Commentary: contrast-induced nephropathy and long-term adverse events: cause and effect?

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Contrast-induced acute kidney injury (CI-AKI) remains an important and potentially avoidable complication after coronary angiography and intervention [1]. In a 2009 issue of the Clinical Journal of the American Society of Nephrology, Solomon and coworkers reported on the long-term outcomes from the Cardiac Angiography in Renally Impaired Patients (CARE) trial. This was a 25 centre, randomized, double-blind parallel-group, trial comparing iso-osmolar iodixanol (n = 210) and low-osmolar iopamidol, 41% (n = 204) in patients with chronic kidney disease (CKD) 41% of whom had diabetes, a mean estimated glomerular filtration rate (eGFR) of 50 ml/min/1.73 m², and were undergoing cardiac angiography [2]. The primary outcome of contrast-induced CI-AKI defined as a rise ≥0.5 mg/dl 45–120 h after coronary arteriography was considerably lower than the expected rate of 15% occurring in 6.7% of those with iodixanol and 4.4% with iopamidol, P = 0.39 [3]. The authors recognized that despite the best attempts, the CARE trial could be interpreted as yet another small, underpowered, randomized trial yielding inconclusive results concerning CI-AKI and that thousands of patients would be needed with such low event rates. This could have been expected as 60% of subjects underwent diagnostic catheterization and either did not require an intervention or were triaged to coronary artery bypass surgery. Importantly, in the original manuscript, there were no major adverse events reported in the first 5 days except for one stroke which was deemed unrelated to the contrast type, but was likely related to the procedure.

In the follow-up study of 294/414 (71%), after 5 days and up to 1 year, 38 (71%) subjects suffered a major adverse event (death, stroke, myocardial infarction, end-stage renal disease [ESRD]). Unfortunately, important information about these 38 subjects is not given such as their baseline eGFR and diabetes status, findings on angiography (normal coronaries to severe multivessel disease), procedural details such as percutaneous coronary intervention, coronary artery bypass surgery, volume of contrast received and the time course of events including the initiation of dialysis. The rates of CI-AKI are not reported for these 38 subjects compared to those who did not suffer events; however, it is disclosed that the major adverse event rates were 22/149 (15%) and 16/145 (11%) for iodixanol and iopamidol, respectively, P = 0.24 (re-computed from 2 × 2 table, relative risk 1.42, 95% confidence interval 0.78–2.62, Epi-Info Version 6.0, Centers for Disease Control, Atlanta, GA, USA). Thus, as in the original trial report, there were no differential in outcomes according to the contrast agent assigned.

Does CI-AKI translate into major adverse events after coronary arteriography? We simply cannot determine this from the CARE trial follow-up as reported. Since 60% of subjects underwent diagnostic catheterization without coronary intervention, 11% had no coronary disease, 14% had single-vessel disease, 19% had two-vessel disease and 24% had three-vessel disease, we can assume a majority of subjects must have had mild to moderate stenoses not warranting revascularization. Thus, in such patients a diagnostic catheterization in the presence of CKD should be carried out with minimal contrast volume, without left ventriculography, and without any early hazard in the days after the procedure. This probably happened in the CARE trial, and these subjects could not have contributed to a translation of events. However, there may have been other subjects, who did incur CI-AKI and were free of major events in the first 5 days, but sustained persistent kidney injury, and had this complicate the clinical course over the following months including the development of heart failure due to volume overload or ESRD.

In this type of study, the authors are advised to simply tell the reader the clinical details of what happened to these patients instead of jumping into multivariate analyses or reporting additional biomarkers such as cystatin C. A flow diagram as shown in Figure 1 would be much more instructive to the practicing and research community. We need to piece together the clinical courses in those rare individuals who sustain CI-AKI in order to devise intelligent strategies for improving safety and outcomes after coronary
revascularization. Perhaps a future report from the CARE trial can inform the reader about these 38 subjects, particularly those who suffered CI-AKI with respect to their courses of treatment and care in the year of follow-up after the trial. By filling in the circles and boxes in Figure 1, the authors could allow inferences on translation of CK-AKI into long-term adverse events and the issue of cause and effect.

Conflict of interest statement. Dr. McCullough is a consultant for GE Healthcare.

References


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Optimizing haemodiafiltration: tools, strategy and remaining questions

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Haemodiafiltration (HDF) is considered the best dialysis therapy currently available in terms of optimal removal of both small and middle molecules. This is obtained by combining diffusive and convective clearance. The efficacy of diffusive transport is usually quantified and monitored by the assessment of small molecule clearance. For this purpose, urea clearance expressed as Kt/Vurea has been widely accepted and used as a parameter for dialysis adequacy. In contrast, it is currently unclear how the efficacy of convective transport should be quantified and monitored.

Pre-dialysis β2-microglobulin (β2M, 11.8 kD) levels have been accepted as a marker for middle molecules [1]. In two large studies, β2M levels have been associated with mortality risk, at least within the range as usually found in haemodialysis patients [2,3]. However, the clinical use of β2M levels to monitor the effects of increased convective clearance by HDF is severely limited by its strong dependence on residual kidney function [4]. To overcome this limitation, the β2M reduction ratio or Kt/Vβ2M could be assessed to measure clearance during HDF, similar to urea. However, in the Hemodialysis (HEMO) study, β2M clearance did not relate to clinical outcome [2].

Alternatively, convective transport could be quantified by monitoring convective volumes. It has been shown that