Author’s response to reviews

Title: Guideline adherence for identification and hydration of high-risk hospital patients for contrast-induced nephropathy

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Author’s response to reviews: see over
Reviewers' comments:

Reviewer #1

1. Cardiology department is used as a reference category in the analysis on guidelines adherence in terms of hydration of high-risk patients. I don’t think this is a proper reference category as cardiology patients are at high risk of acute heart failure due to volume expansion. Cardiologists might therefore be reluctant to use hydration in patients who are at a delicate balance between dehydration vs acute heart failure. I would therefore like to ask the authors to redo the analysis, using another reference category.

   Response 1. We revised the analysis, by selecting internal medicine as reference category instead of cardiology department. Thereby, the results for the association between department and hydration of high-risk patients changed somewhat, as some statistically significant associations were no longer statistically significant (eg ‘other departments’). We processed this in the results, table 3 and the discussion section.

2. The explanation on eGFR can be deleted. However, the authors should add information on the formula used to assess eGFR. Did they use MDRD, CKD-EPI, CG? Was this the same for all hospitals?

   Response 2. We deleted the explanation on eGFR from the Methods. Information about the formula for eGFR included in the guideline is added. We assume all hospitals have used this formula for eGFR, but no information is available about the actual appliance of this formula by the different hospitals as we acquired the eGFR from the patient records.

   Page 3: “Following the guideline, the eGFR should be calculated with the MDRD formula, using information of the creatinine concentration, age and sex [13].”

3. The authors state that all measurements on eGFR in the past twelve months were designated as eGFR value. What do they mean by this? I assume that they used the most recent eGFR value to classify patients as high, or non-high risk?

   Response 3. The most recent eGFR value was used to assess whether the patient was at high risk for CIN. If the measurement of the eGFR value was longer then twelve months ago, this measurement could not be used. We added an explanation to the methods.

   Page 3: “The most recent measurement was used to assess the eGFR value and to define whether the patient was at high-risk for CIN, with a maximum durability of the eGFR measurement of 12 months before contrast administration.”

4. Contrast volume > 150 ml was a risk factor of CI-AKI according to the safety program. How can physicians responsible for CI-AKI prevention have this knowledge prior to the contrast procedure?

   Response 4. The risk factors were included in the checklist and were determined in the records. If the contrast volume was not known before contrast administration, it was not registered in the record. Presumably some risk factors included in the guideline are not known for the applicant physician. We added a sentence to the discussion.

   Page 7: “Possibly, not all risk factors included in the guideline are known when a physician applied contrast administration”.

5. Could the authors also provide information on the mean costs per patient for this safety program (creatinine measurements, hydration, etc)

   Response 5. Unfortunately, costs were not included in this study and cannot be reported.

6. The risk of CI-AKI is thought to be higher after intra-arterial contrast (such as for PTA, PCI, etc) compared with intravenous contrast injections (as used for CT-scans). This might influence guideline adherence. Could the authors show the results on guideline adherence for both groups, individually?

   Response 6. We did not collect data about the method of contrast administration. Therefore, we cannot show the results separately for different methods of contrast administration.
7. To provide further insight on guideline (non)adherence, it would be helpful to present the results split out for inpatients, outpatients, and patients presenting to an emergency department. This is probably taken into account in the multi-level analysis, but break-up of the results would be valuable. **Response 7.** It is not possible to show the results separately for inpatients, outpatients and the emergency department, as only admission department was filled in on the checklist. Outpatients were analyzed in the category ‘no admission/unknown’. A separate question was used to define the acuteness of admission and this variable was used as potential factor associated with hydration.

8. The positive association between admission to day-care department and hydration seems to be the result of the safety program, as outpatients electively scheduled for CT at high-risk of CI-AKI would probably receive hydration at day-care departments. **Response 8.** This may indeed be the explanation of the association between day admission and hydration. We added this explanation to the discussion.

Page 7: “This positive association seems to be the result of the Safety Program, as outpatients at high-risk for CIN scheduled for contrast administration would probably be hydrated at the day admission department”

9. The authors stress that patients not admitted were less often hydrated. How is it possible to give a patient intravenous volume expansion (hydration) when he/she is not admitted to either day care or another department? Same applies for the sentence in the discussion stressing that if a patient was not admitted, 1/3 was hydrated. **Response 9.** The most plausible explanation for the low hydration rate is indeed the lack of time if a patient is not admitted. This was already stated in the discussion, but we adapted the text to state this more firmly.

Page 6: “This low hydration rate seems to be explained mainly by the lack of time when a patient is visiting the hospital for one day, which was mostly an outpatient clinic visit. If patients had to undergo contrast administration acutely, there is insufficient time for hydration.”

10. Please stress that reference 18 was an observational cohort study, not a randomized trial. **Response 10.** Reference 18 was a non-randomized controlled trial, which may influence the interpretation of the results. Therefore, we added this information to the discussion.

Page 7: “However, the usefulness of hydrating lower risk patients for CIN (based on the absence of diabetes mellitus, age >65 year, sCr >1.4 mg/dl) to prevent the incidence of CIN was suggested in a non-randomized controlled trial.”

11. The authors claim that prevention of CIN by infusion of saline or sodium bicarbonate is of importance. However, to my knowledge, there are no randomized placebo controlled studies demonstrating the risks of dialysis and other complications associated with CI-AKI to be lowered by the use of saline (or bicarbonate) versus no hydration. These endpoints reflect the true clinical importance of CI-AKI prevention. **Response 12.** The evidence of the effects of hydration is rare and most studies did not include a control group. As stated in the discussion, only two randomized controlled trials were performed to investigate the effect on developing CIN. The effect on risks of dialysis and other complications were not included in these studies. We added a sentence to the introduction to state that the effect was investigated in only a few studies on developing CIN.

Page 2: “The effect of hydration on the reduction of developing CIN was shown in a few studies [10-15], but only two of these studies included a control group [11,15].”

12. Other points of the safety program were withholding nephrotoxic medication and the use of low contrast volumes. Do the authors know anything about adherence to these guideline recommendations? **Response 12.** We only evaluated the adherence to the prevention method hydration described in the guideline. The other two measures (advising on medication and reducing dose of contrast administration) were not evaluated. We explicated this in the methods.
Page 3: “Besides hydration, two other prevention measures are mentioned in the guideline, including advising on medication and reducing dose of contrast administration, but these prevention measures are not evaluated in the present study.”

13. How many patients were readmitted for complications of hydration (i.e. acute heart failure)?
Response 13. We only evaluated the adherence to the guideline for prevention of CIN, and did not measure clinical outcomes in this study. Therefore, we do not have information about readmissions for complications.

Discretional Revisions:
14. Although the introduction section is already rather long, the authors would strongly improve this section by stressing why it is of clinical importance to describe adherence to their studied safety program.
Response 14. The importance of adherence to clinical guidelines was stated in earlier studies. We added these references to the introduction.

Page 2: “Implementation of guidelines has been proposed to reduce inappropriate care, increase clinical efficiency and better control of health care spending [19,20].”

15. Within the Dutch society, top clinical hospital is a common term. However, I doubt whether colleagues from other parts of the world understand this term.
Response 15. We think tertiary teaching hospital is probably a better international term for this type of hospital. We changed this in the text.

16. First line of the paragraph entitled ‘Guideline adherence to prevent CIN’ seems to miss a verb.
Response 16. Indeed a verb is missing and is now added to the text.

Page 3: “The adherence to the guideline for preventing CIN was determined by evaluating to what extent high-risk patients for CIN were identified and hydrated.”

17. Why should assessing and registration of eGFR and subsequent interventions be reported in medical records other than for study purposes?
Response 17. Information about the eGFR, and subsequent interventions is not only important to register for the performance indicator, but is also important for colleagues to have insight in the prior process. If information about hydration is not registered, this may have impact on patient safety caused by an increased risk of under- or overtreatment. We added a sentence to the discussion.
Page 8: However, if hydration was not registered, this information could similarly not be found by other healthcare providers, “which may have a negative effect on patient safety caused by an increased risk of under- or overtreatment.”

Reviewer #2

The paper Guideline adherence for identification and hydration of high-risk hospital patients for contrast induced nephropathy is interesting and is well written. Statistics should be checked by statistician. Otherwise I have no comments to the paper which is suitable to be published in present form.
Response. The statistics were performed and checked by a statistician.