Unfortunately, the authors did not present own data to substantiate their experience. Other recently published validation studies are in good correlation with our results or show even worse results.\(^3\)

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Lack of renoprotective effect of i.v. N-acetylcysteine in patients with chronic renal failure

Editor—We read with interest the paper by Ristikankare and colleagues\(^1\) regarding the lack of renoprotective effect of N-acetylcysteine (NAC) in patients with pre-existing renal failure undergoing cardiac surgery. We feel that several aspects of this study require further comment. First, a recent meta-analysis of the use of NAC to prevent contrast-induced nephropathy in patients with renal impairment was inconclusive,\(^3\) therefore, reducing the evidence base for the rational use of NAC. We would also wish to question the inclusion of patients with plasma creatinine greater than 100 \(\mu\text{mol l}^{-1}\), which is below the upper limit of normal for many laboratory results in the UK. Therefore, it seems likely that this study may have included patients with normal renal function. We suggest it would have been more appropriate to identify patients with established renal impairment using a more specific measure than plasma creatinine, such as Glomerular Filtration Rate or estimated creatinine clearance.\(^3\)

The power analysis was aimed at detecting a difference in N-acetyl-b-D-glucosaminidase (NAG) and not for any of the other outcome measures. Having powered for 40 patients per group, not reaching this due to the exclusion of three patients reduced the reliability of the results.

After operation, the patients in the NAC arm bled significantly more than the placebo group, we are unclear whether the results were skewed due to large losses from a small number of patients, or a small but significant increase in all. In any event, we wonder about the effect of non-steroidal anti-inflammatory drugs (NSAIDs). In our practice, NSAIDs are avoided as soon as a diagnosis of renal impairment is made. They would certainly not be continued up until the day preceding surgery, rather being managed in the same way as aspirin.

The published fluid balance shows very large i.v. fluid administration in the first 24 h after surgery. Clearly fluid load requirements are different between coronary artery bypass graft (CABG) and valvular surgery and the inclusion of just CABG patients would have been preferable.

There are a number of areas of the study that we feel are unclear. First, as to whether haemofiltration was employed during cardiopulmonary bypass (CPB) for patients with plasma creatinine greater than 100 \(\mu\text{mol l}^{-1}\). It was unclear whether the trend towards longer intensive care unit (ICU) stays in the NAC arm was due to physiological or resource reasons. We are interested in what the criteria for commencing renal replacement therapy were and regarding the patients who died what the cause of death was and whether it was related to renal impairment?

We feel that as this paper was powered for the efficacy of NAC and since there was more bleeding in the NAC arm, questions regarding the safety of NAC have surfaced due to its inherent anticoagulant properties and thus the need for larger fluid requirements.

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Editor—We thank Dr Morgan and colleagues for their interest in our paper.\(^1\) They brought up some interesting points, which we would like to comment on briefly. In 2000, Tepel and colleagues\(^4\) published very promising results of NAC as a renoprotective drug in radio contrast-induced renal failure. Thereafter, a number of new clinical trials of NAC for renal protection have been published. Unfortunately, these studies have not shown that NAC protects the kidneys in either contrast-induced nephropathy or cardiac surgery.\(^5\)

In our study, we included patients who had plasma creatinine above normal limits (90 \(\mu\text{mol l}^{-1}\) for women and 100 \(\mu\text{mol l}^{-1}\) for men, in our hospital). At the department of clinical chemistry in our hospital, serum
creatinine is analysed using an enzyme-based method with NORIP scaling, which is widely used in Scandinavian countries. It gives 10–15% lower values and it is considered more specific than Jaffe-method. We also calculated estimated GFR before operation and in each time point of renal evaluation but did not choose to publish it in accordance with the referees’ guidance. At the time of inclusion of the patients, their GFR was 58 (18) ml min
⁻¹ and after the induction of anaesthesia it was 68 ml min
⁻¹ in both groups. In the recent study, where GFR was found to be a better marker than creatinine for assessment of patients at risk of postoperative renal failure, the preoperative renal insufficiency was defined as 60 ml min
⁻¹ or less.⁶ It is true that the patients had rather mild but also definitive preoperative renal failure. Furthermore, in both groups the patients suffered renal injury after the operation. We agree that the number of the patients in the study could have been greater.

None of the patients had NSAIDs during the study or 1 day before the operation. In general, NSAIDs are rarely used in this group of patients in our hospital.

We were also surprised of the volumes of fluid needed to maintain adequate hydration according to our protocol. The fluid therapy may have been excessive in some patients because, to avoid hypovolaemia, we kept the pulmonary wedge pressure between 10 and 14 mm Hg during the 24 h study period. We believe that patients in the NAC-group received more fluids than the control-group due to the vasodilatory effect of NAC. None of the patients was haemofiltrated during the CPB. If dialysis is needed after cardiac surgery, ICU doctors and consultant nephrologists initiate continuous renal replacement therapy or intermittent haemodialysis depending on the haemodynamic status of the patient.

In our study, we recorded the length of the stay in ICU, but we did not control it in anyway. The longer ICU time in the NAC-group might be a result of the greater fluid input, but it was not determined in our study. Three patients who died had multiorgan failure due to complications of the surgery. In the recent clinical study with patients undergoing abdominal aortic reconstruction,⁷ NAC had anticoagulant and platelet-inhibiting properties, which should be considered if it is administered to patients with increasing bleeding risk.

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Acute lung injury and leptospirosis

Editor—I read with interest the case report on leptospirosis¹ and would like to share my experience in managing this disease while working in an endemic area. Leptospirosis infection has protein manifestations. As a result, it is frequently misdiagnosed even in areas with high prevalence² such as the Indian subcontinent, Latin America, and Southeast Asia. Any delay in diagnosis leads to progression of the disease with its complications. Pulmonary manifestations occur in 20–70% of patients and in many patients can progress to ARDS.³ An Indian study of autopsy findings in 62 cases of leptospirosis⁴ noted most patients were young males who presented with fever, breathlessness, haemoptysis, bleeding, oliguria, and icterus. They died after a brief stay in hospital. A postmortem diagnosis of leptospirosis was made on the basis of characteristic organ findings, aided by results of serology, Levaditi’s staining, and immunohistochemistry (IHC) on kidney sections. Massive intra-alveolar haemorrhage (48 cases), acute interstitial nephritis or acute tubular necrosis (45 cases), and myocarditis (24 cases) were the main autopsy findings. Haemorrhage in various organs such as the heart, gastrointestinal tract, brain, pancreas, and adrenals were also seen. Thirty of 54 kidney sections were positive for leptospiral antigens by IHC. There were extensive haemorrhages in the lungs in 48 (77%) cases and that was the cause of death in most of these cases. Some studies have tried to characterize the severity of


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