Use of NAC to prevent contrast-induced nephrotoxicity remains unsupported

Investigations into whether *N*-acetylcysteine (NAC) can prevent contrast-induced nephropathy have been ongoing for 10 years. Sixty clinical studies, 12 meta-analyses and 2 comprehensive analyses of meta-analyses have been performed, but the results remain heterogeneic. Discovering why there is such variation has proved difficult. In a new meta-analysis, Gonzales *et al*. reassessed 22 randomized, controlled trials to try to resolve some of the issues behind this phenomenon.

Even these carefully chosen trials, which included a total of 2,746 participants, showed notable heterogeneity; yet, no sources for these disparities could be identified. By use of statistical techniques, the authors were able to identify two distinctly different clusters of trials within the meta-analysis. Homogeneity was noted within each group.

The first cluster of 2,445 patients derived no benefit from pretreatment with NAC. By contrast, NAC proved highly beneficial in the second group of 301 patients. Large NAC-induced reductions in serum creatinine levels were an unexpected characteristic of the highly beneficial cluster, which contained relatively small and low-quality trials. Furthermore, post-imaging dialysis was required by patients in the two clusters with much the same frequency, indicating that a positive response to NAC did not markedly improve clinical outcome.

Gonzales *et al*. conclude that there is little evidence to support the use of NAC for prevention of contrast-induced nephrotoxic effects.

Original article Gonzales DA *et al.* (2007) A meta-analysis of N-acetylcysteine in contrast-induced nephrotoxicity: unsupervised clustering to resolve heterogeneity. *BMC Med* **5:** 32

Standardization of creatinine measurement substantially improves GFR estimation

Estimation of glomerular filtration rate (GFR) is generally dependent on creatinine-based equations. Many health professionals fail to recognize that variability in the results of serum creatinine measurement between laboratories can affect diagnoses. Creatinine measurement can be standardized by use of isotope dilution mass spectrometry. Komenda *et al*. report on the implementation of a voluntary standardization program in 107 clinical laboratories in the Canadian province of British Columbia that routinely measured creatinine levels by use of 124 analyzers from 6 different manufacturers.

The accuracy of testing was assessed by comparing the values obtained from analysis of a common set of human serum samples (creatinine levels between 50 and 130 μmol/l [0.6–1.5 mg/dl]) in individual laboratories with those obtained by isotope dilution mass spectrometry in a separate analysis facility. Each laboratory was then provided with a correction factor to standardize all its test results before estimation of GFRs with the Modification of Diet in Renal Disease (MDRD) equation. The average total error in creatinine measurements before standardization was 23.9%; this fell to 8.7% after the program was implemented. The average bias (as overestimation of creatinine concentration) fell from 16.5% to 2.7%.

The authors conclude that standardization is feasible and effective, and they predict that implementing this program on a larger scale could reduce the rate of incorrect classification of stage 3 chronic kidney disease by 84%. They stress that although substantial upfront and maintenance costs are incurred in achieving laboratory standardization, these are far outweighed by the financial and human costs of patient misclassification.

Original article Komenda P *et al.* (2007) Regional implementation of creatinine measurement standardization. *J Am Soc Nephrol* **19:** 164–169

Improved GFR estimates with a new model that incorporates both cystatin C and creatinine

Plasma cystatin C level might better reflect glomerular filtration rate (GFR) than creatinine concentration. Ma *et al.* have developed and tested a new equation to estimate GFR that uses cystatin C and creatinine as independent variables.

GFR values measured via isotope clearance in a training cohort of 376 Chinese adults with chronic kidney disease (CKD) were compared with those estimated by one equation based on cystatin C only and another based on cystatin C plus creatinine. A test cohort of an additional 191 patients was used to validate the results. The accuracy of