

Effects of Renal Sympathetic Blockade on Renal Hemodynamics in Patients Undergoing Major Aortic Abdominal Surgery

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The depressive effects of infrarenal aortic cross-clamping on renal hemodynamics in humans have been previously reported.¹ The marked renal hypoperfusion measured during and after aortic cross-clamping is related to sustained renal vasoconstriction, which can be attributed to the changes in activity of neurogenic and/or humoral factors controlling the renal circulation. These factors include the sympathetic nervous system,² the renin-angiotensin system,² renal prostaglandins,³ and kallikrein.⁴ If renal hypoperfusion is caused by an increase in sympathetic activity, the kidneys being richly innervated by the sympathetic nervous fibers,⁵ interruption of renal sympathetic outflow could prevent the deterioration in renal hemodynamics, which was observed during and after infrarenal aortic cross-clamping in patients receiving general anesthesia alone.¹

Because the incidence of renal failure following aortic abdominal grafting surgery remains an important problem in the postoperative period,⁶ this study was designed to determine whether renal sympathetic blockade obtained by epidural anesthesia provides any protective renal effects in patients undergoing surgical procedures on the abdominal aorta.

PATIENTS AND METHODS

Nine male patients scheduled for elective aortic abdominal grafting surgery consented to participate in this study, which had institutional approval. Their age ranged from 48 to 75 yr (mean 60 yr) and the weight from 57 to 84 kg (mean 70 kg). With the exception of one patient treated with methyldopa for arterial hypertension and a second patient treated with verapamil for paroxysmal

atrial tachycardia, all subjects were free of drugs and of major pathology other than aortic abdominal disease. Surgery consisted of aorto-bifemoral Dacron® grafting and was performed in five patients for aortoiliac occlusive disease and in four patients for nonruptured aortic abdominal aneurysm.

Ninety minutes before arrival in the operating room the patients were premedicated with 0.1 mg/kg morphine sulfate im. After initial hydration of 15 ml/kg of Ringer's lactate, a lumbar epidural catheter was placed *via* the L2-3 interspace. Through this catheter 20 ml of bupivacaine 0.5% was injected, which provided a bilateral sensory anesthesia level of T-6 or above. Additional hydration of 10 ml/kg of Ringer's lactate was administered during the next 20 min. Anesthesia was then induced with fentanyl (2 µg/kg) and thiopental (3-5 mg/kg). Tracheal intubation was facilitated with pancuronium bromide (0.1 mg/kg). Anesthesia was maintained throughout the surgical procedure with nitrous oxide 70% in oxygen. Additional doses of pancuronium were repeated as clinically required and 10 ml of bupivacaine 0.5% was injected through the epidural catheter every 90 min. Mechanical ventilation and fractional inspired oxygen content (FI_O₂) were adjusted to maintain Pa_{CO}₂ between 35-40 mmHg and Pa_O₂ between 80-100 mmHg. No positive end-expiratory pressure was ever applied. Temperature was continuously monitored and maintained above 34.5° C. In all patients heart rate; systolic blood pressure, diastolic blood pressure, and mean arterial pressure using an indwelling arterial catheter; central venous pressure; and urinary output were continuously monitored. In addition, in five patients cardiac output (CO) and pulmonary capillary wedge pressure were measured before, during, and after infrarenal aortic cross-clamping using a quadruple-lumen Swan-Ganz 7F catheter and the thermolulution technique.

Glomerular filtration rate (GFR) and effective or cortical renal plasma flow (ERPF) were measured using standard clearances of ⁵¹Cr EDTA and ¹²⁵I hippuran. These labeled compounds were injected immediately after induction of anesthesia as a bolus of 60 µCi and 30 µCi, respectively, followed by a continuous infusion of 72 µCi of ⁵¹Cr EDTA and 36 µCi of ¹²⁵I hippuran in 500 ml of mannitol 20% administered at a rate of 100 ml/h throughout the study. This methodology allowed us to

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Received from the Departments of Anesthesiology, Surgery and Medicine, University Hospital of Geneva, 1211 Geneve 4, Switzerland. Accepted for publication July 31, 1986. Supported by a grant from the Montus Foundation. Presented in part at the Annual Meeting of the American Society of Anesthesiologists, New Orleans, Louisiana, October 15, 1984.

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Key words: Anesthetic techniques: epidural. Arteries: abdominal aorta. Kidney: blood flow; filtration.

TABLE 1. Systemic Hemodynamic Variables Measured at Midpoint of Preclamp, Perclamp, and Postclamp Period ($\bar{x} \pm SD$)

	Value	n	Preclamp	Perclamp	Postclamp
Heart rate	beats/min	9	75 ± 13	70 ± 8	66 ± 8
Mean arterial pressure	mmHg	9	82 ± 16	90 ± 17	90 ± 11
Central venous pressure	cmH ₂ O	9	6 ± 3	6 ± 2	8 ± 3
Pulmonary capillary wedge pressure	mmHg	5	9 ± 3	8 ± 4	9 ± 2
Cardiac output	l/min	5	6.4 ± 1.4	4.5 ± 0.9	5.4 ± 0.9
Systemic vascular resistance	dyn · s · cm ⁻⁵	5	932 ± 140	1503 ± 242*	1254 ± 216
Renal fraction of cardiac output		5	0.31 ± 0.06	0.22 ± 0.08	0.19 ± 0.07

Statistical difference from preclamp data: **P* < 0.01.

obtain adequate urinary output as well as stable (variation less than 5%) and extremely low blood levels of labeled compounds.¹

After an equilibrium period of 66 ± 9 min ($\bar{x} \pm SD$), the urine was collected during three consecutive investigation periods: 1) before infrarenal aortic cross-clamping for 66 ± 21 min (preclamp); 2) during infrarenal aortic cross-clamping for 51 ± 16 min (perclamp); and 3) after infrarenal aortic cross-clamping for 63 ± 8 min (post-clamp). In the middle of each period of urine collection, to calculate extraction fraction (EF) of ¹²⁵I hippuran and renal clearances, arterial blood was withdrawn from the radial artery, and renal venous blood was sampled by the surgeon, who punctured the left renal vein close to the kidney and withdrew blood slowly to avoid vena cava contamination. At the same time the hemodynamic data were recorded and CO measured in triplicate. Throughout the study the administration of Ringer's lactate and blood were adjusted to maintain the filling pressures and hematocrit at preclamp levels. The decrease or increase of systolic blood pressure of more than 30% of the initial value was treated with mephentermine sulfate 7.5 mg iv or inhalation of halothane, respectively. At the end of the surgery morphine sulfate was administered through the epidural catheter to obtain postoperative analgesia.

The plasma and urinary radioactivity of ⁵¹Cr EDTA and ¹²⁵I hippuran were measured with an auto-gamma scintillation spectrometer (Packard 5230). GFR, ERPF, creatinine clearance (C_{cr}), EF, total renal blood flow (RBF), filtration fraction (FF), free water clearance (C_{H₂O}), renal fraction of CO (RBF/CO ratio), and systemic and renal vascular resistances (SVR, RVR) were calculated using previously reported formulas.¹ Urinary lysozyme and ligandine were measured with standard methods.^{7,8}

The urine was collected during 24 h the day before surgery and the third postoperative day in order to calculate preoperative and postoperative C_{cr}.

The results are expressed as means ± SD. All renal data are reported for a body surface area of 1.73 m². The data between the three study periods were compared with one-way analysis of variance and test of Scheffé for statistical difference, *P* < 0.05 being considered significant.

RESULTS

The preoperative C_{cr} was 88 ± 19 ml/min, which is in the normal range for the age of the patients.⁹ In all subjects the aortic arteriography performed preoperatively showed a normal size of both kidneys, symmetric and adequate secretion of contrast medium, and absence of pathology of renal vessels.

Mephentermine sulfate, 7.5 mg iv, was administered twice in three patients, once during the equilibrium period, and once during the preclamp period. In two patients 0.5% halothane was added for 10 min immediately after aortic cross-clamping. Arterial blood gases remained stable throughout the study. Ringer's lactate, 4,400 ± 550 ml, was infused, as well as 750 ± 250 ml of blood in order to stabilize filling pressures and hematocrit, which was 37 ± 4%, 35 ± 5%, and 38 ± 4% during the three investigation periods, respectively. In addition to the 0.1 mg/kg required for endotracheal intubation, the average dose of pancuronium bromide administered was 3.4 ± 0.7 mg for the entire surgical procedure, which lasted 209 ± 29 min. The mean rectal temperature was 35.8 ± 0.4° C in the preclamp, 34.9 ± 0.4° C in the perclamp, and 34.6 ± 0.3° C in the postclamp period.

Systemic hemodynamic variables are presented in table 1. No significant change was observed with the exception of a significant increase of SVR in the perclamp period when compared with preclamp data.

The results of renal hemodynamics and function are summarized in table 2. During the perclamp and postclamp periods, when compared to preclamp data, GFR, C_{cr}, ERPF, and RBF decreased significantly, whereas FF and RVR increased significantly. The increase in EF is significant only in the postclamp period when compared with preclamp data.

The changes in systemic and renal hemodynamics between the three investigation periods were similar in patients with or without pulmonary artery catheter, as well as in patients undergoing surgical repair of either aortoiliac occlusive disease or aortic abdominal aneurysm.

The indicators of proximal tubular damage lysozyme⁷ and ligandine¹⁰ were never detected in any urine sample.

TABLE 2. Renal Hemodynamic and Functional Changes Produced by Infrarenal Aortic Cross-clamping and Declamping ($\bar{x} \pm SD$) (n = 9)

	Value	Preclamp	Perclamp	Postclamp
Urinary output	ml/min	470 ± 1.77	3.52 ± 1.42	3.58 ± 1.00
Glomerular filtration rate	ml/min	119 ± 41	76 ± 32*	77 ± 28*
Creatinine clearance	ml/min	111 ± 40	72 ± 22*	72 ± 19*
Effective renal plasma flow	ml/min	766 ± 272	393 ± 169†	370 ± 162†
Extraction fraction		0.68 ± 0.04	0.73 ± 0.05	0.74 ± 0.06*
Filtration fraction		0.16 ± 0.02	0.20 ± 0.02*	0.22 ± 0.04†
Renal blood flow	ml/min	1812 ± 677	829 ± 399†	797 ± 378†
Renal vascular resistance	dyn · s · cm ⁻⁵	3808 ± 1490	9905 ± 5525*	10328 ± 5227*
Free water clearance	ml/min	-1.07 ± 1.71	-1.15 ± 1.55	-1.30 ± 1.27

Statistical difference from preclamp data: * $P < 0.05$; † $P < 0.01$.

The mean increase in C_{cr} between the preoperative and the preclamp value, which was measured during epidural anesthesia, was 23 ± 31 ml/min ($P < 0.06$).

At the end of surgery eight of nine patients were extubated and all were pain free, sensory anesthesia level being above T-6. The C_{cr} measured 3 days after surgery (76 ± 21 ml/min) remained significantly lower ($P < 0.05$) when compared with the preoperative value.

DISCUSSION

This study demonstrates that renal sympathetic blockade obtained by epidural anesthesia does not prevent previously documented important alteration in renal hemodynamics following infrarenal aortic cross-clamping,¹ nor significant decrease in postoperative C_{cr} .

The quality of the sympathetic blockade cannot be questioned because the sensory anesthesia level was T-6 or above throughout the surgical procedure. This level of anesthesia implies a complete sympathetic blockade¹¹ of the kidney and the adrenal medulla, which are innervated by spinal nerves from cord levels T6-L2.¹² The efficacy of epidural anesthesia is further confirmed by the small perioperative requirements of muscle relaxants and analgesics. In addition, the preclamp values of renal perfusion are much higher (+80%) than those reported for normal subjects⁹ and are to be related to the combination of renal sympathetic blockade and unimpaired systemic hemodynamics.

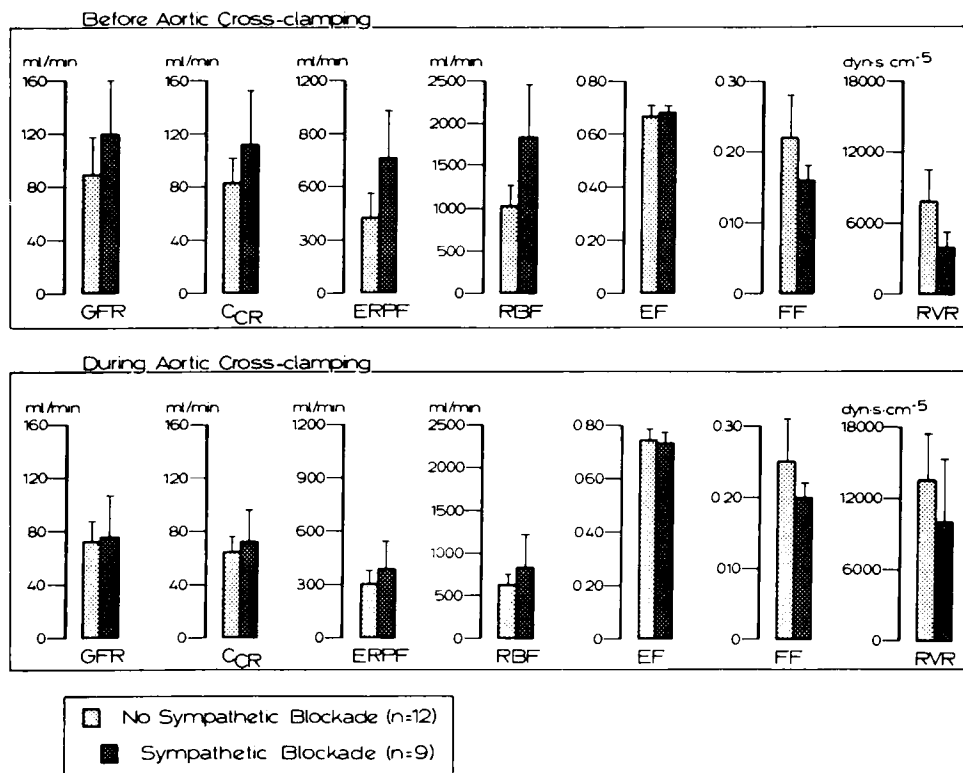
Despite favorable renal hemodynamic conditions in the preclamp period, infrarenal aortic cross-clamping produced a severe impairment of renal perfusion and function characterized by a decrease in RBF of $54 \pm 10\%$ ($P < 0.01$), in ERPF of $48 \pm 13\%$ ($P < 0.01$), and in GFR of $36 \pm 15\%$ ($P < 0.05$) and an increase in RVR of $154 \pm 73\%$ ($P < 0.05$). These renal hemodynamic changes were associated with a significant increase in SVR of $54 \pm 24\%$ ($P < 0.01$). After the release of the aortic clamp, when there was neither further local surgical stimulation nor intraabdominal retractors and packs, renal hemody-

namics did not recover, although the filling pressures remained stable while CO and SVR tended to improve.

This impairment in renal hemodynamics following aortic cross-clamping cannot be attributed to clinical factors such as ventilatory management, infusion of mannitol, or administration of anesthetic drugs. Although controlled mechanical ventilation without positive end-expiratory pressure is known to alter renal perfusion and function,¹³ it cannot explain the observed changes because ventilatory support was not modified throughout the study. An infusion of mannitol at the rate of $0.25 \text{ g} \cdot \text{kg}^{-1} \cdot \text{h}^{-1}$ was started 1 h before the first investigation period and continued until the end of the study in order to increase urinary output and thus improve the accuracy of measurement of renal clearances. A bolus injection or rapid infusion of mannitol was reported to increase ERPF in humans,¹⁴ preserve renal perfusion during aortic cross-clamping,¹⁵ and/or produce an increase in RBF with a concomitant reduction in RVR in hypoperfused kidneys¹⁶ in animals; a slow infusion of this drug, however, probably did not at any time influence renal hemodynamics, but at least cannot be held responsible for its deterioration following aortic cross-clamping. The influence of the anesthetic drugs can also be ruled out because thiopental, fentanyl, and pancuronium were injected at least 1 h before the first measurement period, and nitrous oxide does not affect renal hemodynamics.¹⁷ In addition, there are no known deleterious renal effects of local anesthetics administered *via* the epidural catheter. The observed renal hypoperfusion could only in part be attributed to the changes in systemic hemodynamics. The increase in SVR, probably due to the abrupt occlusion of highly dilated arterial vessels, was only one-third of the increase in RVR; furthermore, RBF decreased twice as much as the CO, and all systemic hemodynamic variables remained in the normal ranges in the perclamp and postclamp periods.

Our study suggests that the sustained deterioration in renal perfusion and function following aortic cross-clamping is mainly related to renal vasoconstriction that

FIG. 1. Comparison (mean \pm SD) of renal functional and hemodynamic variables obtained before and during aortic cross-clamping in patients with and without sympathetic blockade (GFR = glomerular filtration rate; C_{cr} = creatinine clearance; ERPF = effective renal plasma flow; RBF = renal blood flow; EF = extraction fraction; FF = filtration fraction; RVR = renal vascular resistance). The data of patients without sympathetic blockade originate from reference 1.



cannot be attributed to an increased renal sympathetic activity. It is also unlikely that this hypoperfusion is due to a systemic release of catecholamines, because midthoracic sympathetic blockade and analgesia have been shown to abolish neuroendocrine response to surgery.¹⁸ Increased plasma renin activity could be responsible for this intense renal vasoconstriction,^{19,20} but only partly, because interruption of sympathetic outflow attenuates the renin-angiotensin response to anesthesia and surgery.²¹ Thus, the explanation for the observed impairment in renal perfusion should involve other known factors such as renal prostaglandins or kallikrein or unknown intrinsic mechanisms.

Although the results of the present study cannot be scientifically compared with our previous published data investigating the effects of infrarenal aortic cross-clamping on renal hemodynamics in humans under general anesthesia alone,¹ it is interesting to note, as illustrated in figure 1, that before aortic cross-clamping, GFR, C_{cr} , ERPF, and RBF were much higher and FF and RVR were much lower in patients with epidural anesthesia than in patients without sympathetic blockade, whereas the difference in these data became much less important during aortic cross-clamping. Aside from the fact that the patients under epidural anesthesia received about 700 ml of Ringer's lactate more than the others, these two studies are comparable in most other respects. We believe that this dif-

ference in fluid intake was not sufficient to produce important decrease in colloid osmotic pressure with subsequent increase in GFR in the patients of the present study. Thus, these high preclamp values of renal perfusion and function can most probably be attributed to the interruption of renal sympathetic outflow, which could provide some renal protection against surgical stress, but not against aortic cross-clamping. The difference in FF between the two studies can be explained by the fact that sympathetic blockade influences ERPF more than GFR and thus confirms the concept that the increase in FF can be related to the increase in sympathetic tone.²² Our findings are not in agreement with previous work investigating the renal effects of epidural anesthesia, where a deterioration of renal perfusion and function in humans²³ and renal perfusion in animals²⁴ was observed. This difference in results could be due to differences in groups studied; elderly patients with advanced arteriosclerosis receiving epidural and general anesthesia cannot be compared with young healthy volunteers²³ or animals²⁴ receiving epidural anesthesia alone.

In summary, the present study demonstrates the absence of renal protective effects of epidural anesthesia in patients undergoing infrarenal aortic cross-clamping. In addition, our data suggest that the impairment in renal hemodynamics following aortic cross-clamping cannot be related to the increased sympathetic activity.

The authors thank Geneviève Lucot and Djaid Robertson for their excellent technical assistance. The authors are grateful to Marie-Claude Froment for her secretarial work.

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Anesthesiology
65:692-695, 1986

Comparison of Direct Blood Pressure Measurements at the Radial and Dorsalis Pedis Arteries during Sodium Nitroprusside- and Isoflurane-induced Hypotension

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Deliberate systemic hypotension can be induced by vasodilators (nitroprusside and nitroglycerin),¹ ganglionic blockers (trimethaphan),² and potent volatile anesthetics

(halothane and isoflurane).³ A potential hazard of deliberate hypotension is cerebral ischemia.⁴ Other organs susceptible to ischemic damage include the heart, gastrointestinal tract, and liver.⁵ Hence arterial blood pressure is important to monitor during deliberate hypotension.

The most frequently used site for direct arterial blood pressure measurement is the radial artery (RA). Other sites, such as the dorsalis pedis artery (DPA), have been used.⁶ Although differing pressures in RA and DPA may exist,⁷ the influence of deliberate hypotension and drugs used to induce hypotension on this difference have not been clarified. We compared arterial blood pressure obtained from RA and DPA during deliberate hypotension

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Received from the Department of Anesthesiology, Montreal Neurological Institute, McGill University, 3801 University Street, Montreal, Quebec, Canada H3A 2B4. Accepted for publication July 31, 1986.

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Key words: Anesthetic techniques: hypotension, induced. Arteries: dorsalis pedis; radial.