Letter to the Editor

Intravenous hydration according to current guidelines in the prevention of contrast induced nephropathy—the AMACING trial

Estelle C. Nijssen, Patty J. Nelemans, Roger J. Rennenberg, Brigitte A. Essers, Marga M. Janssen, Marja A. Vermeeren, Vincent van Ommen, Joachim E. Wildberger

Maastricht University Medical Center, Maastricht, The Netherlands

Correspondence to: Estelle Claire Nijssen. Maastricht University Medical Centre, P. Debyelaan 25, 6229 HX Maastricht, The Netherlands. Email: cin.groep@mumc.nl.

Provenance: This is an invited Letter to the Editor commissioned by Section Editor Dr. Zhongheng Zhang (Department of Emergency Medicine, Sir Run-Run Shaw Hospital, Zhejiang University School of Medicine, Hangzhou, China).

Response to: Raje V, Feldman G, Jovin IS. Diagnosing and treating contrast-induced acute kidney injury in 2017. J Thorac Dis 2017;9:1443-5.

Sato A, Hoshi T, Aonuma K. No prophylaxis is non-inferior and cost-saving to prophylactic intravenous hydration in preventing contrast-induced nephropathy on requiring iodinated contrast material administration. J Thorac Dis 2017;9:1440-2.

Submitted May 29, 2017. Accepted for publication Jun 05, 2017.

doi: 10.21037/jtd.2017.06.80

View this article at: http://dx.doi.org/10.21037/jtd.2017.06.80

We thank Vikram Raje and Akira Sato and colleagues for their interest in our work. To put the AMACING trial into perspective, the guideline on contrast induced nephropathy (CIN) is one of ten measures to increase patient safety in the Netherlands. Since their introduction and to date, the ten measures have been imposed on hospitals quite strictly, and compliance to these is part of the annual hospital quality assessment carried out by government instances. However, the intravenous hydration to prevent CIN was introduced without its effect having been proven, and its implementation incurs risk of clinical complications as well as increased health care costs.

The aim of the AMACING trial was to evaluate the current guidelines and it was designed to that end (1). The core question was not about the absolute risk of CIN, but rather about the clinical and cost efficacy of prophylactic intravenous hydration according to current guidelines in the prevention of CIN.

The guidelines specify prophylactic intravenous (iv) hydration for all patients with an eGFR <45 mL/min/1.73 m^2, and for all patients with an eGFR <60 mL/min/1.73 m^2 in combination with diabetes or >1 risk factor (age >75 years, cardiovascular disease, nephrotoxic medication or anaemia). We included exactly this patient population in the AMACING trial, except for those with an eGFR <30 mL/min/1.73 m^2 (prevalence ca. 0.5%). The latter were excluded as a safety precaution because incidences of CIN in absence of prophylaxis were unknown, and not giving prophylaxis even more of a controversial topic at the time than it is now. During the two-year inclusion period of the AMACING trial we had to exclude only 157 patients because of an eGFR <30 mL/min/1.73 m^2.

The best way to assure external validity is to conduct the study in a setting that is as close as possible to the one that the program would operate in in clinical routine, and to include those patients that would typically use that setting. We did not interfere with patients' drinking or aspects of daily clinical practice, other than withholding intravenous hydration in the 'no prophylaxis' randomized arm. Furthermore, we included exactly the patient population for which the guidelines recommend prophylactic intravenous hydration with normal saline (2). We excluded all patients with an EGFR lower than 30 mL/min/1.73 m^2 (n=157). Thus the population included in the AMACING trial represents 90% of the patients that receive guideline-recommended intravenous prophylactic hydration.

We found no prophylaxis to be non-inferior to standard intravenous hydration according to the guidelines, and the 95% CI reflects the strength of the results.

The CIN incidences found in our trial are considered by some to be low, however for elective procedures they fall within ranges reported in meta-analyses. For example,

McDonald *et al.* reported post-contrast CIN incidences in the range of 2.1–19% (and 1.3–19.8% without contrast administration), Mehran and Nikolsky reported a range of 0.6–2.3% in the general population (including low risk patients), extending up to 20% in selected subgroups (3,4). It is in specific acute clinical settings that higher incidences are reported.

We would like to emphasize that eGFR<30 mL/min/1.73 m^2, emergency and intensive care status were amongst our exclusion criteria, and such patients are therefore beyond the scope of our trial.

The correspondents suggest future trials are required before changing standard care. Given the non-existent difference intravenous hydration made in the incidence of CIN [incidence in the iv hydration group minus that in the no prophylaxis group =–0.1%, one-sided (95% CI, –2.25 to 2.06), one-tailed P=0.4710], and especially given the 5.5% patients that had serious complications of intravenous hydration, we cannot agree. Any therapy must prove to have benefits exceeding the risks before being generally applied, and this is not so in the case of prophylactic intravenous hydration in the prevention of CIN. The burden of proof must be with intravenous prophylactic hydration and not with no-prophylaxis. We would also counter with the question whether it is ethical to continue giving a treatment that is unproven, carries proven risks, confers significant burden upon patient and hospital, and is so costly. If there are indications that a certain patient group might benefit from intravenous hydration, we would suggest evaluating whether the benefits outweigh the risks before general application tot that group.

Mandrola summarizes on Medscape: "the most provocative aspect of AMACING is how it prompts us to reexamine the very existence of CIN. Perhaps hydration does not prevent CIN because our way of thinking about CIN is flawed. Results of the AMACING study force us to (I) be suspicious of expert opinion; (II) object to quality measures not backed by randomized trial data; and (III) reconsider the existence of an entire disease entity (CIN), and in doing so, think about how our brains can trick us into seeing signal when there is mostly noise" (5).

Cite this article as: Nijssen EC, Nelemans PJ, Rennenberg RJ, Essers BA, Janssen MM, Vermeeren MA, van Ommen V, Wildberger JE. Intravenous hydration according to current guidelines in the prevention of contrast induced nephropathy—the AMACING trial. J Thorac Dis 2017;9(7):E656-E657. doi: 10.21037/jtd.2017.06.80

Acknowledgements

None.

Footnote

Conflicts of Interest: The authors have no conflicts of interest to declare.

References

1. Nijssen EC, Rennenberg RJ, Nelemans PJ, et al. Prophylactic hydration to protect renal function from intravascular iodinated contrast material in patients at high risk of contrast-induced nephropathy (AMACING): a prospective, randomised, phase 3, controlled, open-label, non-inferiority trial. Lancet 2017;389:1312-22.
2. Veligheids Management Systeem. VMS veiligheidsprogramma: voorkomen van nierinsufficiëntie bij intravasculair gebruik van jodiumhoudende contrastmiddelen. September, 2009. Accessed May 17, 2017. Available online: http://www.vmszorg.nl/themas/nierinsufficientie
3. Mehran R, Nikolsky E. Contrast-induced nephropathy: definition, epidemiology, and patients at risk. Kidney Int Suppl 2006;100:S11-5.
4. McDonald JS, McDonald RJ, Comin J, et al. Frequency of acute kidney injury following intravenous contrast medium administration: a systematic review and meta-analysis. Radiology 2013:267:119-28.
5. Mandrola J. Commentary: Contrast-Induced Nephropathy: Signal or Noise? Medscape. March 07, 2017. Accessed May 17, 2017. Available online: http://www.medscape.com/viewarticle/876852

