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Arterial and Pedicle Occlusion in the Hypothermic Pig Kidney

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Summary. Previous laboratory investigation has indicated that during induction of ischaemia the renal artery should be occluded in preference to the whole pedicle. However, in clinical practice the distinction between these may have only a trivial bearing on subsequent renal function compared with the effect of surgery on the parenchyma. The present work was designed to investigate the effects of pedicle and arterial occlusion on the pig kidney after 90 min of hypothermic ischaemia. However, 2 other groups having nephrotomy were also included to give the study more clinical relevance.

The results showed that the combination of nephrotomy and pedicle occlusion gave a significant rise in plasma creatinine in the first 48 h post-operatively compared with the other groups. However, there was no difference between the 4 groups after 8 days and 28 days. Histology of the kidneys removed after 28 days showed comparatively minor changes in terms of glomerular and tubular structural abnormality. Furthermore the vasculature was well preserved though an inflammatory infiltrate was usually found. Semi-quantitative analysis of these changes showed that, paradoxically, they were generally less severe with pedicle than arterial occlusion. Another surprising result of this analysis was that the addition of nephrotomy appeared to be beneficial.

Key words: Warm ischaemia, Hypothermia, Pig kidney, Pedicle occlusion.

INTRODUCTION

The induction of renal hypothermia, either by direct application of cooling medium or by continuous perfusion is now established in urological practice, making possible prolonged surgery on the ischaemic renal parenchyma. However, there is still uncertainty as to the best method of occluding the renal circulation. The kidney can be rendered ischaemic by occluding the artery alone, the whole vascular pedicle or the local circulation around the operating field by direct pressure on the cortex. Most authors recommend that the arterial supply alone should be occluded, either by an external clamp or by an intraluminal balloon (2, 4, 5, 6, 11) to avoid the known hazards of venous stasis, thrombosis and secondary lesions in the renal microcirculation (9, 10). Moreover, there may be more generalised detrimental effects on the circulation (3), which could be more prevalent with arterial and venous clamping. However, in clinical practice renal ischaemia is often achieved by occluding the whole pedicle, apparently without long term ill-effects and with the advantage that venous bleeding through backflow from the vena cava is avoided (8, 12). Moreover since pedicle occlusion requires less dissection of the hilum, damage to individual vessels is more easily avoided.

The aim of the present study was to compare arterial with pedicle occlusion under controlled conditions using hypothermia, ischaemia and nephrotomy. The pig was chosen as an experimental animal since the pig kidney is morphologically and functionally similar to the human kidney.

MATERIALS AND METHODS

Twelve female pigs (large white) weighing between 18 and 24 kg were used. Operations were performed under general anaesthesia and endotracheal intubation. A transperitoneal approach was used and a right nephrectomy was first performed in all animals. Immediately after-

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wards hypothermia was induced in the left kidney with ice sludge applied directly to the cortical surface. The cooling medium was a frozen solution of 5% Glucose, the temperature of which varied between -1°C and -3°C. The core temperature, measured by a probe inserted 1, 5 cm into the parenchyma, varied between 16°C and 20°C. The mean period required for cooling after induction of ischaemia was 5 min. This method was previously found to be a satisfactory form of preservation when used in the pig and to compare favourably with perfusion cooling (1).

The animals were divided into 4 groups, each of 3 animals, according to whether arterial or pedicle occlusion was performed and with, or without, nephrotomy.

The nephrotomy performed was about 4 cm long, 1 cm deep and made longitudinally in the lower pole. Arterial and pedicle occlusion were achieved with a soft intestinal clamp. The duration of ischemia was 90 min.

The following measurements were compared in the 4 groups:

a) Plasma creatinine measured preoperatively and on the 1st, 2nd, 8th and 28th postoperative days.

The analyses were done in the routine clinical biochemistry laboratory by a standard autoanalyser technique.

b) Histological assessment of the left kidney removed after sacrifice 28 days postoperatively.

Histological sections were taken after tissue had been embedded in Paraffin and Methacrylate. Many preparations from different parts of every kidney were examined by one of us (A. Z.), without prior knowledge of their origin, to look for glomerular, tubular, interstitial and vascular changes. Signs of acute and/or chronic inflammation were noted. A quantitative scale (grades 0, 1, 2, 3) was used to denote the severity of the changes. The slides were examined by the investigator in a fixed time period.

RESULTS

Renal Function (Fig. 1)

In all experimental animals in the 4 groups the mean postoperative plasma creatinine concentrations became maximally elevated within the first 48 h. The greatest impairment of function was seen in the group in which pedicle clamping was combined with nephrotomy. A variance analysis showed that the mean levels on Day 2 taken separately and together were significantly higher than those of the other 3 groups ($p = <0.05$, $p = <0.01$, respectively). However, there was no difference between mean levels on Days 8 and 28, and plasm creatinine had not returned to pre-operative levels by the end of the experiment on the 28th post-operative day in any of the 4 groups.

Histopathological Findings

The histological findings were not grossly abnormal even in sections taken near to the site of a nephrotomy. There was some variation between individual animals but there were no striking differences between the four groups. However, all specimens showed signs of a chronic inflammatory infiltrate and protein casts in the tubules were commonly observed (Fig. 2). Slight abnormalities in the glomerular tuft, such as basement membrane thickening and mesangial hypercellularity, were occasionally seen. Focal tubular epithelial cell abnormalities ranging from cell swelling to frank necrosis were seen only in the group that had arterial occlusion without nephrotomy (Fig. 3). Mild vascular lesions, mainly restricted to the venous circulation and taking the form of a peri- or endophlebitis, were seen in groups having arterial occlusion. Arterial lesions were rare and in general the vascular endothelium and tissue in the walls of the arterial tree were well preserved (Fig. 4).

Such changes that were observed were distributed throughout the renal substance and were not necessarily related to the nephrotomy site.

These results were examined by variance analysis of the numbers denoting severity of histological change, obtained in each category from the quantitative estimates . A figure was then obtained for the sum of all the histological categories in each of the four groups of animals (Table 1). The addition of nephrotomy appeared to confer significant benefit in terms of severity of histopathological change, whether the artery or pedicle was occluded. Furthermore the changes appeared to be generally less severe after pedicle than after arterial occlusion.

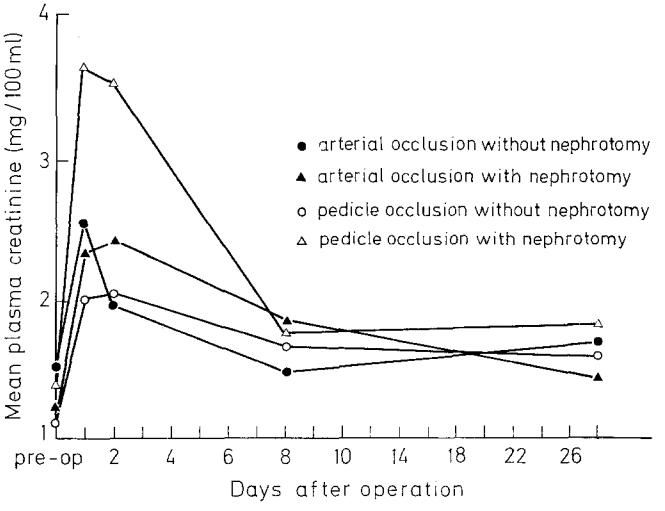

Fig. 1. Graph comparing plasma creatinines in the four groups

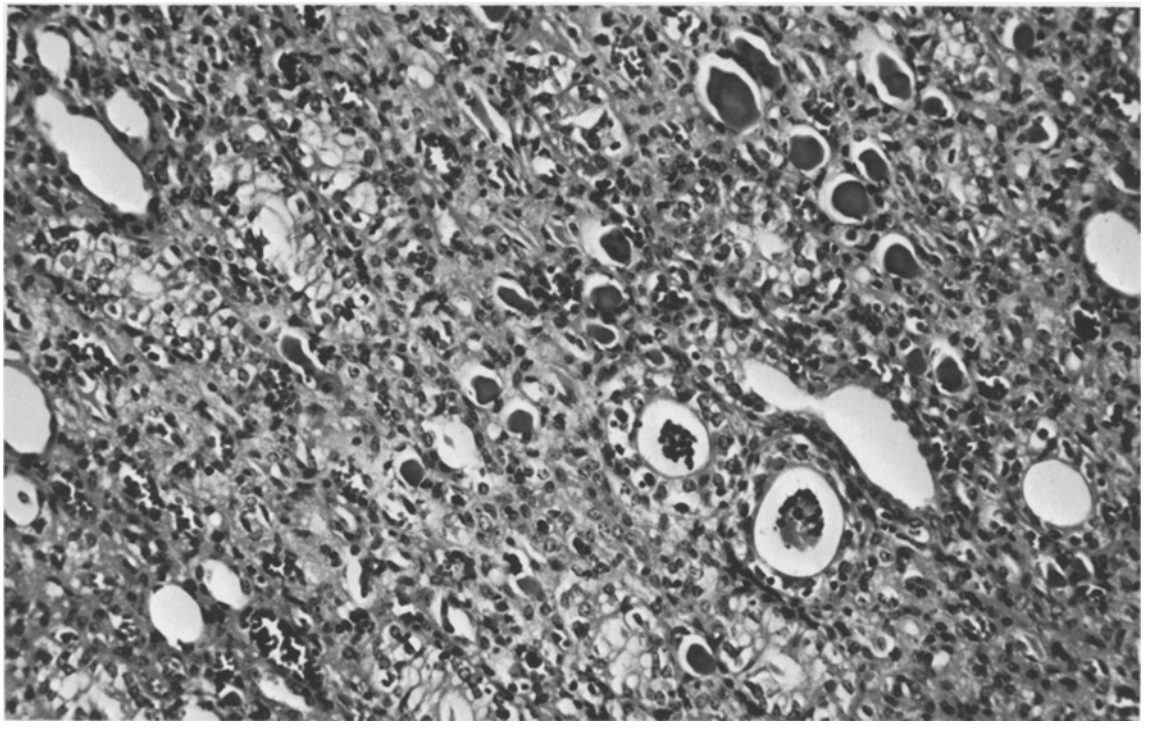

Fig. 2. Photomicrograph showing protein casts in tubules

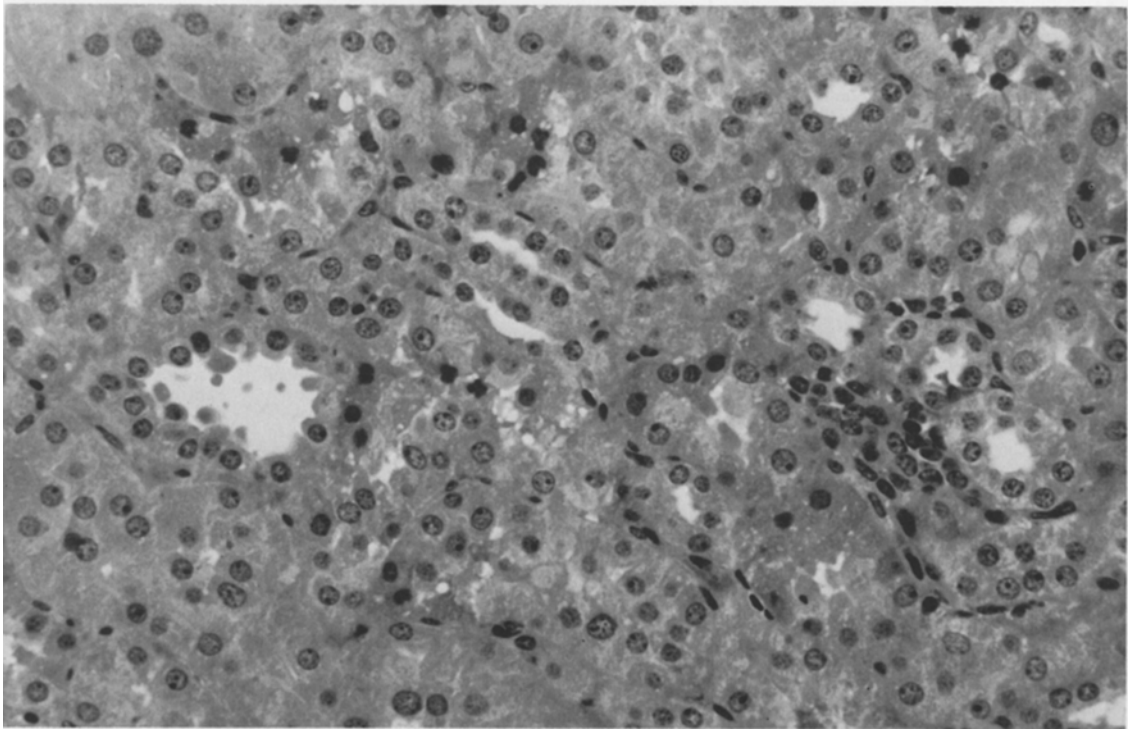

Fig. 3. Photomicrograph showing swelling of tubular epithelial cells and derangement of tubular architecture

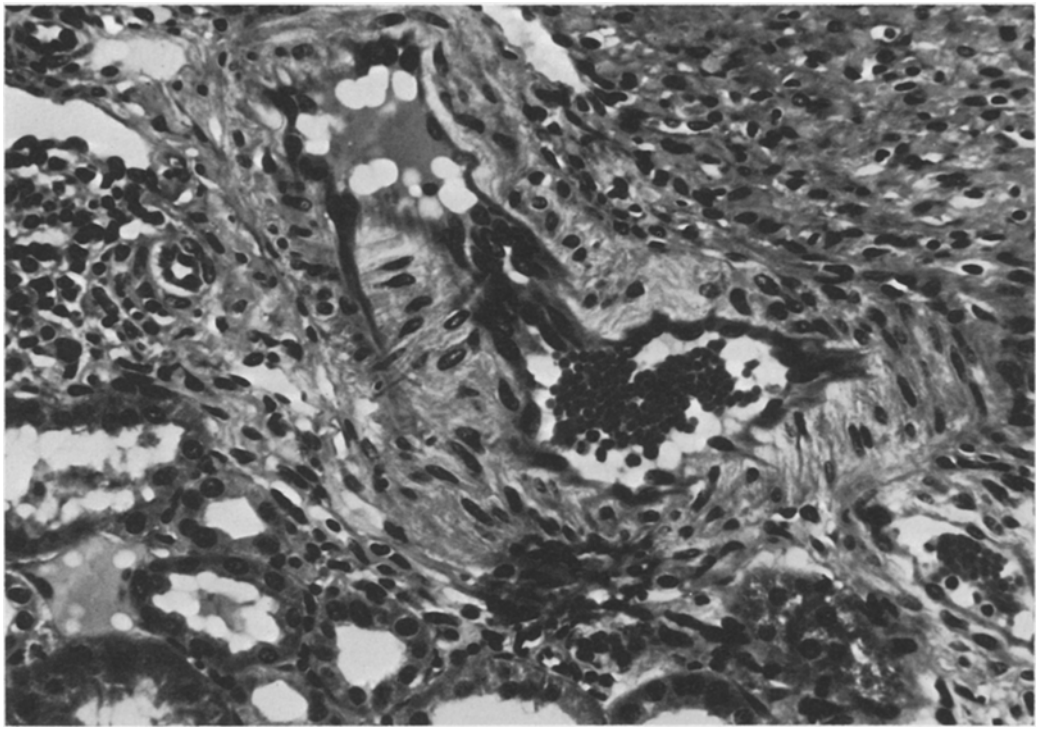

Fig. 4. Photomicrograph showing morphology of an arteriole well preserved

Table 1. Semi-quantitative assessment of histological changes. Degree of abnormality expressed on a scale 0-3 (for each category, most severe change = N° of observations x 3)

Histological categories	N°. of observations (3 kidneys)	Severity of changes			
		Arterial occlusion		Pedicle occlusion	
		+ Nephrotomy	- Nephrotomy	+ Nephrotomy	-Nephrotomy
Inflammatory reactions	21	13	18	13	20
Glomerular lesions	15	5	8	5	1
Tubular lesions	12	1	11	0	3
Vascular lesions	18	6	4	1	0
Protein deposit in tubular lumen	9	5	8	1	4
Total "severity count"		30	49	20	28

DISCUSSION

It has been a matter of some controversy whether the renal artery or the whole pedicle should be occluded prior to hypothermic ischaemia and renal surgery. There has been little experimental work to test this point and rather more comment based only on theoretical considerations. However, Birkeland et al. (2) showed that arterial occlusion in the dog caused less impairment of renal function than arterial and venous clamping: The maximum periods of hypothermic ischaemia tolerated before irreversible changes occurred were 12 h and 7 h respectively. This was supported by the work of Neely and Turner (7) who demonstrated adverse effects of pedicle compared with arterial occlusion upon renal blood flow during recovery from ischaemia in

the dog kidney. Subsequently the more recent reports of experiments in the rat by MacLoughlin et al. (6) confirmed these earlier observations. The drawback of these studies is that important issues may have been clouded by oversophisticated tests of renal function and by experimental techniques which did not correspond precisely to the clinical situation. The importance of performing a nephrotomy in the experimental kidney was also discussed by Birkeland et al. They suggested that drainage of blood through the cut surface of a kidney whose pedicle was clamped was tantamount to keeping the renal vein patent during the ischaemic period. However, they did not specifically investigate this point.

The present study was therefore designed simply to compare arterial with pedicle occlusion and to demonstrate the effects of nephrotomy in an animal whose kidney has structural and functional similarities with the human. Plasma creatinine was the only measure of renal function used as it probably has more bearing upon life support than other more complex tests. The results showed little difference between experimental groups though in the first 48 h the combination of pedicle clamping and nephrotomy appeared to be particularly disadvantageous. This result is difficult to explain in terms of venous stasis if it can be assumed that the nephrotomy allowed venous drainage and decompression during the ischaemic period. In any event these early differences in function were irrelevant to subsequent progress which was equal in the 4 groups from the 8th day onwards.

It is perhaps not surprising that by the 28th day there were few major differences in the histopathological appearances between the groups or even that for some of the parameters the 2 groups having had pedicle clamping showed paradoxically fewer abnormalities. An earlier biopsy might have shown a more obvious though reparable lesion such as tubular necrosis to parallel the relatively greater functional impairment. However, it is of interest that a simple analysis of these comparatively mild changes showed that nephrotomy is apparently beneficial where either the artery or pedicle is occluded. Here the effect of incising the kidney substance could be to reduce pressure beneath the capsule which might increase due to oedema developing during the ischaemic period. This is the same argument which has been put forward for capsulotomy as a procedure likely to improve the tolerance of a kidney to ischaemia.

Finally, a longer period of ischaemia near to the limit of the animal's tolerance might have magnified any slight structural and functional differences between groups to give a more conclusive result. However, such an adjustment would have limited the clinical relevance of the experiment.

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