Renal function not impaired by hip arthroplasty

A prospective study of 26 patients

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To evaluate the importance of various changes during major surgery, 26 patients, electively chosen for total hip replacement (THR), were investigated for renal function preoperatively and postoperatively. In most of the patients, surgery was performed ad modum Charnley (n 25), and anesthesia was given mainly by continuous administration of bupivacaine or mepivacaine through an epidural catheter.

Postoperatively, there was an improvement in glomerular filtration rate (GFR) and a reduction in renal concentrating ability (RCA), but no change in diurnal albumin excretion. No correlation was found between the change in GFR and, e.g., the degree of peroperative hypotension, bleeding, transfusions, or volume of infusions. There was a correlation between the impairment of RCA and the lowering of serum albumin concentration. In 3 patients the GFR was slightly impaired. The risk of contracting severe, acute renal failure seems low in THR performed on patients with reduced or normal kidney function.

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Submitted 91-04-22. Accepted 91-09-16

The risk of incurring impaired renal function after major surgery is considerable (Gornick and Kjellstrand 1983, Wilkins and Faragher 1983, List et al. 1985, Cameron 1986, Beaman et al. 1987, Davis 1987). The surgical trauma may even lead to renal failure, and the risk of such failure occurring increases with the extent of tissue damage, from hypotension, from multiple blood transfusions (Sherman 1982, Shin et al. 1986), and in cases with postoperative infections (Heloury et al. 1983, Wilkins and Faragher 1983, Myers and Moran 1986). In total hip replacement (THR), these risk factors are often present, and severely impaired renal function has been reported to occur in more than 10 percent of the patients (Gelman et al. 1979, Isacson and Collert 1984, Hedström and Hybbinette 1988). To our knowledge, no prospective study of THRs has evaluated the changes in kidney function on a more definitive basis by plasma clearance as regards glomerular filtration rate.

The aim of this prospective study was to investigate the extent of kidney impairment possibly occurring in the course of a THR operation. The importance of various risk factors for renal impairment was also considered.

Patients and methods

Patients. Thirty consecutive patients scheduled for a THR were examined preoperatively. None of them had known renal disease. Three of the patients were considered unfit for surgery at the time of the operation and were therefore excluded. A fourth patient had to be excluded after the operation because of an extensive myocardial infarction. The median age of the remaining 26 patients was 75 (49–86) years for the 16 men and 72 (50–85) years for the 10 women. Approval was obtained from the ethics committee of our hospital; and all the patients were informed, and their consent was obtained before the studies began.

Technique. THR was performed ad modum Charnley in 25 cases, whereas an intertrochanteric osteotomy (Schatzker 1984) was performed in one 50-year-old woman. As a fixative for the prosthesis, bone cement containing gentamicin granules (Schéring Corp., Kenilworth, NJ, U.S.A.) was used in 2 patients who received a revised THR. Bone cement without antibiotics (Simplex®, monomethyl methacrylate, Howmedica, Rutherford, NJ, U.S.A., and CMW, Thackray Orthopaedic, Leeds, England) was used in all the other patients. Preoperatively, all the patients were given ephedrine 5–15 mg i.v. (Kabi, Stockholm, Sweden), pethidine 25–100 mg i.m. (Kabi, Sweden), and diazepam 2–10 mg p.o. (Dumex, Copenhagen, Denmark), the doses depending on body size and age.

All the patients were kept fasting for 10–12 hours before the operation. No fluids were given i.v. before surgery.

In 24 patients, the anesthesia was given by the continuous administration of bupivacaine or mepivacaine through an epidural catheter. In 2 patients, the anesthetist was unable to gain entry into the epidural space, and a general anesthetic was given instead. The latter was also given to a third patient in whom the effect of the epidural anesthesia was not sufficient. Peroperatively, infusions, as well as blood transfusions, were given in relation to blood loss. Infusions of dextran 70 were preceded by an initial dose of dextran hapten (Promiten®, Pharmacia AB, Uppsala, Sweden) to avoid anaphylactic reactions (Renck et al. 1983). Thereafter, 500 of mL dextran 70 (Macrodex®, Pharmacia AB, Uppsala, Sweden) was given peroperatively. In addition, 500 mL of dextran 70 was given on the day of the operation, as well as on the first postoperative day, and thereafter every other day until the patient was ambulatory.

In the early phase of anesthesia, 500 mL of a modified Ringer's solution (mmol/L: Na^+ 130, K^+ 4, Ca^{2+} 2, Mg^{2+} 1, Ac^- 30, Cl^- 110) was infused. At least 500 mL of the same fluid was given peroperatively and minimally 450 mL of a 2.5 percent glucose solution (also containing in mmol/L Na^+ 70, Ac^- 25, Cl^- 45).

During the first 24 hours after the operation, bupivacaine was given through the epidural catheter to produce analgesia. Thereafter, paracetamol and dextropropoxyphene were given orally if necessary. Fourteen patients had additional injections of pethidine (meperidine) i.m. in total doses of 25 to 375 mg.

On the first postoperative day, all the patients stood up beside their bed for at least 5 minutes. Daily physiotherapy was given that included active hip and leg exercises.

As infection prophylaxis, dicloxacillin (Bristol, Solna, Sweden) was used. One patient received double doses of dicloxacillin, whereas another patient was given ceftacidim and cefuroxim (Glaxo, Mölndal, Sweden) after having recalled that earlier treatment with dicloxacillin had resulted in side effects. The remaining patients received 1 g of dicloxacillin i.v. during the operation and thereafter 1 g orally three times daily for 3 days.

Blood transfusions were given as concentrated erythrocyte solutions, stored at + 4 °C.

The glomerular filtration rate (GFR), expressed as mL/min per 1.73 m^2, was determined preoperatively a median of 26 (2–94) days before the operation, as well as postoperatively on the fourth to seventh day by the administration of 3.2 MBq of ^{51}Cr-EDTA. Calculations were performed according to Bröchner-Mortensen (1972).

The ability to concentrate urine within the collecting ducts of the nephrons was investigated by the subcutaneous administration of 4 μg of desmopressin (Tryding et al. 1987). The desmopressin test (DT) was performed preoperatively, as well as postoperatively within 2 days after the GFR determination. Urine was collected at the start and 3 h after the injection of desmopressin, and was analyzed for osmolality (mosmol/kg). This was done in 16 unselected patients. A seventeenth patient had side effects after the first injection, and the test was discontinued.

Preoperatively, the urine was analyzed for diurnal Na and K, whereas dip sticks were used to determine glucose, protein, hemoglobin, nitrite, and, in 15 unselected patients to determine dU-albumin (detection limit > 40 mg/L). The analyses were repeated on the fourth postoperative day.

Before the operation, blood serum or plasma was analyzed for creatinine, Na, K, albumin (Alb), urea, creatine phosphokinase (CPK), aspartate aminotransferase (ASAT), alanine aminotransferase (ALAT), lactate dehydrogenase (LD), fibrinogen degradation products (FDP), plasma thromboplastin component (PTC), activated partial thromboplastin time (APTt), erythrocyte sedimentation rate (ESR), blood concentration of leukocytes (WBC), and hemoglobin (Hb). The sampling was repeated 2 hours postoperatively for CPK and for the remaining tests on the fourth postoperative day.

Blood pressure (BP), temperature, fluid consumption, and urine volumes were measured daily.

Postoperative complications. A postoperative infection was present in 2 patients, 1 of whom had a lower urinary tract infection, while the other had a wound infection. Postoperative hypotension was noted in 1 of these patients; the systolic blood pressure fell from a preoperative value of 100 mmHg to 70 mmHg for 5 minutes during the initial stage of the cementation procedure and then stabilized at 100 mmHg. Postoperatively, generalized discomfort and vomiting occurred, and the systolic BP was 80 mmHg for 2.5 hours and 90 mmHg for another 3 hours despite a Hb of 118 g/L and an additional volume substitution of 2,000 mL of Ringer's solution and 500 mL dextran 70. The most pronounced reduction in GFR was observed in this patient (from 87 to 63). A possible myocardial infarction may have occurred. This was not investigated. No deep vein thrombosis or pulmonary embolism was recorded in any of the patients.

Statistics. Two-tailed tests were used, as described by Siegel (1956), using commercially available software computer programs (SPSS 1986). Spearman's rank correlation coefficient (given as r_s in text) was calculated using a Fortran program (Kempi 1985). The Mann Whitney *U*-test was used for analysis of inter-

group differences of ^{51}CrEDTA in both the patients that received and did not receive dextran 70 during the ^{51}CrEDTA. Multiple stepwise regression was performed using SAS® (SAS Institute Inc. Cary, NC, U.S.A.) for the IBM computer.

Results (Table 1)

Glomerular filtration rate showed an overall increase after the operation ($P < 0.05$, Table 2). This was indirectly verified by a simultaneous lowering of serum creatinine ($P < 0.0001$). In 3 patients the glomerular filtration was decreased. In 2 of them a temporary drop in systolic blood pressure had occurred during the cementing procedure. The third patient had had a minor fall in systolic blood pressure peroperatively together with a postoperative wound infection.

^{51}Cr-EDTA measured preoperatively correlated with the corresponding values postoperatively (r_s = 0.77; $P < 0.001$). The GFR was lower in older patients ($P < 0.001$). Their degree of change in GFR was not related to the preoperative or postoperative glomerular filtration (e.g., no appreciable change if a high initial ^{51}Cr EDTA) or to the age of the patient.

There was a negative correlation between GFR and the corresponding values of serum creatinine only if the serum creatinine was above 115 µmol/L (r_s = –0.43; $P < 0.05$). The postoperative change in ^{51}Cr EDTA did not correlate with the change in any other parameter given in Table 1 or 2, or with the extent of pethidine administered postoperatively.

Postoperatively, the values of GFR were not affected whether dextran 70 infusions were given or not given during the investigation (Mann-Whitney *U*-test, $n_1 = 9$, $n_2 = 12$, $P = 0.48$).

Multiple stepwise regression was performed for change in preoperative and postoperative ^{51}Cr-EDTA as the dependent variable compared with the independent peroperative variables: bleeding, infusion, transfusion, lowest systolic blood pressure, degree of reduction from highest to lowest systolic blood pressure, duration of hypotension (systolic BP below 100

Table 1. Peroperative data

	n	Median	Range
Bleeding (mL)	26	950	300–8,000
Transfusion (units)	26	1	0–12
Infusion (mL) 1,500–7,200	26	2,700	
Lowest BP (mmHg)	26	90	65–120
BP diff. (mmHg)[a]	26	67	15–125
Duration of hypotension (min)	17[b]	10	5–35
Duration of operation (hours)	26	2.4	1.3–8.0
Dose of ephedrine (mg)	26	10	0–45

[a]Difference between maximum and minimum values of peroperative systolic blood pressure.
[b]Patients with a peroperative systolic blood pressure below 100 mmHg.

Table 2. Preoperative and postoperative glomerular filtration rates, as well as other urine and blood data. *P*-values obtained for the difference between postoperative and preoperative data are given

	Preoperative			Postoperative			Difference
	n	Median	Range	n	Median	Range	*P*-value
^{51}Cr-EDTA (mL/min per 1.73 m^2)	26	70	34–92	26	74	37–154	<0.05
U-osmolality[a] (mosm/kg)	19	753	435–937	19	657	382–956	< 0.001
dU-Albumin (mg/d)	19	54	40–158	18	55	40–106	NS
dU-potassium (mmol/d)	23	59	16–101	22	36	16–80	< 0.001
dU-sodium (mmol/d)	23	126	33–381	20	100	29–261	< 0.02
s-creatinine (µmol/L)	26	87	55–130	26	86	50–144	< 0.001
s-albumin (g/L)	26	40	31–47	26	27	21–44	< 0.001
s-Na (mmol/L)	26	140	136–144	26	140	136–150	NS
s-K (mmol/L)	26	4.2	3.1–5.3	26	3.9	3.0–4.7	< 0.001
s-urea (mmol/L)	26	6.7	3.4–9.6	26	5.9	2.4–10.7	< 0.001
s-LD (nkat/L)	26	6.3	2.6–10.5	26	5.8	3.0–23.3	NS
s-ASAT (nkat/L)	26	0.40	0.23–0.75	26	0.58	0.23–2.54	< 0.001
s-ALAT (nkat/L)	26	0.25	0.05–1.27	26	0.38	0.17–4.80	< 0.001
s-CPK (nkat/L)	21	1.1	0.4–2.7	17	4.5	1.8–17.1	< 0.001
PTC (%)	24	101	50–158	21	95	76–125	NS
APTt (sec)	21	24	21–30	19	25	13–25	NS
Hb (g/L)	26	147	109–173	26	114	91–145	< 0.001
WBC (10^9/L)	24	6.9	4.4–9.8	22	8.0	4.9–12.6	< 0.005
ESR (mm/h)	24	12	3–54	21	108	45–143	< 0.001

[a]Desmopressin test.

mmHg), and dose of epinephrine. Variables significant for entry were bleeding (R-square = 0.33) and reduction in blood pressure (R-square = 0.18). These two parameters in the model supplied a possible explanation of changes in ^{51}Cr-EDTA in about 50 percent of the patients (R-square = 0.51).

Urine osmolality by the desmopressin test. The results of the desmopressin test are also apparent from Table 2. There was a significant reduction in the ability of the kidney to concentrate urine after the operation. The change in urine osmolality postoperatively was more pronounced if the preoperative urine osmolality was high (n 16, r_s = 0.73, P = 0.001). By linear regression analysis, impairment of urine osmolality correlated negatively with the postoperative concentration of serum albumin (n 15, r = – 0.57, P = 0.028). There was no correlation between the change of the urine osmolality and the corresponding change of other recorded variables mentioned previously. Postoperatively, the urine osmolality was not influenced whether or not dextran 70 had been given during the desmopressin test (Mann-Whitney U-test, n_1 = 4, n_2 = 10, P = 0.41). Stepwise regression analysis was not performed because of the low number of desmopressin tests.

Diurnal urine albumin. The diurnal urinary albumin before and after the operation did not change (Table 2). No correlation was found between dU albumin and any above-mentioned variable.

Miscellaneous. There was a significant increase in values of CPK, ASAT, ALAT, ESR, and WBC (Table 2). A significant decrease occurred postoperatively in the serum samples of creatinine, urea, albumin, K, diurnal urinary Na, and K, and in blood hemoglobin. No change was found for serum-LD, Na, PTC, and APTt.

Fibrin degradation products in the serum were measured preoperatively and postoperatively in 16 patients, and were found in all the patients to be less than 10 mg/L preoperatively and less than 10 mg/L in 15 patients (1 of them had a FDP of 40 mg/L) postoperatively.

A correlation was found between the amount of bleeding and the duration of hypotension (n 17, r_s = 0.63, P = 0.007), but not with the degree of hypotension. This indicated that the anesthetists were anxious to transfuse during prolonged hypotension.

In 7 patients the peroperative systolic BP was 80 mmHg or lower (Table 1). The lowest systolic BP peroperatively was 65 mmHg in 2 patients. In these 2 patients the GFR changed from 40 (mL/min per 1.73 m^2) and 92 preoperatively to 50 and 90, respectively, after the operation.

Discussion

The main findings in this study were the overall improvement in glomerular filtration rate, which on a multianalysis basis was shown to be negatively correlated with the amount of bleeding and the extent of the fall in systolic blood pressure peroperatively. A reduction in the ability of the kidneys to concentrate urine (as an indicator of distal tubular impairment) was more pronounced when the preoperative values were higher and when the postoperative concentration of serum albumin was lower.

Because the patients operated on in this study suffered from a number of classical risk factors for acute renal failure (e.g., hypotension, duration of operation, transfusion), we expected an overall reduction in GFR postoperatively. Therefore, it was surprising that the filtration rate improved. This outcome may be due to the extensive hydration and peroperative treatment with dextran 70 used in this protocol. Peroperative and postoperative infusions of dextran 70 act as an adjuvant colloid, and may prevent severe hypovolemia, and thus the development of severe renal failure. This effect may be prolonged, because after an infusion, dextran 70 is present within the body for more than 48 hours (Terry et al. 1953). This would favor a long-term renal circulation and, to some extent, protect against renal damage. However, such prophylaxis by dextran 70 was also used in studies where more pronounced renal dysfunctions were observed (Isacson and Collert 1984, Hedström and Hybbinette 1988). It is notable that in animal experiments isolated acute volume depletion per se is tolerated well, whereas on the other hand, acute volume expansion protects against ischemic injury of the kidneys (Zager 1986).

The change in GFR could not be related to indicators of the extent of muscular damage, such as CPK, ASAT, ALAT, which increased postoperatively.

With only one exception, all the patients were treated with dicloxacillin as an antibiotic prophylaxis. Two studies (Isacson and Collert 1984, Hedström and Hybbinette 1988) have claimed that dicloxacillin may be nephrotoxic. One of these studies was retrospective (Isacson and Collert 1984) and the other was prospective (Hedström and Hybbinette 1988). In an editorial comment (Nordbring 1984), the need of a study using ^{51}Cr-EDTA was pointed out. However, our present study could not verify a general nephrotoxic effect on GFR by the use of dicloxacillin. Caution is, however, urged because interactions with other factors or drugs may be of importance for nephrotoxicity.

An evidence of a minor interference in tubular function by the operation was the lowered ability of the kidneys to concentrate urine during the desmopressin test. This reduction in renal concentrating ability was

correlated negatively (only by linear regression analysis) with the concentration of serum albumin. These data may indicate a rather mild degree of medullary ischemia, because a drop in the concentrating ability of the kidneys has been shown to occur after rather mild ischemia in animal studies (Mason et al. 1987). Albumin is, within physiologic levels, important for the maintenance of the intravasal colloid-osmotic pressure, thus preventing edema, reducing blood viscosity, and enabling optimal microcirculation. Other reports have shown that renal failure, which is probably due to hypoalbuminemia, may be prevented by infusing albumin (Levy et al. 1986), and that depression of serum albumin levels may be associated with the development of acute renal failure (Levy et al.1986, Karnad et al. 1987, Ward 1988, Llach et al. 1988). These results indicate that a correction of hypoalbuminemia (e.g., by infusing albumin or plasma) to optimize the colloid-osmotic pressure within the capillaries may be favorable for protecting kidney function.

The hypopotassemia may have been due to an active secretion of potassium from the collecting ducts or due to passive losses of potassium in the proximal tubule. No diuretic medication was given postoperatively. The drop in urinary potassium and sodium measured in the urine on the fourth day postoperatively may have been due to an increased loss during the first postoperative days, and may also be an indicator that tubular reabsorption was disturbed.

A THR did not cause a change in the diurnal amount of albuminuria. The interpretation may be that the operation procedure did not affect the permeability of the glomerular basement membrane by endotoxic or immunologic processes.

In conclusion, our present study showed that there was a minor reduction in renal glomerular function in 3 of the patients, although they had overall improvement. Evidence was found that supports a slight dysfunction of the collecting ducts, indicating early stages of acute renal failure owing to medullary involvement. The only important evidence of the classical risk parameters for impairment in GFR was found by multiple stepwise regression as regards the extent of bleeding and the drop in blood pressure peroperatively. The reduction in intravascular colloid osmotic agents by bleeding may be of importance.

Acknowledgements

The authors would like to express their thanks to Dr. Kjerstin Lindberger, to the nurses in the orthopedic ward, and to the statistician Mats Nilsson. Financial support was obtained from the Norrland Njursjukas Förening.

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