ACUTE KIDNEY INJURY

Intravenous hydration for the prevention of CIAKI

Carlo Briguori and Giuseppe Signoriello

Iodinated contrast media are essential for diagnostic and interventional radiological and cardiological procedures, but may cause kidney damage. Intravenous hydration is the current cornerstone for prevention of contrast-induced acute kidney injury; however, new data from the AMACING trial suggest that this approach might not be beneficial in low-risk patients.

Refers to Nijssen, E. C. *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* http://dx.doi.org/10.1016/S0140-6736(17)30057-0 (2017)

In patients undergoing procedures that require use of iodinated contrast media (CM), intravenous hydration induces an increase in urine flow rate, reduces the concentration of CM in the tubule and expedites CM excretion, thus reducing the exposure time of tubular cells to the toxic effects of CM. The general consensus, therefore, is that hydration is beneficial for the prevention of contrast-induced acute kidney injury (CIAKI)[1,2], but new findings from the AMACING trial do not support this view[3]. Indeed, this trial reports that in 660 patients deemed to be at risk of CIAKI, no prophylaxis was non-inferior to intravenous hydration for the prevention of CIAKI and was also cost-saving. Moreover, a previous study reported that a high ratio of hydration volume to weight is associated with an increased risk of CIAKI and worse outcomes overall[4]. Before adopting these conclusions in clinical practice, the results of the AMACING trial should be interpreted within the boundaries of the study population and the hydration protocol utilized.

> “no prophylaxis was non-inferior to intravenous hydration for the prevention of CIAKI and was also cost-saving”

Importantly, the incidence of CIAKI observed in the AMACING trial (2.6–2.7%) is at the low end of the range previously reported in the scientific literature (0 to >50%). Thus the results of this study refer to a low-risk population and cannot be generalized to all patients. This conclusion is supported by several findings. First, only 35% of the trial participants had an estimated glomerular filtration rate (eGFR) <45 ml/min/1.73 m^2 at baseline. Previous data suggest that the incidence of CIAKI is significantly higher in patients who are exposed to CM than in control patients only when baseline eGFR is <45 ml/min/1.73 m^2 (REF. 2).

Second, the majority (52%) of the trial participants received intravenous rather than intra-arterial CM. Much of the risk attributed to intravenous CM exposure has been extrapolated from studies of intra-arterial CM administration. Indeed, a large, single-centre, propensity-score-adjusted retrospective study failed to demonstrate an excess risk of CIAKI, short-term mortality or excess incidence of emergent dialysis among patients who were exposed to intravenous CM compared with a similar matched group of patients who were not exposed to CM[5]. In the AMACING trial, the results were reportedly consistent across the subgroups with intravenous versus intra-arterial CM administration, but this end point was not pre-specified and the study was not powered to address this issue.

Third, a clear direct association between CM volume and CIAKI occurrence has been documented and strategies to minimize CM volume are strongly recommended. The risk of CIAKI has been demonstrated to exponentially increase with CM volume exceeding the cut-off value of three times the baseline eGFR[6]. In the AMACING trial, the mean volume of CM administered was low; the estimated mean cut-off value was 140 ml (that is, three times the mean GFR of 47 ml/min/1.73 m^2), which is much higher than the reported mean volume of CM administered (91 ml). The participants were, therefore, at low risk of developing AKI.

> “targeted protocols have been shown to be superior to conventional hydration regimens for the prevention of CIAKI”

At present no consensus exists on how hydration for prevention of CIAKI should be carried out. The European Society of Cardiology (ESC)/European Association for Cardio-Thoracic Surgery (EACTS) and Kidney Disease: Improving Global Outcomes (KDIGO) guidelines both recommend a 1 ml/kg per h infusion of normal saline 12 h before and 12 h after CM exposure[1,2]. In the AMACING trial, the standard hydration protocol (based on a Dutch recommendation) was intravenous infusion of normal saline at 3–4 ml/kg per h during the 4 h before and 4 h after CM administration. The limitations of all current hydration regimens must also be emphasized; that is preclusion in urgent or emergent settings; the risk of pulmonary oedema; and suboptimal efficacy in high-risk patients.

In the AMACING trial, 4% of patients in the hydration group experienced complications that led to hydration being stopped prematurely. This rate is quite high and unexpected in such a low-risk population. Indeed, in studies that enrolled patients at higher risk of CIAKI than those included in the AMACING trial, the reported rate of pulmonary oedema was substantially lower (1–1.5%)[7,8]. This finding reinforces the concept of targeted hydration protocols — a single hydration protocol should not be applied to all patients.

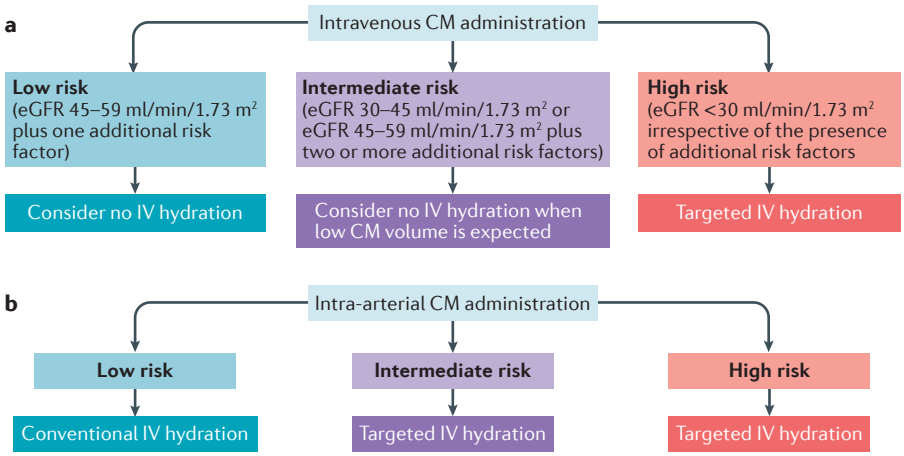

Figure 1 | **Proposed hydration strategy for the prevention of contrast-induced acute kidney injury (CIAKI). a** | Intravenous (IV) contrast media (CM) administration. Additional risk factors for CIAKI are age >75 years, diabetes mellitus, anaemia, female sex, cardiovascular disease, non-steroidal anti-inflammatory drug or diuretic nephrotoxic medication. **b** | Intra-arterial CM administration. Risk groups are defined according to the Mehran[9] or Gurm[10] risk scores. The conventional hydration regimen is a 1 ml/kg per h infusion 12 h before and 12 h after CM exposure. Targeted hydration regimens include left-ventricular end-diastolic pressure-guided hydration, urine flow rate-guided hydration; central venous pressure-guided hydration; and bioimpedence-guided hydration.

Several targeted hydration regimens have been proposed including left-ventricular end-diastolic pressure-guided hydration, urine flow rate-guided hydration; central venous pressure-guided hydration; and bioimpedence-guided hydration. These targeted protocols have been shown to be superior to conventional hydration regimens for the prevention of CIAKI, and are associated with a reduced risk of pulmonary oedema[7,8].

> “the decision on whether to use intravenous hydration should take into account the method of CM infusion ... and the patient’s baseline risk of CIAKI”

In patients undergoing CM exposure, we suggest that the decision on whether to use intravenous hydration should take into account the method of CM infusion (intravenous versus intra-arterial) and the patient’s baseline risk of CIAKI (FIG. 1). According to the results of the AMACING trial, no prophylaxis can be considered for low-risk patients and for intermediate-risk patients undergoing intravenous low-volume CM exposure. In all other clinical scenarios we strongly recommend use of targeted hydration regimens to prevent CIAKI, use of low doses of CM and avoidance of closely spaced, repetitive studies (within 48–72 h). Future studies are necessary to clarify which targeted hydration regimen is the most appropriate according to the patient’s baseline risk profile and the route of CM administration.

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Competing interests statement
The authors declare no competing interests.