Conclusion of recent ‘osmolality trials’ in preventing contrast-induced nephropathy by NAC—what is the standard?

Sir,

We read with great interest Dr Kimmel et al.’s report on the use of cystatin C as a more reliable parameter for estimating GFR and its value in assessing the renoprotective potential of putative prophylactic agents, and we believe that this study makes an important contribution to the scientific literature [1]. However, in the paper’s discussion, when explaining their rationale for using a low-osmolar contrast agent, Kimmel et al. incorrectly state that our clinical trial, RECOVER [2], does not support the results of NEPHRIC [3], which concluded that contrast-induced nephropathy (CIN) may be less likely to develop in high-risk patients when the iso-osmolar contrast agent, iodixanol, is used rather than a low-osmolar contrast agent.

NEPHRIC was a double-blind, prospective, multicentre trial in which 129 patients with diabetes and serum creatinine (SCr) levels of 1.5 to 3.5 mg/dL undergoing coronary or aortofemoral angiography were randomized to receive either ioxixanol or iohexol, a low-osmolar contrast agent. Defining CIN as an increase in SCr of ≥0.5 mg/dL from baseline, Aspelin et al. determined that 3% of patients in the ioxixanol group developed CIN compared to 26% of patients in the iohexol group (P = 0.002).

RECOVER was a double-blind, prospective, single-centre trial in which 300 patients with creatinine clearance (CrCl) rates ≤ 60 mL/min undergoing coronary angiography were randomized to receive either ioxixanol or ioxaglate, a low-osmolar contrast agent. Technically, if we had used the same definition of CIN as Aspelin et al. (only SCr increase ≥0.5 mg/dL from baseline), the difference in CIN incidence between ioxixanol and ioxaglate would have trended in favour of ioxixanol but would not have achieved statistical significance (3.6% versus 8.9%, P = 0.067). However, in our study we used the more common definition of CIN [4,5]—the one used as a study endpoint in [1] and given in the European Society of Urogenital Radiology (ESUR) guidelines [6]—that is, an increase in SCr of ≥25% or ≥0.5 mg/dL from baseline, and we determined that 7.9% of patients in the ioxixanol group developed CIN compared with 17.0% of patients in the ioxaglate group (P = 0.021). We also investigated the incidence of CIN in subgroups of at-risk patients and found the incidence of CIN to be significantly lower in the ioxixanol group compared to the ioxaglate group in patients with severe renal impairment (CrCl < 30 mL/min; 12.5% versus 53.3%, P = 0.023) and in those with diabetes (10.4% versus 26.5%, P = 0.041). We concluded that the iso-osmolar contrast agent, iodixanol, was significantly less nephrotoxic than the low-osmolar contrast agent, ioxaglate.

In summary, the RECOVER trial confirmed the findings of the NEPHRIC trial in reporting significantly lower CIN rates with iodixanol when compared to a low-osmolar contrast agent.

Conflict of interest statement. None declared.

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Reply

Sir,

In the part of our paper mentioned by Jo et al., we are not explaining the rationale for using low-osmolar contrast agent [1]. Our study was designed before the publication...