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CRITICAL CARE

Hypotensive epidural anaesthesia in patients with preoperative renal dysfunction undergoing total hip replacement

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Background. Hypotensive anaesthesia does not impair renal function after surgery in normal patients but there are no reports of hypotensive anaesthesia in patients with chronic renal dysfunction (CRD).

Methods. From a database of 1893 consecutive patients undergoing total hip replacement (THR) under hypotensive epidural anaesthesia (HEA) from 1999 to 2004, 54 patients were identified with CRD (preoperative serum creatinine $\geqslant$124 μmol litre^{-1}). Fifty matched pairs were identified for patients with normal renal function who have hypertension (n=50) or no hypertension (n=50). Changes in serum creatinine and blood urea nitrogen (BUN) were recorded daily for 3 days. Acute renal failure was defined as an increase in serum creatinine of 44 μmol litre^{-1}.

Results. The mean duration of hypotension (MAP<55 mm Hg) was 94 min (range 35–305 min). The mean age was 71 yr. All patients with a creatinine level of 124 μmol litre^{-1} had a creatinine clearance of <40 ml min^{-1} 1.73 m^{-2} (range: 13–56). Patients with CRD received more crystalloid during surgery (1755 ml) than the other two groups (1435 ml) (P<0.001). Otherwise, all three groups were similar. No patients developed evidence of acute renal dysfunction immediately after or by 24 h after surgery. Three patients with CRD had an increase in creatinine of >44 μmol litre^{-1} at 48 and 72 h after surgery in the setting of volume depletion (acute blood loss in two patients and early ileus in one). Renal function subsequently improved.

Conclusion. HEA, *per se*, when carefully managed does not appear to predispose patients with CRD to acute renal failure after THR.

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Chronic renal dysfunction (CRD) defined as a creatinine clearance of <60 ml min^{-1} 1.73 m^{-2} is present in at least 11 million people in the USA,[1] who are thus at increased risk of mortality and morbidity from vascular disease[1 2] and from acute renal failure after major surgery.[3 4] Perioperatively, 80–90% of cases of renal failure in patients with CRD is triggered by episodes, as short as 60 min,[5 6] of relative hypovolaemia and reduced renal blood flow. For these reasons, anaesthetic management of patients with CRD is based on preserving central venous and arterial pressure. Not surprisingly, it is said that hypotensive anaesthesia is contraindicated in patients with CRD.[7]

Hypotensive anaesthesia, induced with general anaesthesia, typically results in a reduction in glomerular filtration and urine production, but deterioration in renal function postoperatively has not been observed.[8–10] However, these studies have all been performed in patients with normal renal function. Hypotensive epidural anaesthesia (HEA) involves substantial if not complete sympathectomy,[11 12] and cardiac output and central venous pressures may be maintained with a low dose epinephrine infusion.[13 14] In a large series of patients with normal preoperative renal function who received HEA, postoperative renal dysfunction was not observed.[15 16] However, avoidance of HEA in patients with CRD[17] has been recommended, as a greater

reduction in glomerular filtration rate and renal blood flow was noted when epinephrine rather than phenylephrine was utilised to control blood pressure during HEA.[18]

However, patients with CRD could potentially benefit from HEA, which offers many advantages in total hip replacement (THR), such as reduced blood loss and blood transfusion, low rate of venous thromboembolism,[19] improved cement fixation[20] and a low postoperative mortality rate.[21] For these reasons, we began utilising increasing degrees of HEA in patients with CRD so that by 1998–99, our routine practice was to utilise HEA in all patients with CRD. This study describes the experience of using HEA in 50 patients with preoperative CRD.

Methods

A database of all HEA for THR performed by the senior author (NES) from October 1999 to June 2004 was retrospectively reviewed to identify patients with a preoperative diagnosis of CRD. The Hospital for Special Surgery is an elective orthopaedic specialty hospital performing ∼2500 THR per annum. Patients with a preoperative creatinine of $\geqslant$124 μmol litre^{-1} were identified as the group with CRD. In addition, two matched pair control groups with (i) hypertension but normal serum creatinine (<124 μmol litre^{-1}) or (ii) normal arterial pressure and serum creatinine were identified. Matching was based upon gender; age $\pm$5 years, surgical diagnosis and surgery performed within $\pm$3 month period. If more than one match was available, the match closest in age was chosen.

A total of 54 patients with an elevated creatinine were identified out of a database of 1893 patients. Suitable matches were identified for 50 patients. Hospital charts were reviewed. Perioperative serum creatinine, blood urea nitrogen (BUN), haematocrit, duration of surgery, duration of mean arterial pressure (MAP) <55 mm Hg, intraoperative fluid, blood loss and blood transfusions were recorded.

All patients received HEA and were monitored with radial artery and central venous catheters. HEA was induced by injecting 20–30 ml 0.75% bupivacaine plain via a 17-gauge Tuohy needle inserted at L1–2 to T11–12 interspaces. An epidural catheter was placed, through which additional local anaesthetic could be injected. The catheter was used for postoperative epidural analgesia for 24–48 h. MAP was maintained at 40–55 mm Hg with a low dose intravenous epinephrine infusion and intravenous crystalloid to maintain central venous pressure at normal or baseline values (usually 1–3 mm Hg). Patients breathed spontaneously and were sedated during surgery with a combination of midazolam and fentanyl or a propofol infusion. Urine output was not monitored during surgery. Urinary catheters were placed in all patients in the PACU immediately after surgery.

Surgery was performed in the lateral decubitus position using the posterior approach. Patients included primary, revisions, or one-staged bilateral procedures using either cemented or non-cemented prostheses. NSAIDs were not administered for pain control. All patients received cephalozin 1–2 g every 8 h perioperatively for 24 h. Two patients received vancomycin and the other 148 patients received cephalozin for antibiotic prophylaxis. Aspirin 325 mg BID or warfarin was used for thromboprophylaxis begun the evening after surgery. Postoperatively, all patients had epidural analgesia (PCEA) for 24–48 h with a mixture of bupivacaine 0.06% and hydromorphone 10 μg ml^{-1}.

Changes in serum creatinine from the preoperative value (baseline) were measured for each patient. Perioperative renal failure was defined as an increase in creatinine level of 44 μmol litre^{-1}.[22–25] Preoperative creatinine clearance was determined for all patients using the modification of diet in renal disease (MDRD) equation. This has been validated and used in multiple studies.[1 2]

Statistics

Changes between groups were assessed by unpaired *t*-test or chi square analysis using StatView® (SAS Institute Inc.). Stasistical significance was set at *P*<0.05.

Results

The three patient groups were similar in age, height, weight, BMI and gender. The CRD group tended to have a higher ASA classification and had significantly lower preoperative haematocrit. There were 36 males and 14 females in each of the three groups (Table 1). The calculated creatinine clearance (CC) was 40 ml min^{-1} 1.73 m^{-2} for the CRD group and 80.5 and 79.5 ml min^{-1} 1.73 m^{-2} for the groups with hypertension and normotension, respectively. All patients in the CRD group had a CC of <60 ml min^{-1} 1.73 m^{-2} (range 14–58). Ten patients had a CC of $\leqslant$30 ml min^{-1} 1.73 m^{-2}.

The mean duration of intraoperative hypotension (MAP 40–55 mm Hg) was ∼95 min (NS) and the mean epinephrine infusion rate was 3.5 μg min^{-1} (NS) in each group. Patients

Table 1 Baseline characteristics of the three groups

	Patients with normotension and normal creatinine (*n*=50)	Patients with hypertension and normal creatinine (*n*=50)	Patients with CRD (*n*=50)
Age (years)	71±10	71±10	72±10
Height (cm)	171.1±9.4	167.5±12.3	171.3±9.3
Weight (kg)	78±14	85±20	85±20
BMI (kg m^{-2})	26±3.5	30±6.2	29±5.9
ASA I	5	0	0
ASA II	24	17	5
ASA III	20	33	41
ASA IV	1	0	4
Preop creatinine (μmol litre^{-1})	84±17	84±17	157±52
Preop BUN (mmol litre^{-1})	6.2±1.7	6.8±2.4	11±3.2
Preoperative creatinine clearance (ml min^{-1} 1.73 m^{-2})	79.5±15	80.5±17.6	40±10.3
History of coronary artery disease	11	5	16
History of congestive heart failure	5	3	7

Table 2 The duration of hypotension, mean epinephrine infusion rate and total volume of crystalloid administered during surgery. No patients received colloid or blood products during surgery. *$P<0.05$ compared with patients with normotension and hypertension

	Patients with normotension and normal creatinine (*n*=50)	Patients with hypertension and normal creatinine (*n*=50)	Patients with CRD (*n*=50)
Duration (min) of hypotension MAP 40–55 mm Hg	95±40	91±37	97±46
Mean epinephrine infusion rate (μg min^{-1})	3.2±1.6	3.7±1.8	3.4±2.3
Total intraoperative crystalloid (ml)	1394±568	1475±605	1755±619*

Table 3 Perioperative haematocrit and allogenic blood transfusion in each group. *Compared with patients with normotension and hypertension
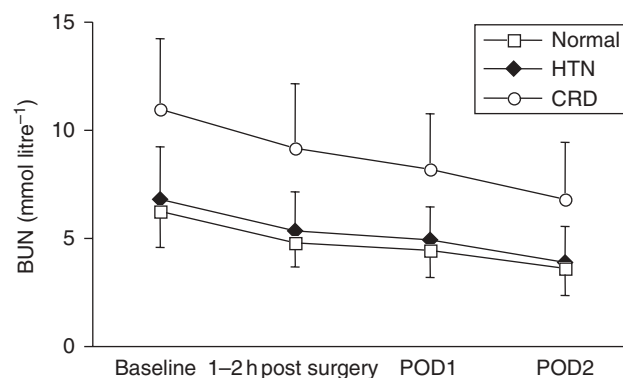
	Patients with normotension and normal creatinine (*n*=50)	Patients with hypertension and normal creatinine (*n*=50)	Patients with CRD (*n*=50)	*P*-value*
Preop Hct (%)	40.5±4.8	40.3±4.5	37.2±5.8	0.005
Postop Hct (%) (PACU)	33±4.2	34±3.9	30.6±4.7	0.01
Hct 24 h (%)	33.7±4.6	35±3.4	31.6±3.8	0.01
Hct 48 h (%)	32.4±4.6	33.5±3.3	30.8±4.5	0.01
Hct 72 h (%)	32.1±5	33.2±3.5	29.5±3.6	0.05
# Patients transfused with allogenic blood	8 (16%)	3 (6%)	8 (16%)	
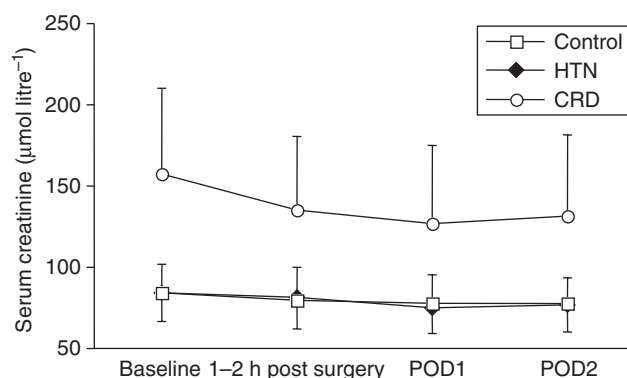
Fig 1 Mean serum creatinine for each group after total hip replacement.

Fig 2 Mean serum BUN for each group after total hip replacement.
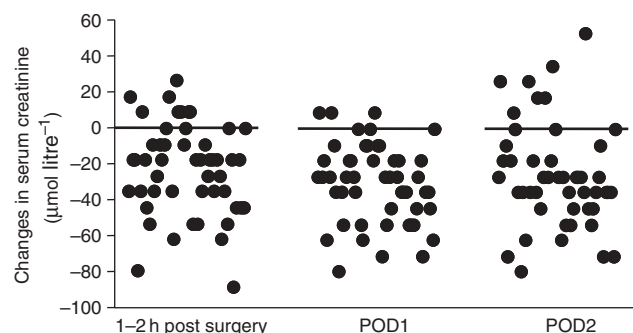
Fig 3 Individual changes in serum creatinine from baseline to 1–2 h after surgery, the following day (POD1) and 48 h after surgery (POD2) in the 50 patients with chronic renal insufficiency. No patients exhibited an increase in creatinine of 44 μmol litre^{-1} after surgery or by POD1.

in the CRD group received significantly more fluid during surgery (250–300 ml) but estimated blood loss during surgery was not significantly different (Table 2). Haematocrit fell by ∼7% perioperatively in each group (Table 3).

Serum creatinine declined from baseline, 1–2 h after surgery ($P<0.001$) in patients with CRD and remained unchanged thereafter (Fig. 1). BUN declined from baseline in both groups (Fig. 2). The changes in serum creatinine from baseline to 1–2 h after surgery, and to 1 and 2 days postoperatively for each patient with CRD, was calculated (Fig. 3). Serum creatinine did not increase by >44 μmol litre^{-1} in any patient immediately after surgery or on postoperative day 1. One patient with a preoperative CC of 52.9 had an increase of creatinine from 124 to 177 μmol litre^{-1} on postoperative day 2, which decreased to 159 μmol litre^{-1} by postoperative day 3. Two other patients (CC 35.2 and 47.2) had a 44 and 53 μmol litre^{-1} increase in creatinine by day 3. No patient in the control groups developed an increase in creatinine >35 μmol litre^{-1}. No patients exhibited persistent renal dysfunction or required dialysis after surgery.

The number of patients requiring blood transfusion was similar between groups (Table 3). Patients who required homologous blood transfusion had a significantly lower preoperative haematocrit (36.4 *vs* 39.8; $P<0.01$) but were of similar age.

Twenty of the 100 controls and 19 of the 50 CRD patients were taking ACE inhibitors preoperatively. These patients did not exhibit a greater decline in creatinine after surgery. However, two of the three CRD patients who developed an increase >44 μmol litre^{-1} in the setting of hypovolaemia after surgery were taking ACE inhibitors.

The causes for the postoperative renal failure in three of the patients with CRD were assessed by reviewing the charts and is shown in Table 4. All three were elderly patients, having a preoperative diagnosis of congestive heart failure or severe cardiac disease. One patient developed a mild ileus and became dehydrated. The other two had episodes of

Table 4 Characteristics of the three patients with CRD who had increases in serum creatinine of >44 μmol litre^{-1} after total hip replacement

Medical History		Preop Hct	Lowest Hct	Preoperative Cr (μmol litre^{-1})/ creatinine clearance	Highest Cr (μmol litre^{-1})	Transfusion
Patient 1	Male 86 y.o. High BP CHF Rx: Topol, lasix	44	32 (POD3)	133/47	203 (POD4)	No
Patient 2	Male 72 y.o. S/P CABG CHF A Fib Rx: lasix, atenolol, amiodarone, ranipril (altace)	37	26 (POD2)	124/53	177 (POD2)	2
Patient 3	Female 81 y.o. CHF MI Rx: Coreg, digoxin, captorpil, furusamide	39	23 (POD2)	133/35	177 (POD3)	3 Units + albumin 500 ml (presumptive case: ileus, dehydration)

bleeding after surgery, necessitating blood transfusion. In these three patients, serum creatinine did not elevate immediately postoperatively or in the first 24 h after surgery but increased on the second to fourth day after surgery.

Discussion

There is no universally accepted definition for new onset of acute renal failure after surgery.[3 26] However, an increase of 44 μmol litre^{-1} in serum creatinine is generally considered to be a reasonable measure.[22–24] Using this definition, none of our patients developed acute renal dysfunction within 24 h of surgery with HEA but 3 of the 150 patients had increases observed by 48–72 h after surgery. This suggests that HEA, *per se*, does not increase the risk of developing acute renal dysfunction (ARD) in patients with CRD or a preoperative diagnosis of hypertension.

The hormonal and renal response to thoracic epidural anaesthesia[27] and extensive spinal anaesthesia[28] to HEA has been studied.[18] When intravenous phenylephrine or crystalloid were used to maintain blood pressure at 50–60 mm Hg, renin and noradrenaline concentrations were decreased and renal blood flow was relatively well maintained.[18] However, cardiac output and stroke volume declined making control of the circulation difficult. With low dose epinephrine, cardiac output and filling pressures were preserved providing a more stable circulation. However, the epinephrine resulted in an increase in renin release and a decline in renal plasma flow. As a result of these studies, we were hesitant to use HEA in patients with CRD. However, over the last 7 or 8 yr, HEA with low dose epinephrine infusion has been utilised safely in patients with renal dysfunction, being mindful of the need to preserve filling pressures and monitor patients carefully. This retrospective review of our experience verifies that HEA can be safely used in patients with CRD.

The major risk factor for acute renal dysfunction after surgery is a preoperative diagnosis of CRD[3 6] and the most frequent precipitating factor is hypovolaemia leading to a reduction in renal function.[5] The extent of surgery, blood loss and use of nephrotoxic agents, e.g. contrast material and antibiotics, are other factors.[29] The risks of acute renal failure after major surgery (such as THR) in patients with CRD is unknown, but may be as high as 10–15%.[6 23]

HEA is utilised to reduce blood loss by lowering mean arterial pressure and preserving filling pressure at preoperative levels. During liver resection, anaesthetic techniques have been developed to keep central venous pressure normal. These result in less intraoperative blood loss and no increase in the risk of postoperative renal failure.[24] Techniques to minimize blood loss by lowering vascular pressure (venous or arterial) do not appear to increase the risk of acute renal dysfunction providing there is adequate monitoring.

Angiotensin converting enzyme (ACE) inhibitors may contribute to acute renal failure if mean arterial pressure decreases to levels that cannot sustain renal perfusion or if patients become volume depleted.[4 22 30] Thirty-nine of the patients we reviewed were taking ACE inhibitors preoperatively and these patients did not exhibit an increased risk of acute renal failure. This probably reflects the physiology of HEA and the care taken to prevent volume depletion in these patients in the immediate perioperative period. Other potentially nephrotoxic agents were avoided. Patients did not receive NSAIDs or COX II inhibitors. No patients with CRD received vancomycin.

There are a number of more sensitive markers of renal injury available, which we did not measure. These may have demonstrated changes in renal function not detectable by serum creatinine or BUN.[26 31] However, these are not utilised clinically at present but could be used to study the timing and factors contributing to acute renal failure after surgery in patients with CRD.

All these patients were carefully monitored with arterial and central venous catheters and patients with CRD received additional crystalloid during surgery to preserve filling pressure. Furthermore, the majority of the patients with CRD were monitored in the PACU for 12–24 h and had excellent postoperative analgesia. Hypotensive anaesthesia limited fluid shift resulting in low intraoperative blood loss (mean 197 ml). The only incidents of decline in renal function occurred after transfer to the wards where less monitoring was available. This favourable experience using HEA in patients with CRD does not mean that other means of achieving hypotensive anaesthesia are safe to use in patients with CRD. This must be subject to further study.

We included a control group with hypertension and normal preoperative creatinine. None of these patients exhibited an increase in creatinine (>44 μmol litre^{-1}) after surgery.

This is consistent with previous publications demonstrating that patients with hypertension tolerate hypotensive anaesthesia without sequelae.[8 16] The control group demonstrated that patients with preoperative renal dysfunction received an additional 300 ml of crystalloid intraoperatively, but were otherwise managed in a similar fashion. The ideal control group would be patients with renal dysfunction undergoing normotensive anaesthesia, but normotensive anaesthesia has been difficult to justify at our institution.[15]

The duration of renal hypoperfusion influences the likelihood of developing postoperative CRD and a duration of 60 min is often mentioned as critical.[5 6] The mean duration of hypotension (<55 mm Hg) was 94 min and the range was 35–305 min. The three patients who developed CRD between 48 and 72 h after surgery had MAP of <55 mm Hg for 75, 95 and 80 min, respectively. The mean duration for the other patients with CRD was 97 min. In addition, the average MAP of these 3 patients was 45, 50 and 51 mm Hg, similar to the average mean pressure of 46 mm Hg of the others who did not develop renal failure after surgery. It does not appear that duration of HEA is a factor in contributing to CRD after surgery.

Only 10 of the 50 patients with CRD had a CC of ⩽30, so it is difficult to generalise the safety of this technique in patients with more severe renal dysfunction. None of the patients with a CC<30 developed renal dysfunction after HEA. No patients with renal allografts were operated upon during this period.

References

1 Anavekar NS, McMurray JJ, Velazquez EJ, *et al*. Relation between renal dysfunction and cardiovascular outcomes after myocardial infarction. *N Engl J Med* 2004; **351**: 1285–95

2 Go AS, Chertow GM, Fan D, McCulloch CE, Hsu CY. Chronic kidney disease and the risks of death, cardiovascular events, and hospitalization. *N Engl J Med* 2004; **351**: 1296–305

3 Novis BK, Roizen MF, Aronson S, Thisted RA. Association of preoperative risk factors with postoperative acute renal failure. *Anesth Analg* 1994; **78**: 143–9

4 Lameire N, Van Biesen W, Vanholder R. Acute renal failure. *Lancet* 2005; **65**: 417–30

5 Wilson WC, Aronson S. Oliguria. A sign of renal success or impending renal failure? *Anesthesiol Clin North America* 2001; **19**: 841–83

6 Suen WS, Mok CK, Chiu SW, *et al*. Risk factors for development of acute renal failure (ARF) requiring dialysis in patients undergoing cardiac surgery. *Angiology* 1998; **49**: 789–800

7 Van Aken H, Miller ED Jr. Deliberate hypotension. In: Miller RD, editor. *Anesthesia*. 4th edn. New York: Churchill Livingstone, 2000; 1470–90

8 Thompson GE, Miller RD, Stevens WC, Murray WR. Hypotensive anesthesia for total hip arthroplasty: A study of blood loss and organ function (brain, heart, liver, and kidney). *Anesthesiology* 1978; **48**: 91–6

9 Lessard MR, Trepanier CA. Renal function and hemodynamics during prolonged isoflurane-induced hypotension in humans. *Anesthesiology* 1991; **74**: 860–5

10 Hara T, Fukusaki M, Nakamura T, Sumikawa K. Renal function in patients during and after hypotensive anesthesia with sevoflurane. *J Clin Anesth* 1998; **10**: 539–45

11 Sharrock NE, Mineo R, Urquhart B. Hemodynamic response to low-dose epinephrine infusion during hypotensive epidural anesthesia for total hip replacement. *Reg Anesth* 1990; **15**: 295–9

12 Sharrock NE, Mineo R, Go G. The effect of cardiac output on intraoperative blood loss during total hip arthroplasty. *Reg Anesth* 1993; **18**: 24–9

13 Sharrock NE, Bading B, Mineo R, Blumenfeld JD. Deliberate hypotensive epidural anesthesia for patients with normal and low cardiac output. *Anesth Analg* 1994; **79**: 899–904

14 Bading B, Blank S, Sculco TP, Pickering TG, Sharrock NE. Augmentation of calf blood flow by epinephrine infusion during lumbar epidural anesthesia. *Anesth Analg* 1994; **78**: 1119–24

15 Williams-Russo P, Sharrock NE, Mattis S, *et al*. Randomized trial of hypotensive epidural anesthesia in older adults. *Anesthesiology* 1999; **91**: 926–35

16 Sharrock NE, Mineo R, Urquhart B. Haemodynamic effects and outcome analysis of hypotensive extradural anaesthesia in controlled hypertensive patients undergoing total hip arthroplasty. *Br J Anaesth* 1991; **67**: 17–25

17 Sharrock NE, Salvati EA. Hypotensive epidural anesthesia for total hip arthroplasty. *Acta Orthop Scand* 1996; **67**: 91–107

18 Zayas V, Blumenfeld J, Bading B, *et al*. Adrenergic regulation of renin secretion and renal hemodynamics during deliberate hypotension in man. *Am J Physiol* 1993; **265**: F686–92

19 DiGiovanni CW, Restrepo A, Della Valle AG, *et al*. The safety and efficacy of intraoperative heparin in total hip arthroplasty. *Clin Orthop Relat Res* 2000; **379**: 178–85

20 Ranawat CS, Beaver WB, Sharrock NE, Maynard MJ, Urquhart B, Schneider R. Effect of hypotensive epidural anaesthesia on acetabular cement-bone fixation in total hip arthroplasty. *J Bone Joint Surg [British]* 1991; **73-B**: 779–82

21 Sharrock NE, Cazan MG, Hargett MJL, Williams-Russo P, Wilson PD Jr. Changes in mortality after total hip and knee arthroplasty over a ten-year period. *Anesth Analg* 1995; **80**: 242–8

22 Schoolwerth AC, Sica DA, Ballermann BJ, Wilcox CS. Renal considerations in angiotensin converting enzyme inhibitor therapy: a statement for healthcare professionals from the Council on the Kidney in Cardiovascular Disease and the Council for High Blood Pressure Research of the American Heart Association. *Circulation* 2001; **104**: 1985–91

23 Conzen PF, Kharasch ED, Czerner SF, *et al*. Low-flow sevoflurane compared with low-flow isoflurane anesthesia in patients with stable renal insufficiency. *Anesthesiology* 2002; **97**: 578–84

24 Melendez JA, Arslan V, Fischer ME, *et al*. Perioperative outcomes of major hepatic resections under low central venous pressure anesthesia: blood loss, blood transfusion, and the risk of postoperative renal dysfunction. *J Am Coll Surg* 1998; **187**: 620–5

25 Singri N, Ahya SN, Levin ML. Acute renal failure. *JAMA* 2003; **289**: 747–51

26 Cittanova ML. Is peri-operative renal dysfunction of no consequence? *Br J Anaesth* 2001; **86**: 164–6

27 Ecoffey C, Edouard A, Pruszczynski W, Taly E, Samii K. Effects of epidural anesthesia on catecholamines, renin activity, and vasopressin changes induced by tilt in elderly men. *Anesthesiology* 1985; **62**: 294–7

28 Kennedy WF, Everett GB, Cobb LA, Allen GD. Simultaneous systemic and hepatic hemodynamic measurements during high

peridural anesthesia in normal man. *Anest Analg* 1971; **50**: 1069–78

29 Hou SH, Bushinsky DA, Wish JB, Cohen JJ, Harrington JT. Hospital-acquired renal insufficiency: a prospective study. *Am J Med* 1983; **74**: 243–8

30 Lote CJ, Harper L, Savage CO. Mechanisms of acute renal failure. *Br J Anaesth* 1996; **77**: 82–9

31 Loef BG, Henning RH, Epema AH, *et al.* Effect of dexamethasone on perioperative renal function impairment during cardiac surgery with cardiopulmonary bypass. *Br J Anaesth* 2004; **93**: 793–8