 27 | (37%) | 73 |  | 37 | (39%) | 94 |
|  | Sepsis | 3 | (4%) | 73 |  | 1 | (1%) | 94 |
|  | Multi-organ failure | 0 | (0%) | 73 |  | 2 | (2%) | 94 |
|  | Respiratory failure | 1 | (1%) | 73 |  | 2 | (2%) | 94 |
|  | Aspiration pneumonia | 0 | (0%) | 73 |  | 2 | (2%) | 94 |
|  | Procedural complications | 3 | (4%) | 73 |  | 4 | (4%) | 94 |
|  | Cancer | 0 | (0%) | 73 |  | 2 | (2%) | 94 |
|  | Other | 2 | (3%) | 73 |  | 0 | (0%) | 94 |
| **Age (years)** | |  |  |  |  |  |  |  |
|  | Mean (SD) | 76 | (9) | 66 |  | 74 | (9) | 81 |
|  | Median (IQR) | 77 | (72–82) | 66 |  | 77 | (67–82) | 81 |
| **Sex (№)** | |  |  |  |  |  |  |  |
|  | Male | 41 | (62%) | 66 |  | 55 | (68%) | 81 |
|  | Female | 25 | (38%) | 66 |  | 26 | (32%) | 81 |
| **Body-mass index (kg/m2)** | |  |  |  |  |  |  |  |
|  | Mean (SD) | 26 | (4) | 59 |  | 26 | (4) | 60 |
|  | Median (IQR) | 35 | (30–42) | 59 |  | 26 | (24–29) | 60 |
| **Medical history (№)** | |  |  |  |  |  |  |  |
|  | Diabetes mellitus | 19 | (29%) | 66 |  | 30 | (37%) | 81 |
|  | Hypertension | 41 | (63%) | 65 |  | 56 | (69%) | 81 |
|  | Congestive heart failure | 26 | (43%) | 61 |  | 42 | (54%) | 78 |
| **Left ventricular ejection fraction (%)** | |  |  |  |  |  |  |  |
|  | Mean (SD) | 38 | (16) | 49 |  | 35 | (12) | 58 |
|  | Median (IQR) | 41 | (30–50) | 49 |  | 35 | (30–42) | 58 |
| **Mehran risk (score)** | |  |  |  |  |  |  |  |
|  | Mean (SD) | 12 | (4) | 44 |  | 12 | (4) | 60 |
|  | Median (IQR) | 11 | (9–15) | 44 |  | 11 | (9–13) | 60 |
| **Contrast volume (mL)** | |  |  |  |  |  |  |  |
|  | Mean (SD) | 182 | (98) | 52 |  | 171 | (129) | 73 |
|  | Median (IQR) | 165 | (115–210) | 52 |  | 140 | (80–200) | 73 |
| **Serum creatinine (mg/dL)** | |  |  |  |  |  |  |  |
|  | Mean (SD) | 1·4 | (0·5) | 66 |  | 1·4 | (0·4) | 81 |
|  | Median (IQR) | 1·4 | (1·0–1·7) | 66 |  | 1·3 | (1·1–1·6) | 81 |
|  | |  |  |  |  |  |  |  |
|  | |  |  |  |  |  |  |  |
|  | | Sodium Bicarbonate (№=73) | | |  | Sodium chloride (№=94) | | |
|  | | Events or mean | | Total |  | Events or mean | | Total |
| **Estimated GFR (mg/min per 1·73 m2)** | |  |  |  |  |  |  |  |
|  | Mean (SD) | 48 | (23) | 66 |  | 49 | (16) | 80 |
|  | Median (IQR) | 40 | (32–57) | 66 |  | 42 | (33–59) | 80 |
| **Co-intervention (№)** | |  |  |  |  |  |  |  |
|  | N-acetylcysteine | 42 | (62%) | 69 |  | 54 | (62%) | 87 |

GFR=glomerular filtration rate. №=number of participants. SD=standard deviation. IQR=interquartile range. To convert units of serum creatinine from mg/dL to μmol/L, multiply by 88·4.

# Table e6: Meta-analyses of sodium bicarbonate versus sodium chloride for contrast-associated nephropathy

|  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  | **Trials** | **N\*** | **FE** | **RE** | **RR** | **OR** | **Effect** | **(95% CI)** | **p value** | **I2** |
| Jang 2012[13](#_ENREF_13) | 19 | 3609 | ○ | ● | ○ | ● | 0·56 | (0·36–0·86) | 0·008 | 58% |
| Kunadian 2011[14](#_ENREF_14) | 7 | 1509 | ○ | ● | ○ | ● | 0·33 | (0·16–0·69) | 0·003 | 65% |
| Trivedi 2010[15](#_ENREF_15) | 10 | 1090 | ● | ○ | ○ | ● | 0·57 | (0·38–0·85) | .. | 39% |
| Brar 2009[16](#_ENREF_16) † | 3 | 1145 | ○ | ● | ● | ○ | 0·85 | (0·63–1·16) | .. | 0% |
| Brar 2009[16](#_ENREF_16) ‡ | 12 | 1145 | ○ | ● | ● | ○ | 0·50 | (0·27–0·93) | .. | 56% |
| Brown 2009[17](#_ENREF_17) | 10 | 1594 | ○ | ● | ● | ○ | 0·65 | (0·40–1·05) | 0·08 | 55% |
| Hoste 2009[18](#_ENREF_18) | 18 | 3055 | ○ | ● | ● | ○ | 0·66 | (0·45–0·95) | 0·03 | 52% |
| Kanbay 2009[19](#_ENREF_19) | 17 | 2448 | ○ | ● | ● | ○ | 0·54 | (0·36–0·83) | .. | .. |
| Meier 2009[20](#_ENREF_20) | 17 | 2633 | ○ | ● | ○ | ● | 0·52 | (0·34–0·80) | 0·003 | 48% |
| Navaneethan 2009[21](#_ENREF_21) | 12 | 1652 | ○ | ● | ○ | ● | 0·46 | (0·26–0·82) | 0·008 | 56% |
| Zoungas 2009[22](#_ENREF_22) | 23 | 3563 | ○ | ● | ● | ○ | 0·62 | (0·45–0·86) | .. | 49% |
| Joannidis 2008[23](#_ENREF_23) | 9 | 1843 | ○ | ● | ○ | ● | 0·45 | (0·26–0·79) | .. | 57% |
| Hogan 2008[24](#_ENREF_24) | 7 | 1307 | ○ | ● | ● | ○ | 0·37 | (0·18–0·74) | 0·005 | .. |

●=Yes. ○=No. CI=confidence interval. FE=fixed-effect. RE=random-effects. RR=risk ratio. OR=odds ratio.

\*Note: these effect estimates are reportedly based on various distinct treatment effect estimators (eg, intention-to-treat, per-protocol). In addition, the reported estimator was not always the one actually used to inform the calculations that yielded these effect estimates. As such, these effect estimates should be interpreted with caution and none should be quoted as presented without further reference to the original records, with an in depth analysis of the methods and results used therein. This table is instead meant to give a general sense of what aggregate data meta-analyses of this topic have reported.

†Large trials

‡Small trials

# References: reference list for sources cited throughout this supplementary appendix

1. 1. DerSimonian R, Laird N. Meta-analysis in clinical trials. *Controlled clinical trials.* 1986;7(3):177–188.
2. 2. Higgins JP, Thompson SG, Deeks JJ, Altman DG. Measuring inconsistency in meta-analyses. *Bmj.* 2003;327(7414):557–560.
3. 3. Brar SS, Shen AY, Jorgensen MB, et al. Sodium bicarbonate vs sodium chloride for the prevention of contrast medium-induced nephropathy in patients undergoing coronary angiography: a randomized trial. *JAMA.* 2008;300(9):1038–1046.
4. 4. Masuda M, Yamada T, Okuyama Y, et al. Sodium bicarbonate improves long-term clinical outcomes compared with sodium chloride in patients with chronic kidney disease undergoing an emergent coronary procedure. *Circulation journal : official journal of the Japanese Circulation Society.* 2008;72(10):1610–1614.
5. 5. Ueda H, Yamada T, Masuda M, et al. Prevention of contrast-induced nephropathy by bolus injection of sodium bicarbonate in patients with chronic kidney disease undergoing emergent coronary procedures. *The American journal of cardiology.* 2011;107(8):1163-1167.
6. 6. Solomon R. Evaluation of Sodium Bicarbonate to Reduce the Incidence of Contrast Induced Chronic Kidney Injury in Patients With Kidney Disease (BOSS). Paper presented at: 25th Annual Symposium of the Transcatheter Cardiovascular Therapeutics; 29 Oct 2013, 2013; San Francisco, CA.
7. 7. Gomes VO, Lasevitch R, Lima VC, et al. Hydration with sodium bicarbonate does not prevent contrast nephropathy: a multicenter clinical trial. *Arquivos Brasileiros de Cardiologia.* 2012;99(6):1129–1134.
8. 8. Maioli M, Toso A, Leoncini M, et al. Sodium bicarbonate versus saline for the prevention of contrast-induced nephropathy in patients with renal dysfunction undergoing coronary angiography or intervention. *Journal of the American College of Cardiology.* 2008;52(8):599–604.
9. 9. Maioli M, Toso A, Leoncini M, Micheletti C, Bellandi F. Effects of hydration in contrast-induced acute kidney injury after primary angioplasty: a randomized, controlled trial. *Circulation. Cardiovascular interventions.* 2011;4(5):456-462.
10. 10. Recio-Mayoral A, Chaparro M, Prado B, et al. The reno-protective effect of hydration with sodium bicarbonate plus N-acetylcysteine in patients undergoing emergency percutaneous coronary intervention: the RENO Study. *Journal of the American College of Cardiology.* 2007;49(12):1283–1288.
11. 11. Thayssen P, Lassen JF, Jensen SE, et al. Prevention of contrast-induced nephropathy with N-acetylcysteine or sodium bicarbonate in patients with ST-segment-myocardial infarction: a prospective, randomized, open-labeled trial. *Circulation. Cardiovascular interventions.* 2014;7(2):216-224.
12. 12. Klima T, Christ A, Marana I, et al. Sodium chloride vs. sodium bicarbonate for the prevention of contrast medium-induced nephropathy: a randomized controlled trial. *European heart journal.* 2012;33(16):2071–2079.
13. 13. Jang JS, Jin HY, Seo JS, et al. Sodium bicarbonate therapy for the prevention of contrast-induced acute kidney injury – a systematic review and meta-analysis. *Circulation journal : official journal of the Japanese Circulation Society.* 2012;76(9):2255–2265.
14. 14. Kunadian V, Zaman A, Spyridopoulos I, Qiu W. Sodium bicarbonate for the prevention of contrast induced nephropathy: a meta-analysis of published clinical trials. *European journal of radiology.* 2011;79(1):48–55.
15. 15. Trivedi H, Nadella R, Szabo A. Hydration with sodium bicarbonate for the prevention of contrast-induced nephropathy: a meta-analysis of randomized controlled trials. *Clinical nephrology.* 2010;74(4):288-296.
16. 16. Brar SS, Hiremath S, Dangas G, Mehran R, Brar SK, Leon MB. Sodium bicarbonate for the prevention of contrast induced-acute kidney injury: a systematic review and meta-analysis. *Clinical journal of the American Society of Nephrology : CJASN.* 2009;4(10):1584–1592.
17. 17. Brown JR, Block CA, Malenka DJ, O'Connor GT, Schoolwerth AC, Thompson CA. Sodium bicarbonate plus N-acetylcysteine prophylaxis: a meta-analysis. *JACC. Cardiovascular interventions.* 2009;2(11):1116–1124.
18. 18. Hoste EA, De Waele JJ, Gevaert SA, Uchino S, Kellum JA. Sodium bicarbonate for prevention of contrast-induced acute kidney injury: a systematic review and meta-analysis. *Nephrology, dialysis, transplantation : official publication of the European Dialysis and Transplant Association - European Renal Association.* 2010;25(3):747–758.
19. 19. Kanbay M, Covic A, Coca SG, Turgut F, Akcay A, Parikh CR. Sodium bicarbonate for the prevention of contrast-induced nephropathy: a meta-analysis of 17 randomized trials. *International urology and nephrology.* 2009;41(3):617–627.
20. 20. Meier P, Ko DT, Tamura A, Tamhane U, Gurm HS. Sodium bicarbonate-based hydration prevents contrast-induced nephropathy: a meta-analysis. *BMC medicine.* 2009;7:23.
21. 21. Navaneethan SD, Singh S, Appasamy S, Wing RE, Sehgal AR. Sodium bicarbonate therapy for prevention of contrast-induced nephropathy: a systematic review and meta-analysis. *American journal of kidney diseases : the official journal of the National Kidney Foundation.* 2009;53(4):617–627.
22. 22. Zoungas S, Ninomiya T, Huxley R, et al. Systematic review: sodium bicarbonate treatment regimens for the prevention of contrast-induced nephropathy. *Annals of internal medicine.* 2009;151(9):631–638.
23. 23. Joannidis M, Schmid M, Wiedermann CJ. Prevention of contrast media-induced nephropathy by isotonic sodium bicarbonate: a meta-analysis. *Wiener klinische Wochenschrift.* 2008;120(23-24):742–748.
24. 24. Hogan SE, L'Allier P, Chetcuti S, et al. Current role of sodium bicarbonate-based preprocedural hydration for the prevention of contrast-induced acute kidney injury: a meta-analysis. *American heart journal.* 2008;156(3):414–421.