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The Impact of in-situ Balloon Occlusion of the Renal Artery and Hypothermic Perfusion on Renal Blood Flow

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Summary. Unilateral renal blood flow was evaluated in-situ in 13 dogs by cineangiodensitometry and microsphere distribution studies before and after intermittent balloon occlusion with and without hypothermic perfusion of one kidney. The contralateral kidney served as control. No significant difference in renal blood flow and vascular resistance was noted before, and 5, 30 and 60 minutes after unilateral intra-arterial manipulation. Compartmental flow distribution studies in 5 dogs revealed no evidence of alteration of intra-renal haemodynamics. In a clinical pilot study, unilateral renal blood flow measured by cineangiodensitometry showed no change of clinical significance 5 and 60 minutes after intraluminal balloon occlusion of the renal artery for 60 seconds.

Key words: Balloon occlusion of the renal artery - Hypothermic renal perfusion - Renal blood flow - Intra-renal flow distribution - Cineangiodensitometry - Microspheres - Renal ischaemia.

Intraluminal balloon occlusion of the renal artery and simultaneous hypothermic perfusion have proved to be valuable adjuncts to extended in-situ surgery of the kidney (9, 10). This method provides a bloodless operative field and improves the tolerance of the kidney to ischaemia during prolonged procedures on the renal parenchyma. The catheter is introduced percutaneously, so that the renal pedicle does not need to be dissected and arterial occlusion is achieved with a minimum of mechanical irritation of the vessel. Surgical manipulation of the renal artery is known to have a significant impact on renal haemodynamics (3, 6, 12, 18). It was therefore necessary to study renal blood flow following temporary balloon occlusion. As simultaneous hypothermic perfusion might also be a factor in any haemodynamic changes (3, 5, 17), its effect was likewise investigated.

MATERIALS AND METHODS

13 adult mongrel dogs weighing 17 to 32 kg were anaesthetised with 30 mg sodium pentobarbital/kg i.v. (Nembutal^R, Abbott, FRG) and intubated. They were well hydrated with approx 1000 ml 0.45% saline in 5% dextrose via a continuous i.v. drip (Fig. 1). An urethral catheter was inserted for continuous bladder drainage and arterial blood pressure measured continuously with a catheter in the right iliac artery (Statham strain gauge p 23 Db, Stato Rey, USA; polygraph, 19, Hellige, FRG).

Renal haemodynamics were evaluated by cineangiodensitometry and distribution studies of radionuclide-labelled microspheres (MAP). These methods provide comparable haemodynamic data without the need for any surgical manipulation near the renal arteries. For densitometric determination of the renal blood flow (RBF), the passage of a bolus of contrast dye through the renal arteries was documented on 35 mm film at a speed of 90 exposures per sec (Arriflex, R35-90 camera, Arritechna, FRG). 15 ml 60% meglumine diatrizoate (Angiografin^R, Schering, FRG) were injected with a motor syringe (20 ml/s, Contrax KME 500, Switzerland) through a Hettler catheter with side holes, which was introduced into the aorta from the right carotid artery, with its tip positioned approximately 15 cm proximal to the

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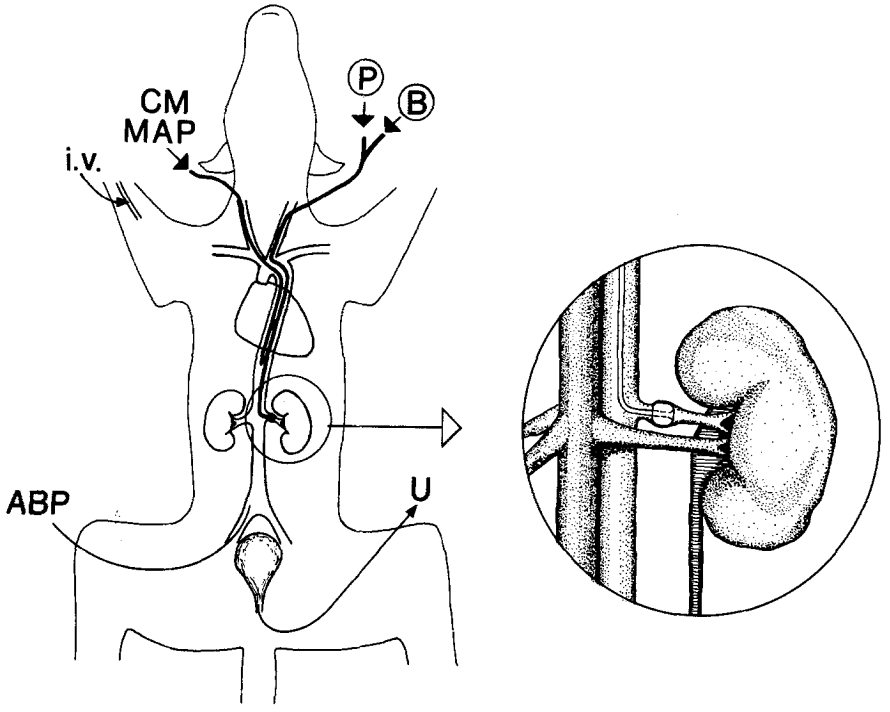

Fig. 1. Schematic drawing of experimental arrangement (ABP: arterial blood pressure; CM, MAP: Hettler catheter for injection of contrast media and MAP; BP: double-lumen Swan Ganz catheter for balloon occlusion (B) and perfusion (P) of renal artery; U: urethral catheter

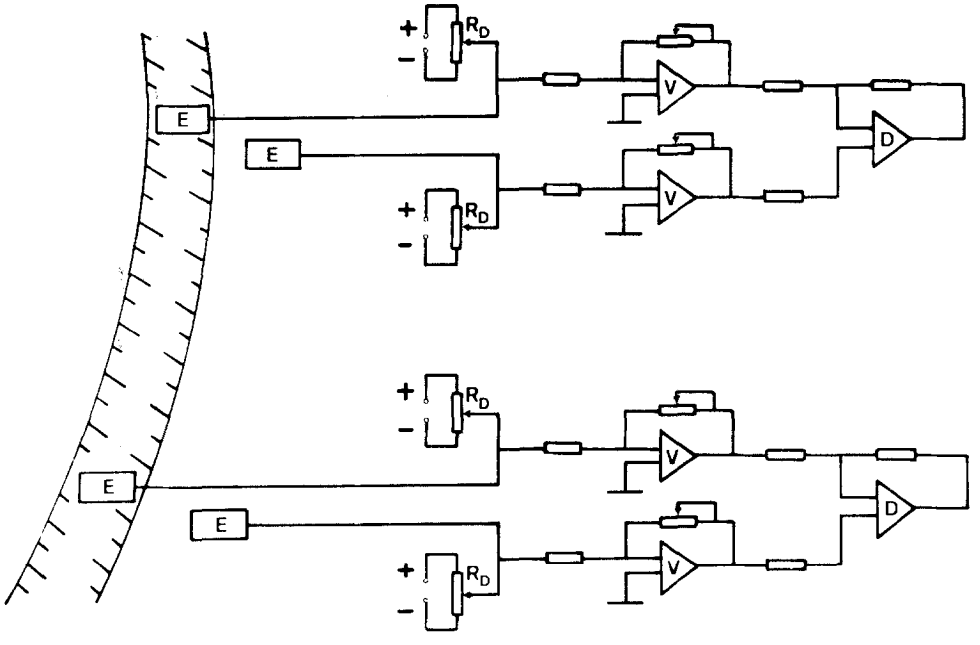

Fig. 2. Schematic drawing for recording system of dye density profile over 2 points of renal artery (E: photo element; R: rheostat; V: amplifier; D: differential potentiometer)

renal arteries. During this phase, breathing was stopped by deliberate hyperventilation followed by short-term apnoea. The time-related dye density profile was then measured from the film over 2 sections of the renal artery about 2 cm apart with 2 photo elements, each of which was connected to a reference element (Fig. 2). Using a system of amplifiers, 2 differential potentials were thus obtained representing the time concentration curve of the dye at the specific points of the artery. From the time difference of the mean transit time of the dye particles at the 2 arterial sections, the absolute blood flow in the vessel can be calculated with the formula $RBF = \pi \cdot r^2 \cdot \Delta l \cdot \frac{f}{\Delta t}$

(r = radius of artery; Δl = distance between cross sections; Δt = difference of mean transit times; f = exposures/s). In the dog, this technique has a coefficient of variation of dual measurements of $\pm$ 6% (13, 14). In addition, the cinefilm provides good morphological documentation of the renal arterial system. It was also found helpful to video-tape each angiographic phase and review it for its validity before going on with the experiment.

For the MAP-studies, human albumin particles 8 to 35μ in diameter and labelled with 99 mTc (3-M Deutschland GmbH, FRG), 113 mIn (INK-5, Commisariat a l'Energie Atomique, France) or 131 I (I 1215, Behring Institut, FRG) were used. 50,000 to 100,000 particles diluted in 1 ml dextrose, were rapidly injected into the aorta via the Hettler catheter, which was immediately flushed with 20 ml saline. With the tip of the catheter high up in the aorta, the MAP are mixed thouroughly with the aortic blood before reaching the renal arteries (15). The amount of MAP entering the renal tissue is therefore a precise function of the fraction of aortic flow to the tissue. As all the microspheres are trapped in the capillaries within a single passage (15), the determination of the MAP content of both kidneys permits precise determination of the distribution of the total renal blood flow between both kidneys at the time of injection. By determining the MAP content of the tissue of well-specified parts of the kidney, alterations of intrarenal blood flow can likewise be evaluated (4).

Baseline measurements were first obtained with both methods. A 5 F Swan Ganz balloon catheter (Nr. 93-111-5F, Edwards Laboratories, USA) was then advanced into the renal artery of one of the kidneys under fluoroscopic control from the left carotid artery. Two groups of experiments were performed. In Group I (6 dogs), the balloon catheter was simply inflated and deflated 5 times with 0.4 ml saline. This is a volume known to over-distend the canine renal

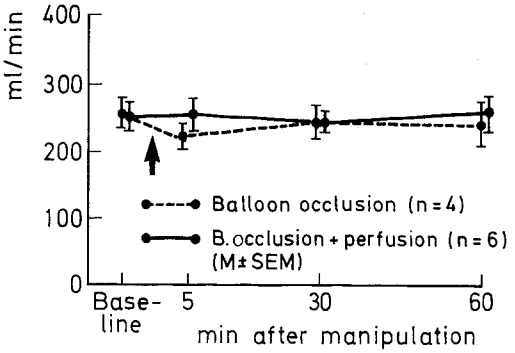

Fig. 3. Renal blood flow to manipulated kidney, as evaluated by cineangiodensitometry
(↑ : manipulation)

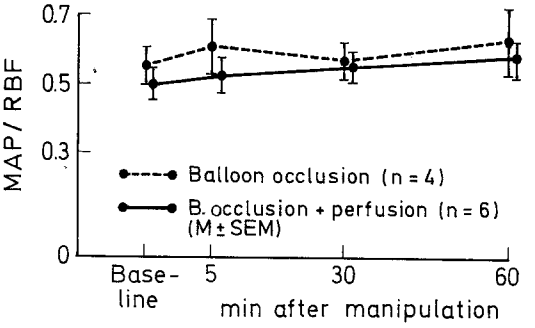

Fig. 4. Renal vascular resistance of manipulated kidneys

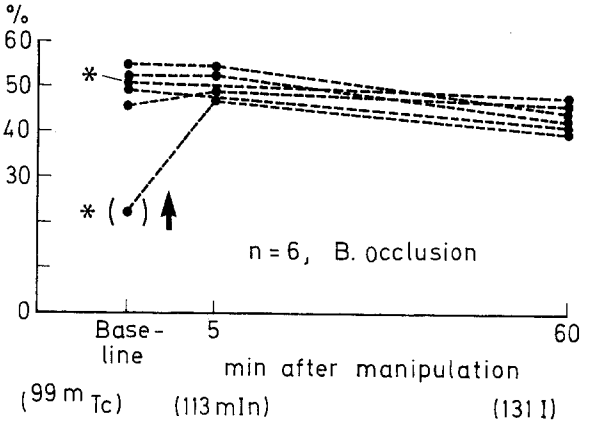

Fig. 5. Group I. Fraction (%) of total renal blood flow going to manipulated kidney, as evaluated by MAP distribution. The value marked (•) is probably due to too slow MAP injection, and was not further considered.
(* Dogs in which postocclusive densitometric flow studies were impossible because of vascular dilatation)

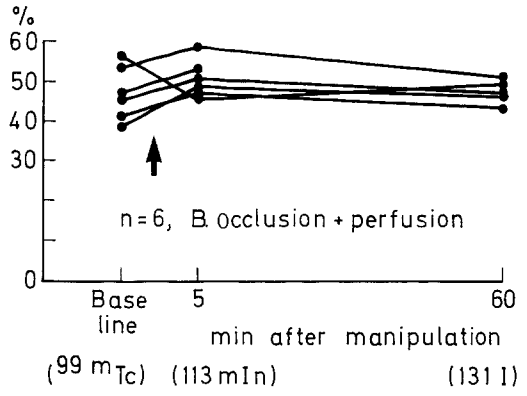

Fig. 6. Group II. Fraction (%) of total renal blood flow going to manipulated kidney, as evaluated by MAP distribution

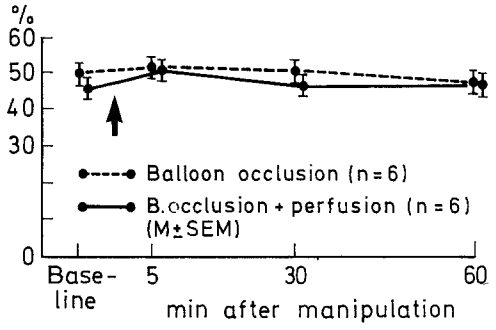

Fig. 7. Groups I and II. Fraction (%) of total blood flow going to manipulated kidney, as evaluated by densitometry and MAP distribution

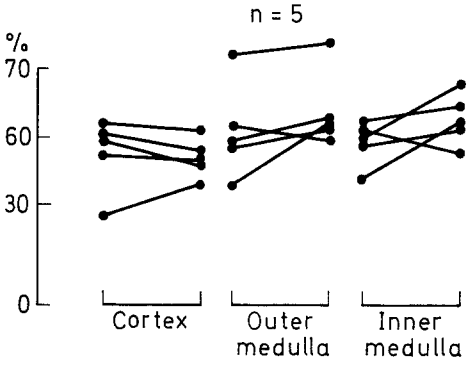

Fig. 8. Group II. Compartmental MAP distribution in 5 manipulated kidneys (in % of MAP content/g compartmental tissue of both kidneys) before and after manipulation

artery (9). The catheter was then immediately removed. In Group II (7 dogs), the renal artery was occluded by filling the balloon with 0.3 ml saline. The kidney was immediately thereafter perfused in-situ with a roller pump (Blutpumpe 742, Fresenius, FRG) via the second lumen of the catheter. 250 ml of Ringer's lactate solution, brought to an osmolarity of 430 mOsmol/l by the addition of 27 g mannitol/l, and cooled to 4° C, were administered at a flow rate of 50 ml/s (8, 9). The completeness of occlusion at the end of the perfusion was checked with a bolus of contrast dye. Thereafter the balloon was deflated and the catheter removed. Follow-up MAP studies were done 5 (113 mIn) and 60 minutes (131 I) and densitometric studies 5, 30 and 60 minutes after the procedure. The dogs were then sacrificed and the kidneys removed, weighed, and the MAP content measured in-vitro using semi-conductor counting equipment (Geli-Crystal detector, Plurimat, Intertechnique, FRG).

For intrarenal flow studies, the kidneys of 5 dogs of Group II were bi-valved and immersed in 10% formaldehyde for 24 hours. Cortex, outer and inner medulla could then be clearly differentiated macroscopically. Specimens of approximately 1 g were taken from each of these zones from the upper and lower pole and the central portion of each kidney. The aglomerular outermost part of the cortex was avoided. The content of MAP-I^{131} and MAP-TC^{89} per g of each zone was determined, and the specimens examined histologically.

RESULTS

One dog (Group II) was excluded from the study because of haemorrhage and hypotension. In 2 dogs of Group I, the renal artery was obviously over-distended and showed persistent dilatation at the site of balloon occlusion, making densitometric studies impossible. These 2 dogs had renal arteries with a diameter of less than 3 mm. Subsequently, therefore, only larger dogs were used. All other renal arteries remained angiographically normal throughout the experiment and significant vasospasm was never observed.

The results of renal blood flow determination by densitometry are given in Figure 3. After balloon occlusion only (Group I), there was a slight, but statistically insignificant (Student t test, $p < 0.05$) drop in the blood flow after 5 minutes, which promptly returned to normal. In Group II, no significant changes were noted. In virtually all dogs, a slight increase in arterial blood pressure was noted during the experiment (138 $\pm$ 6 mmHg SE before balloon occlusion, 149.8 $\pm$ 7 mmHg SE 60 minutes later), probably due to the haemoconcentration resulting from the large amounts of contrast medium (average 70 ml). The renal vascular resistance, calculated as the ratio of mean arterial blood flow in mm Hg to renal blood flow per ml per

Table 1. Renal blood flow (RBF) in 2 patients with idiopathic haematuria before and after retrograde renal phlebography with simultaneous balloon occlusion (1 minute) of the renal artery

	RBF (ml/min) baseline	RBF (ml/min) after balloon occlusion 5 min	60 min
K.G., 52 yrs., m.			
right kidney	630[a]	570[a] (-9%)	560[a] (-11%)
left kidney	540	550 (+2%)	500 (- 7%)
K.H., 62 yrs., f.			
right kidney	540[a]	610[a] (+12%)	580 (+ 7%)
left kidney	620	580 (- 6%)	570 (- 8%)

[a]manipulated kidney

min is given in Figure 4. There was a slight increase in the mean vascular resistance throughout the experiment in both groups, but this was not statistically significant.

The MAP studies likewise revealed no significant alterations in the percentage fraction of the total renal blood flow distributed to the manipulated kidney (Figs. 5 and 6). Surprisingly, the aneurysmal renal arteries occurring in 2 kidneys did not seem to reduce the blood flow significantly. The MAP values correlated satisfactorily with the percentage of the total renal blood flow to the manipulated kidney as determined by densitometry. (Mean variation of MAP results from densitometric results + 0.8% SE $\pm$ 2%; SD $\pm$ 9%). It therefore seemed justified to draw individual mean values where the results were obtained by both methods, and plot a summary of all percentage values available (Fig. 7). Again, no statistically significant alteration of the RBF fraction flowing to the manipulated kidney was noted, with a clustering of the values around the 50% line.

The results of the intra-renal flow distribution studies performed in Group II are given in Figure 8. They suggest a slight drop in the cortical blood flow and a slight increase in the outer and inner medullary blood flow. However, the changes are so small that it is doubtful if they are of any functional significance.

DISCUSSION

The re-establishment of renal circulation after temporary ischaemia is characterised by transient hyperaemia, the extent and duration of which depend on the time of renal artery occlusion and increase progressively with prolonged ischaemia (1, 3, 7). After only 10 minutes of ischaemia, it was virtually absent, even when the experiment was repeated at short intervals (7). In the present series ischaemia never exceeded 3 minutes in Group I and 8 minutes in Group II, so that a significant haemodynamic effect from this factor seems improbable. Likewise, the influence of contrast medium can be excluded. The RBF alterations seen after selective arteriography return to normal within 3-4 minutes (16). As the contralateral kidney always served as an individual control, other potential influences on RBF, such as prolonged anaesthesia, hypercapnia and haemoconcentration need not be considered. Any unilateral alteration of renal haemodynamics seen in the present investigation would therefore be a result of balloon occlusion and/or hypothermic perfusion. However, no changes of clinical significance were noted.

Obviously vasoreaction after intraluminal dilatation of the arterial wall by the balloon is considerably less pronounced than after dissection and external compression of the vessel. The latter invariably results in a reduction of RBF (6), and with severe manipulation, vasospasm (18), probably due to stimulation of the nerves located around the renal artery. In agreement with the results reported in this paper, McCaughan (11) never observed vasospasm after intraluminal occlusion of arteries in dogs, and Lyrdal (7) reported the same experience with renal arteries of rabbits. Although these results should only be applied to human arteries

with extreme caution because of species differences, extensive clinical use of balloon occlusion has not given evidence of any different vasoreaction (10). A clinical pilot study seems to confirm this (Table 1).

The renal vasoresponse to perfusion depends on the composition and temperature of the perfusate, the flow rate and perfusion pressure, time of perfusion and any accompanying ischaemic damage to the kidney (8, 17). Hypothermia is known to reduce all vascular reactions (3). As has been shown consistently in transplant surgery, hypothermic, short-term, rapid flow perfusion with an acellular "physiological" perfusates prevents severe vasoconstriction after removal of a donor kidney. In in-situ hypothermic perfusion of kidneys, Eisenberger (1), however, observed a transient RBF decrease lasting several hours after re-establishing renal circulation. His experiments, however, involved extensive mobilization and tourniquet occlusion of the renal artery, so that his results cannot be compared to those reported herein. In addition, to simulate the clinical situation (10), mannitol was added to the perfusate in the present investigation. In spite of the low total dosage, this could have transiently lowered renal vascular resistance (2), and thus have neutralised a slight vasocontrictive effect.

It is concluded that the impact of balloon occlusion of the renal artery and hypothermic perfusion has a surprisingly little impact on renal haemodynamics. This justifies the further promotion of the technique for renal surgery. The present investigation also seems to suggest that vasodilator agents are unnecessary in combination with this technique. However, it must be noted that in the extensive surgical procedures in which the technique is employed, ischaemia, the surgical manipulation of the kidney and the release of endogenous catecholamines also have a detrimental effect on post-occlusive haemodynamics (3, 7). Pretreatment of patients subjected to this kind of surgical treatment with Phenoxybenzamine, 20 to 30 mg/d for at least 3 days, as we have recommended previously (10), still seems justified.

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