Dialysis and iodinated contrast media

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Contrast media are excreted mainly by glomerular filtration. There is thus, a significant correlation between both body and renal clearances of contrast media and glomerular filtration rate, and their renal excretion will be delayed in patients with renal insufficiency. Contrast media can be efficiently removed from blood by hemodialysis (HD). Since most contrast media are middle-sized molecules, the main factors potentially influencing their removal by HD are blood flow, membrane surface area, molecular size, transmembrane pressure, and dialysis time. Peritoneal dialysis is also effective in removing contrast agents from the body but takes longer than HD. Dialysis immediately after radiographic contrast studies has been suggested for two groups of patients. Those on chronic HD and those at very high risk for contrast nephropathy. Three studies have examined the necessity of immediate dialysis after intravascular injection of contrast media in chronic HD patients; the authors found no evidence that it is effective at preventing contrast nephropathy. The reasons why HD treatment was not beneficial in those three studies are not known. Perhaps, the rapid onset of renal injury after administration of contrast media is one answer. It is also possible that HD *per se* was nephrotoxic and might have offset the beneficial effect of the removal of contrast media. Marenzi *et al*. randomized 114 consecutive patients with chronic renal failure undergoing coronary interventions to either hemofiltration in an intensive care unit or isotonic saline hydration. The authors concluded that periprocedural hemofiltration given in an intensive care unit setting appears to be effective in preventing the deterioration of renal function due to contrast agent induced nephropathy and is associated with improved in-hospital and long term outcomes. The concentration of contrast media can effectively be reduced by HD and peritoneal dialysis. HD does not offer any protection against contrast media induced nephrotoxicity. Hemofiltration may decrease the risk of contrast induced nephropathy and have some long-term benefits, but additional studies are needed to better define the appropriate population for this treatment.

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PHARMACOKINETIC PROPERTIES OF WATER SOLUBLE IODINATED CONTRAST MEDIA

The pharmacokinetic properties of water-soluble iodinated contrast media are such that they are distributed in the extracellular fluid only, are minimally protein bound, are not metabolized, and are excreted mainly by glomerular filtration.

In patients with normal kidney function, iodinated contrast media are rapidly eliminated through glomerular filtration.[1,2] All contrast media are distributed into the extracellular body compartments after intravenous injection,[3] and this leads relatively quickly to a decrease in their serum concentration. This can be explained by the fact that contrast media, because of their chemical structure, diffuse into the extravascular spaces until the diffusion equilibrium has been attained, at the same time, there is excretion of the contrast medium with the first glomerular passage in normal kidneys. The decrease of the serum level caused by renal elimination leads to a rediffusion of the contrast medium out of the tissue and back into the intravascular space,[3] and the decrease in plasma concentration follows a two-part exponential function.[4–8] In normal subjects and in subjects with mild, moderate, and severe renal impairment, the plasma concentration of the low osmolar contrast medium iomeprol declines biexponentially after intravenous administration.[8] Comparison of the fractions of the area under curve for each phase and comparison of the volume terms indicate that the first phase can be regarded as the distribution phase and the terminal phase as the elimination phase. The mean body clearance and mean renal clearance values are progressively reduced with an increasing degree of renal impairment. There is a progressive increase in the elimination half-life with increasing degree of renal impairment. There is thus, a significant correlation between both body and renal clearances of contrast media and glomerular filtration rate. The half-life for iodinated contrast media in patients with normal glomerular function is between 40 and 120 min for ionic contrast media.[4–6] The half-life for nonionic iopromide has been reported to be 110 min.[6] Cumulative mean 120 h urinary excretion of low osmolar contrast medium iomeprol averages 93.5 and 63.8% in healthy subjects and those with severe renal impairment, respectively.

In normal subjects, elimination takes place rapidly: after 2 h approximately 50% of the injected dose is recovered in the urine. In subjects with severe renal impairment, the

elimination is slower, with approximately 50% of the injected dose recovered in urine between 16 and 84 h after injection.[8] In patients with end-stage renal failure, there is long-lasting retention of the injected contrast medium because the compensating alternative of biliary elimination is particularly slow.

REMOVAL OF IODINATED CONTRAST MEDIA BY DIFFERENT EXTRA CORPOREAL TREATMENT

Hemodialysis

Contrast media can be efficiently removed from blood by hemodialysis (HD).[9–22] Removal of solute by HD occurs predominantly by diffusion with a lesser contribution due to bulk flow of fluids across the membrane. Contrast media have some properties favoring rapid transfer across the dialytic membrane, that is, water solubility, low protein binding, and low intracellular penetration. However, the removal rate is limited by their molecular weight, which approximates that of the hypothetical 'middle-sized molecules' and is considerably higher than that of readily dialyzed molecules such as urea and creatinine.

In one study,[11] the time course of iodine elimination by HD was assessed in eight patients with chronic renal failure (serum creatinine level $\geqslant 1.3$ mg/dl) and 12 patients under chronic HD. High flux dialysers with a membrane area of 1.0–1.9 m^2 were used and the blood flow rate was 120–200 ml/min. The mean reduction rate of iodine by HD was $46.6 \pm 5.3\%$ at 1 h, $65.2 \pm 2.9\%$ at 2 h, $75.1 \pm 2.2\%$ at 3 h, and $80.6 \pm 4.3\%$ at 4 h. No correlation was observed between the initial plasma concentration and the removal rate of iodine by HD. Other studies found similar results.[10,12,15–17] Low osmolar contrast medium clearance was in the range from 147 to 180 ml/min.

The postdialysis concentration of contrast media has been assessed in two studies.[15,16] Matzkies *et al.*[15] found no evidence for major redistribution processes 1 h after HD. On the contrary, the blood concentration of iohexol increased significantly 3 and 6 h after HD, suggesting a rebound effect attributed to variations in blood flow distribution between compartments.[16]

Since most contrast media are middle sized molecules, the main factors potentially influencing their removal by HD are: blood flow, membrane surface area, molecular size, transmembrane pressure, and dialysis time. *In vitro* Teraoka *et al.*[13] observed a high correlation between clearance and blood flow rate. It is likely based on studies with other drugs that the same correlation should be observed *in vivo* for contrast media.

Dialysis membrane surface area and membrane material will influence contrast media elimination.[15] Marked increase in plasma clearance (from 156 ± 12 to 204 ± 36 ml/min) could be seen with increasing surface area for patients dialyzed with polysulfone dialysers. Additional ultrafiltration further increased plasma iodine clearance. A comparable increase in plasma clearance was observed with cuprophan membranes with different surface areas.[15]

Most studies[12,15,19–21] have shown that high-flux HD (with polysulfone, PF14, or PAN) is superior to low-flux membranes for elimination of contrast media. Those studies are in accordance with *in vitro* studies.[13–14] In contrast, Matzkies *et al.*[18] demonstrated no difference in iopromide clearance between high flux and low flux dialysers *in vivo*. The reason for this discrepancy is unclear.

Peritoneal dialysis[23–26]

In three patients with chronic renal failure who underwent coronary angiography with iohexol, intermittent automated peritoneal dialysis (36–60 l dialysis fluid) was able to remove 43–72% of the iohexol over 16–18 h. In another study, intermittent peritoneal dialysis for 64 h removed 56% of the injected high osmolar contrast media. Continuous ambulatory peritoneal dialysis of 10 patients in chronic renal failure removed 54% (range 36–80%) of the administrated dose of iopamidol 300 (30 ml) over 7 days using 8 l of dialysis fluid daily. During the same period, 27% (range 36–80%) of the injected contrast medium was excreted in the urine.[23] Thus, peritoneal dialysis is also effective in removing contrast agents from the body but takes longer than HD.

POSTCONTRAST DIALYSIS

Dialysis immediately after radiographic contrast studies has been recommended for two groups of patients. Those on chronic HD and those at very high risk for contrast nephropathy.

Three studies[27–29] have examined the necessity of immediate dialysis after intravascular injection of contrast media in chronic HD patients. All patients were in-patients maintained on a routine HD schedule of three times per week and who required intravascular administration of contrast media. Patient tolerance to the contrast load was closely monitored. One study[29] included 22 patients who received 85–225 ml of contrast media and the incidence of side effects was observed over the next 5 days. The authors found that the patients had no more side effects than those without renal failure. None of the patients had postprocedural side effects that warranted dialysis before the next routinely scheduled session. Similar conclusions were reached in the two other studies, which included 10 (50–300 ml of iobitridol) and eight patients (50 ml of iopamidol) also given nonionic contrast media. The results of those studies suggest that low osmolar contrast medium may be given safely to patients with end-stage renal disease being maintained on HD without the added expense or inconvenience of emergent postprocedural dialysis. Additional investigation in a larger number of cases involving patients with poor cardiac condition and peritoneal dialysed patients with residual renal function is warranted.

Several studies investigated the effect of HD after contrast medium procedure on renal outcome.

In a study[30] of 13 patients with serum creatinine 2.4–7.4 mg/dl, dialysis was carried out within 1–18 h of the procedure. No patient had a rise in serum creatinine within 15 days. The authors concluded that dialysis is helpful in

preventing contrast nephropathy. However, the absence of a control group makes these findings difficult to interpret.

However, several studies have suggested that although HD eliminates contrast medium effectively, it may not influence the incidence or outcome of contrast induced nephropathy (CIN). The influence of HD on the pharmacokinetics of nonionic contrast media and the outcome of CIN in patients at risk undergoing angiography was prospectively studies in 30 patients with reduced renal function (2.4 ± 0.2 mg/dl).[31] The patients were randomized into two groups. In group 1, HD was started as soon as possible (63 ± 6 min) after termination of contrast medium administration.

HD was performed for 3 h without fluid withdrawal. The dialyser used in all cases was a high-flux polysulfone membrane. The average blood flow was 139 ± 8 ml/min and the dialysate flow was 500 ml/min. Group 2 received no HD. All patients received an intravenous infusion of 0.9% saline. Serum iopentol concentration in the HD group declined significantly faster than in the control group (11 ± 1.6 and 17 ± 2.3% of the peak concentration 24 h after iopentol application in groups 1 and 2, respectively). Except for the first 24 h after HD, the course of serum creatinine was parallel in both groups. The rate of CIN (an increase of at least 0.5 mg/dl within 48 h) was not significantly different between the two groups (53 vs 40% in groups 1 and 2, respectively). Neither was the incidence of CIN in the diabetic and non-diabetic patients.

Vogt *et al.*[32] studied 113 patients with chronic stable renal failure (serum creatinine levels >2.26 mg/dl). Patients underwent either selective percutaneous transluminal renal angiography ($n=36$), percutaneous transluminal angioplasty of the lower extremities ($n=26$), coronary angiography ($n=38$), computed tomography ($n=11$), or other radiographic investigation. Patients were assigned randomly to receive either intravenous saline at 1 ml/kg/h for 12 h before and after administration of the contrast agent or saline before and HD after administration of contrast agent. HD was started between 30 and 280 min (median 120 min) after administration of the first bolus of contrast media. The dialyser used was a high-flux polysulfone membrane. The mean blood flow was 180 ± 42 ml/min and the duration of dialysis averaged 3.1 ± 0.7 h with a dialysate flow was 500 ml/min. The rate of CIN (maximal increase in serum creatinine level >1.5 mg/dl or >50% above baseline at any time point) and evolution of serum creatinine did not differ between the groups. Because the volume of contrast media administered to patients in the non-HD group was approximately 30% less than that administered in the HD group (143 ± 115 vs 210 ± 143 ml, $P=0.007$), they compared the effects of HD among patients who received >150 ml of contrast media. There was no beneficial effect of HD on serum creatinine levels in this subgroup of patients. The authors found that a greater percentage of patients who were treated with prophylactic HD after the administration of contrast media required additional HD treatment or had a decline in renal function (8 vs 3 patients).

In total, 32 patients with reduced renal function (serum creatinine >1.7 mg/dl) were randomly selected to undergo either HD or standard treatment following angiographic examination.[33] Glomerular filtration rate was determined the day before and 1 week after administration of the contrast medium by iohexol clearance, which correlates excellently with renal inulin clearance, and is thus a reliable marker of glomerular filtration rate. HD lowered the level of contrast medium in plasma by approximately 80%. In spite of this, no significant difference in renal iohexol clearance was noted between groups. Renal clearance of iohexol correlates excellently with renal inulin clearance and is thus a reliable marker of glomerular filtration rate. Therefore, in spite of the obvious effect of HD on plasma contrast levels, the authors found no evidence that it is effective at preventing contrast nephropathy.

The reasons why HD treatment was not beneficial in those three studies are not known. Perhaps, the rapid onset of renal injury after administration of contrast media is one answer. Renal hypoperfusion occurs within 20 min after the injection of contrast media; however, a delay between contrast medium exposure and institution of an HD procedure of <30 min does not seem feasible. However, one study has assessed the effects of simultaneous HD with contrast administration on the rate of CIN.

Frank *et al.*[34] have prospectively studied 17 patients with known chronic renal insufficiency (serum creatinine >3 mg/dl) yet dialysis independent who were undergoing coronary angiography. Patients were randomized to receive hydration (1000 ml 0.9% saline) over a time period of 6 h before and after contrast administration or the same volume of saline with high flux HD without ultrafiltration over 6 h simultaneously with the contrast media application. At 24 h creatinine clearance was similar at baseline (19.4 ± 9.6 vs 17.4 ± 7.2 ml/min) and 1 and 8 weeks after angiography. No patients developed oliguria. This first study with HD simultaneously to contrast media application showed that the overall clearance of the contrast media was significantly increased by dialysis. However, the peak plasma concentration of iomeprol 15 min after contrast media application was not changed significantly by simultaneous dialysis.

Another limitation of all those studies is the small size of the population studied. Frank *et al.*[34] have analyzed the sample size needed to treat to obtained a significant end point. With regard to the incidence of end-stage renal failure in their study and previous data showing a risk for the need of dialysis after coronary intervention between 12% for non-diabetic and 43% for diabetic, they postulated that simultaneous dialysis should reduce the risk for developing end-stage renal failure by 50% to be considered clinically beneficial. This risk reduction seems reasonable to justify the potential side effects and expenditure of this procedure. With a type 1 and type 2 test error set at 0.01, the hypothesis could be accepted if none of the next 48 sequential patients with simultaneous dialysis would need dialysis during the 8 weeks after contrast media exposure. On the other hand, 239

sequential patients with simultaneous dialysis had to be included to reject the hypothesis. Based on these numbers, we may assume that none of the already performed studies had the power to detect any effect of dialysis on the rate of CIN.

It is also possible that HD *per se* was nephrotoxic and might have offset the beneficial effect of the removal of contrast media. Nephrotoxicity due to dialysis has been linked with the activation of inflammatory reactions and the induction of hypovolemia and hypotension. In contrast to HD, hemofiltration is a continuous form of renal replacement therapy that constitutes an alternative strategy for the prevention of contrast-agent-induced nephropathy in high-risk patients. Hemofiltration is associated with greater hemodynamic.

Marenzi G *et al.* have[35] studied 114 consecutive patients with chronic renal failure (serum creatinine concentration >2.0 mg/dl (176.8 μmol/l)), who were undergoing coronary interventions. Patients were randomly assigned to either hemofiltration in an intensive care unit or isotonic saline hydration at a rate of 1 mml/kg/h in a 'step-down' unit. For patients in the hemofiltration group, a treatment session was started 4–6 h before the scheduled coronary procedure. Treatment was resumed after the procedure was completed and continued for 18–24 h. Hemofiltration treatment was stopped during the coronary procedure itself. Contrast agent-induced nephropathy was defined as an increase of more than 25% from the baseline value in the serum creatinine concentration. An increase in the serum creatinine concentration of more than 25% from the baseline value after the coronary procedure occurred less frequently among the patients in the hemofiltration group than among the control patients (5 vs 50%). Temporary renal replacement therapy (HD or hemofiltration) was required in 25% of the control patients and in 3% of the patients in the hemofiltration group. The rate of in-hospital events was 9% in the hemofiltration group and 52% in the control group ($P<0.001$). In-hospital mortality was 2% in the hemofiltration group and 1% in the control group ($P=0.02$), and the cumulative 1-year mortality was 10 and 30%, respectively ($P=0.01$). The authors concluded that periprocedural hemofiltration given in an intensive care unit setting appears to be effective in prevention of the deterioration of renal function due to contrast agent induced nephropathy, and is associated with improved in-hospital and long-term outcomes.

Those provocative data were then challenged by several authors who raised several keys points:

- Why should hemofiltration that was stopped during the exposure to contrast media have prevented CIN when the experience with HD suggests that the renal injury occurs during that initial exposure to contrast media?
- Is it possible that the heparin infusion used in the hemofiltration group have protected the patients from contrast media induced ischemia reperfusion injury?
- Relying on an increase in the serum creatinine concentration to define acute renal failure creates a bias toward the finding of less acute renal failure in the hemofiltration group, which had creatinine concentrations artificially lowered below baseline at day 1.
- The benefits of randomization were attenuated when confounding by indication was built into the treatment protocols.

As outlined by the authors in their answer to these comments,[36] a preventive strategy based on hemofiltration cannot be directly applicable to all patients at risk, given the relative high cost of this procedure and the limited availability of beds in intensive care unit. Further studies are needed for a better delineation of the risk profile of patients exposed to contrast media and for the selection of those in whom a preventive strategy with hemofiltration might be justified and cost effective.

CONCLUSIONS

Delayed excretion of iodinated contrast media in patients with renal insuffciency has led to concerns about increased toxicity in such patients after radiographic procedures, which require intravascular injection of iodinated contrast. The concentration of contrast media can effectively be reduced by HD and peritoneal dialysis. HD does not offer any protection against contrast media induced nephrotoxicity. Hemofiltration may decrease the risk of CIN and have some long-term benefits but additional studies are needed to better define the appropriate population for this treatment.

REFERENCES

1. Cattell WR, Fry IK, Spencer AG, Purkiss B. Excretion urography. Factors determining the excretion of Hypaque. *Br J Radiol* 1967; **40**: 561–571.
2. Tornell G. Influence of contrast media on the central nervous system. *Acta Radiol* 1963; **11**: 932–940.
3. Schlungbaum W. Verteilung, Ausscheidung und Resorption nierengängiger mit 131 jod markiert Röntgenkontrasmittel. *Fortschr Röntgenstr* 1962; **96**: 795–806.
4. Bahlmann J, Gollnisch HJ, Krüskemper HL. Der Einflub der nierenfunktion auf die kontrastmittelelimination nach infusionspyelographie. *Eur J Clin Pharmacol* 1972; **4**: 162–169.
5. Herms HJ, Taenzer V. Infusions urographie:methodische variationen und ihre bedeutung für die Ausscheidungskinetik. *Radiologe* 1967; **7**: 221–223.
6. Krause W, Schuhmann-Giampieri G, Staks T, Kaufmann J. Dose proportionality of iopromide pharmacokinetics and tolerbility after IV injection in healthy volunteers. *Eur J Clin Pharmacol* 1994; **46**: 339–343.
7. Siemesen HC, Augustin HJ. Pharmacokinetic von diatrizoate unter hamodialyse. *Int J Clin Pharmacol* 1973; **8**: 22–28.
8. Lorusso V, Taroni P, Alvino S, Spinazzi A. Pharmacokinetics and safety of iomeprol in healthy volunteers and in patients with renal impairment or end stage renal disease requiring haemodialysis. *Invest Radiol* 2001; **36**: 309–316.
9. Morcos SK, Thomsen HS, Webb JAW. Dialysis and contrast media. *Eur Radiol* 2002; **12**: 3026–3030.
10. Horiuchi K, Yoshida K, Tsuboi N *et al.* Elimination of non-ionic contrast medium by hemodialysis in patients with impaired renal function. *J Nippon Med School* 1999; **66**: 17–18.
11. Shinoda T, Hata T, Nakajima KI *et al.* Time-course of iodine elimination by hemodialysis in patients with renal failure after angiography. *Therapeutic Apheresis* 2002; **6**: 437–442.
12. Matzkies FK, Reinecke H, Tombach B *et al.* Reduced iopromide elimination in hemodialysis with cuprophan membranes. *Acta Radiol* 2000; **41**: 671–673.
13. Teraoka T, Sugai T, Nakamura S *et al.* Prediction of iopromide reduction rates during hemodialysis using an *in vitro* dialysis system. *Nephrol Dial Transplant* 2005; **20**: 754–759.

14. Bailie GR, Eisele G, Sala J, Wu D. Determination of iodixanol hemodialysis clearance using a novel *in vitro* system. *Clin Res Reg Affairs* 1996; **13**: 111–124.
15. Matzkies FK, Reinecke H, Tombach B *et al.* Influence of dialysis procedure, membrane surface and membrane material on iopromide elimination in patients with reduced kidney function. *Am J Nephrol* 2000; **20**: 300–304.
16. Johnsson E, Attman PO, Samuelsson O, Haraldsson B. Improved clearance of iohexol with longer haemodialysis despite similar Kt/V for urea. *Nephrol Dial Transplant* 1999; **14**: 2407–2412.
17. Hudson JQ, Comstock TJ, Feldman GM. Evaluation of an *in vitro* dialysis system to predict drug removal. *Nephrol Dial Transplant* 2004; **19**: 400–405.
18. Matzkies FK, Tombach B, Kisters K *et al.* Clearance of iopromide during haemodialysis with high-and low-flux membranes. *Acta Radiol* 1999; **40**: 220–223.
19. Rault RM. Hemodialysis for removal of iodinated contrast media. *Intern J Artif Organs* 2001; **24**: 331–334.
20. Gouge SF, Moore J, Atkins F, Hirszel P. Radiocontrast removal by dialysis membranes. *Blood Purif* 1991; **9**: 182–187.
21. Schindler R, Stahl C, Venz S *et al.* Removal of contrast media by different extracorporeal treatments. *Nephrol Dial Transplant* 2001; **16**: 1471–1474.
22. Marenzi GC, Bartorelli AL, Lauri G *et al.* Continuous veno-venous hemofiltration for the treatment of contrast-induced acute renal failure after percutaneous coronary interventions. *Catheterization Cardiovasc Interventions* 2003; **58**: 59–64.
23. Donnelly PK, Burwell N, McBurney A *et al.* Clearance of iopamidol, a non ionic contrast medium, by CAPD in patients with end-stage renal failure. *Br J Radiol* 1992; **65**: 1108–1113.
24. Milman N, Christensen E. Elimination of diatrizoate by peritoneal dialysis in renal failure. *Acta Radiol Diagn* 1974; **15**: 265–272.
25. Iwamoto M, Hiroshige K, Suda T *et al.* Elimination of iomeprol in patients undergoing continuous ambulatory peritoneal dialysis. *Peritoneal Dial Int* 1999; **19**: 380–385.
26. Marx MA, Shuler CL, Golper TA. Plasma iohexol clearance in automated peritoneal dialysis – its role in adequacy determination. *Peritoneal Dial Int* 1998; **18**: 512–515.
27. Younathan CM, Kaude JV, Cook MD *et al.* Dialysis is not indicated immediately after administration of non-ionic contrast agents in patients with end-stage renal disease treated by maintenance dialysis. *Am J Roentgenol* 1994; **163**: 969–971.
28. Hamani A, Petitclerc T, Jacobs C, Deray G. Is dialysis indicated immediately after administration of iodinated contrast agents in patients on haemodialysis? *Nephrol Dial Transplant* 1998; **13**: 1051.
29. Harazawa H, Yamazaki C, Mazuki K. Side effects and pharmacokinetics of non ionic contrast medium in hemodialyzed patients. *Nippon Igazku Hoashasen gakkai Zasshi* 1990; **50**: 1524–1531.
30. Moon S, Back SE, Kurkus J, Nilson-Ehle P. Hemodialysis for elimination of the non-ionic contrast medium iohexol after angiography in patients with impaired renal function. *Nephron* 1995; **70**: 430–437.
31. Lenhnert T, Keller E, Gondolf K *et al.* Effect of haemodialysis after contrast medium administration in patients with renal insufficiency. *Nephrol Dial Transplant* 1998; **13**: 358–362.
32. Vogt B, Ferrari P, Schönholzer C *et al.* Prophylactic hemodialysis after radiocontrast media in patients with renal insufficiency is potentially harmful. *Am J Med* 2001; **111**: 692–698.
33. Sterner G, Frennby B, Kurkus J, Nyman U. Does post-angiographic hemodialysis reduce the risk of contrast-medium nephropathy? *Scand J Urol Nephrol* 2000; **34**: 323–326.
34. Frank H, Werner D, Lorusso V *et al.* Simultaneous hemodialysis during coronary angiography fails to prevent radiocontrast-induced nephropathy in chronic renal failure. *Clin Nephrol* 2003; **60**: 176–182.
35. Marenzi G, Marana I, Lauri G *et al.* The prevention of radiocontrast-agent-induced nephropathy by hemofiltration. *N Engl J Med* 2003; **349**: 1333–1340.
36. Marenzi G, Marana I, Lauri G *et al.* The prevention of radiocontrast-agent-induced nephropathy by hemofiltration. *N Engl J Med* 2004; **350**: 836–838.