

Prophylactic hemodialysis for the prevention of contrast-induced nephropathy after coronary angiography

Original article Lee PT *et al.* (2007) Renal protection for coronary angiography in advanced renal failure patients by prophylactic hemodialysis: a randomized controlled trial. *J Am Coll Cardiol* 50: 1015–1020

SYNOPSIS

KEYWORDS chronic kidney disease, contrast-induced nephropathy, coronary angiography, prophylactic hemodialysis

BACKGROUND

Patients with chronic kidney disease (CKD) are particularly susceptible to contrast-induced nephropathy (CIN).

OBJECTIVE

To ascertain whether prophylactic hemodialysis reduces the risk of CIN in patients with advanced CKD who are undergoing coronary angiography.

DESIGN

This prospective, randomized, controlled trial was carried out at Kaohsiung Veterans General Hospital, Kaohsiung, Taiwan from August 2003 to June 2006, in patients referred for coronary angiography. The inclusion criteria were age >20 years, serum creatinine level >309 $\mu\text{mol/l}$ (>3.5 mg/dl), and change in serum creatinine of <44.2 $\mu\text{mol/l}$ (<0.5 mg/dl) over the period of 1 month. Patients with newly-diagnosed and uncontrolled diabetes and patients on long-term dialysis were among those excluded. Angiotensin-converting-enzyme inhibitors were withheld on the day of angiography; acetylcysteine, theophylline, dopamine and mannitol were withheld throughout the study.

INTERVENTION

Patients were randomized to receive an intravenous infusion of normal saline 1 ml/kg/h for 6 h before and 12 h after administration of contrast (iohexol) plus 4 h of hemodialysis, or infusion of saline only. Dialysis was initiated as soon as possible after angiography.

OUTCOME MEASURE

Change in creatinine clearance between baseline (before angiography) and day 4, as measured by 24 h urine collection, was the primary end point.

RESULTS

Screening of 3,724 patients undergoing coronary angiography yielded 318 patients with CKD, of whom 90 consented to enter the study. A total of 82 patients were available for analysis. Baseline demographic and clinical characteristics did not differ significantly between the patients assigned to saline infusion and hemodialysis ($n=42$) and those assigned to saline infusion only ($n=40$); mean creatinine clearance was also similar in the two groups (13.2 ml/min/1.73 m² vs 12.6 ml/min/1.73 m²). The dialysis group experienced a smaller reduction in creatinine clearance by day 4 than did the control group (-0.4 ml/min/1.73 m² vs -2.2 ml/min/1.73 m²; $P=0.001$). Multivariate regression analysis identified only two factors significantly associated with a change in creatinine clearance: prophylactic dialysis (increase of 1.938 ml/min/1.73 m²; $P<0.001$) and baseline creatinine clearance (increase of 0.324 ml/min/1.73 m² per 1 ml/min/1.73 m² increase in baseline value; $P=0.011$). Both temporary dialysis and maintenance dialysis were required by a greater number of patients in the control group than in the prophylactic hemodialysis group (temporary dialysis 14 patients vs 1 patient [35% vs 2%]; $P<0.001$, and maintenance dialysis 5 patients vs 0 patients [13% vs 0%]; $P=0.018$). Permanent renal damage (increase in serum creatinine of >88.4 $\mu\text{mol/l}$ [>1 mg/dl] or permanent need for dialysis) occurred in 18 of the control patients and 2 of the patients who received prophylactic hemodialysis (45% vs 5%; $P<0.001$). There were no major complications of prophylactic hemodialysis.

CONCLUSION

Prophylactic hemodialysis might provide protection from CIN in patients with advanced CKD who are undergoing coronary angiography.

[ED: please delete a line from column 2]

COMMENTARY

Giancarlo Marenzi

The potential for renal replacement therapies to protect against CIN in patients with advanced CKD has been a matter of intense investigative interest and debate in recent years. Contrast media are excreted mainly by glomerular filtration; the elimination of these agents is prolonged in patients with renal insufficiency, resulting in longer exposure of the kidney to their toxic effects.

In spite of the obvious effect of hemodialysis on plasma contrast levels, there are conflicting (but mostly negative) data regarding the utility of this technique in preventing CIN. Even the benefit of pre-emptive hemofiltration has been ascribed to mechanisms different to those of contrast removal.¹ Although the reasons for the apparent lack of efficacy of hemodialysis are unknown, possible explanations include delay between contrast exposure and the start of treatment, failure to reduce the peak plasma concentration of contrast agent, and hemodialysis-associated nephrotoxicity. The conflicting results of various studies might also reflect differences in the contrast procedure, type and volume of contrast agent, baseline renal function, time from contrast exposure to start of hemodialysis, treatment duration, characteristics of dialysis, and clinical end points. In 2006, two expert panels and a meta-analysis concluded that there was insufficient evidence to recommend hemodialysis for prevention of CIN in patients with advanced CKD.^{2–4}

The positive results of Lee and colleagues revive interest in the use of prophylactic hemodialysis, and reopen the question of whether hemodialysis can prevent CIN. The major limitations of previous studies include small sample sizes (only 3 studies had at least 20 patients in each group), absence of randomization or of a control group, and use of serum creatinine (which can be artificially lowered by hemodialysis) as a marker of renal function. Only the study by Vogt *et al.*⁵ can be compared with that by Lee *et al.* in terms of design and sample size. Both are randomized prospective trials, include relatively large populations (113 and 82 patients, respectively), and have similar treatment protocols (comprising hydration before contrast

exposure and use of nonionic low-osmolality contrast agents, with similar treatment delay and duration, filter characteristics, and blood and dialysate flows, and no pharmacologic prophylaxis). The two studies yielded opposite conclusions in terms of CIN incidence and clinical outcome, however: no benefit—or even harm—in the Vogt *et al.* trial, and clear benefit in the study by Lee and co-workers.

The only differences between the Vogt *et al.* and the Lee *et al.* studies are the mean (\pm SD) contrast volume administered (210 ± 143 ml vs 107 ± 44 ml) and the baseline average serum creatinine ($318 \mu\text{mol/l}$ [3.6 mg/dl] vs $433 \mu\text{mol/l}$ [4.9 mg/dl])[Au: in the hemodialysis groups?]. The latter difference implies that a critical threshold of renal impairment determines whether prophylactic hemodialysis has a clinical effect, and that this threshold is higher than that proposed in previous studies. Only patients with low residual renal function (creatinine clearance <25 ml/min/1.73 m²) seem to benefit, particularly when contrast volume is minimized.

Should the outcomes of the study by Lee *et al.* change clinical practice? Probably not. The effectiveness of prophylactic hemodialysis has yet to be confirmed convincingly, and further studies using more-accurate indices of renal function (e.g. scintigraphic estimates of clearance) are required to validate the effects of this intervention and to better identify patients in whom preventive hemodialysis would be justified and cost-effective.

References

- 1 Marenzi G *et al.* (2003) The prevention of radiocontrast-agent-induced nephropathy by hemofiltration. *N Engl J Med* **349**: 1333–1340
- 2 Stacul F *et al.* (2006) Strategies to reduce the risk of contrast-induced nephropathy. *Am J Cardiol* **98** (Suppl 1): S59–S77
- 3 Solomon R *et al.* (2006) How to prevent contrast-induced nephropathy and manage risk patients: practical recommendations. *Kidney Int* **69** (Suppl 100): S51–S53
- 4 Cruz DN *et al.* (2006) Extracorporeal blood purification therapies for prevention of radiocontrast-induced nephropathy: a systematic review. *Am J Kidney Dis* **48**: 361–371
- 5 Vogt B *et al.* (2001) Prophylactic hemodialysis after radiocontrast media in patients with renal insufficiency is potentially harmful. *Am J Med* **111**: 692–698

G Marenzi is Director of the Intensive Cardiac Care Unit at the Centro Cardiologico Monzino, Istituti di Ricovero e Cura a Carattere Scientifico, Institute of Cardiology, University of Milan, Milan, Italy.

Acknowledgments

The synopsis was written by Chloé Harman, Associate Editor, Nature Clinical Practice.

Competing interests

The author declared no competing interests.

Correspondence

Centro Cardiologico Monzino
Via Parea 4
20138 Milan
Italy
giancarlo.marenzi@ccfm.it

Received 5 October 2007

Accepted 24 October 2007

Published online

XXXX 2007

www.nature.com/clinicalpractice
doi:10.1038/ncpneph0697

PRACTICE POINT

Prophylactic hemodialysis should be considered as a means of reducing the risk of contrast-induced nephropathy in patients with severe chronic kidney disease who are undergoing coronary angiography