DEM Journal Club

Article Appraisal

Article: 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

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Resident Reviewer Name(s) and Residency Affiliation: Trisha Mackle (EM R3) and Kevin Fairbairn (CCFP EM)

Faculty Methodology/Bio-statistics Resource Person: Dr. Frank Scheuermeyer

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Background and Study Objective(s):

In patients with compromised renal function, intravenous (IV) contrast material is often withheld out of concern for causing contrast-induced nephropathy (CIN). Some guidelines recommend hospital admission for prophylactic prehydration to prevent CIN in high-risk patients. These recommendations are based on expert consensus and until now, there has not been a prospective, randomized trial of IV hydration versus no hydration in patients considered high risk for CIN.

Study Design:

This was a prospective, randomised, phase 3, controlled, open-label, non-inferiority trial. From 2014 to 2016 at a single center in Holland, patients were assigned 1:1 to receive prophylactic hydration or no hydration in an open-label format. Inclusion were: eGFR 45-60 with diabetes or two of the following (age>75 yr, anemia HCT <0.39L/L male <0.36 L/L female, cardiovascular disease, NSAID or diuretic nephrotoxic medication), multiple myeloma, or lymphoplasmacytic lymphoma with small chain proteinuria. Exclusion criteria were: eGFR<30, renal replacement therapy, emergency procedures, intensive care patients, known inability to plan primary endpoint data collection, no referral for prophylactic hydration, participation in another RCT, or isolation/infection control. IV hydration included either a short protocol (0.9% NaCL 3-4ml/kg/hr 4hr pre and post contrast) or a long protocol (0.9% NaCL 1ml/kg/hr 12hr pre and post contrast). Contrast administration was done using minimum volume pre-warmed, low-osmolar, monomer, non-ionic, contrast material lopromide, at 300mg iodine per ml. The primary outcome was a creatinine rise greater than 25% or 44 umol/L in days 2-6. Prespecified subgroups included diabetes (yes/no), eGFR <45 or >45, contrast route (intravenous or intraarterial) and procedure type (diagnostic or interventional). Creatinine was measured at 2-6 days and again at 26-35 days, and secondary endpoints included mean change in serum creatinine from days 2-6 to days 26-35. Adverse events such as all-cause mortality, renal replacement therapy, intensive care admission, and sequelae of fluid administration were also included, and the cost effectiveness of hydration therapy was performed.

Results:

A total of 66O patients were randomized with similar baseline characteristics between groups. Mean total hydration volume administered was 1637mL. Overall, there were no statistically significant results for any of the primary or secondary outcomes related to renal injury. Data for the primary outcome of CIN at days 2 - 6 was available for 91% of patients, and the incidence of CIN was 2.7% in the hydration group and 2.6% in the no hydration group ($p = 0.47$). No patients sustained renal failure (GFR <15) or required dialysis within 35 days .All-cause mortality was 0% in the hydration group and 0.9% in the no hydration group ($p = 0.13$). Symptomatic heart failure occurred in 4% of the hydration group compared with 0% in the no hydration group ($p = 0.0001$). Pre-planned subgroup analysis demonstrated outcome similarity between all groups, but wide confidence intervals due to smaller sample sizes. In this setting no hydration was considered overall more cost effective than hydration.

Validity of Results:

The initial aim of the study was to enrol 1300 patient over 2 years. However, this was adjusted and upon revision it was determined that 660 patients would provide sufficient power. The results for the primary outcome appear to be valid in establishing non-inferiority, and the absolute difference of -0.10 falls just under the non-inferiority margin of 2.1%. However, the rationale for the 2.1% non-inferiority threshold is unclear. No subgroup analyses had significant results, likely due to small sample size.

Generalizability of Results:

The contrast material was different from prior high-osmolar contrast in previous study, but similar to that used locally. The inclusion of “high risk” patients provides clinical relevance for our practice. Overall, the results are pertinent to a relevant population of patients, albeit limited by the single center nature of the study. However, this study excluded patients undergoing “emergency procedures” or those in Intensive Care Unit, which may limits the generalizability of results to our setting. Furthermore, current BC guidelines do not recommend hydration for patients with a eGFR >30 in any case, and these results may be more applicable to centers that mandate prophylactic hydration.

The Bottom Line:

Withholding prophylactic IV hydration therapy before contrast administration for high risk patients with an eGFR >30 was shown to be non inferior to prophylactic hydration in the prevention of CIN. Additionally, a potential cost saving was associated with not giving prophylactic intravenous fluid (IVF). Secondary outcomes included a significantly increased incidence of symptomatic heart failure associated with IV prophylaxis at the high volumes mandated by their protocol. The study was well designed, although the establishment of the 2.1% non-inferiority margin remains in question. While perhaps not generalizable to the ED patients, withholding IVF in patients with an $30 < eGFR < 60$ before contrast administration may be considered.