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# Angiographic Evaluation of Machine Perfused Kidneys

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Summary. An intact and patent renal vascular system is a prerequisite for even and complete perfusion during machine preservation and the reestablishment of renal blood flow after transplantation. Most of the so called "viability tests" for machine perfused kidneys refer to the cellular viability, not taking into account possible lesions of the vascular system. Angiography during machine preservation is a simple, safe and reliable means of examining alterations of the renal vascular system and detecting occult vascular pathology. The degree and reversibility of vasoconstriction can easily be demonstrated, as well as normal and pathologic perfusion patterns. Angiographic examination during preservation may be useful in addition to the tests of cellular viability in order to evaluate borderline kidneys prior to transplantation.

Key words: Renal preservation, Viability tests, Renal angiography, Machine perfusion.

The increasing use of cadaver donors for renal transplantation necessitates viable preservation methods for periods ranging from several hours to several days in order to perform tissue-typing, recipient selection and organ transport on the basis of national and international organ exchange programs.

Continuous hypothermic perfusion has proved to be the method of choice for medium and long term preservation.

One of the major problems of organ preservation is the lack of simple and reliable methods for assessing the functional state and prospective capacity of the organs preserved. In vitro assays that can predict the viability and quality of a kidney prior to transplantation are a prerequisite for the clinical use of organ preservation in order to evaluate borderline kidneys and eliminate non viable oragans.

Numerous tests have been described for the evaluation of the preserved kidneys but not a single test is entirely reliable and satisfactory.

Table 1 shows the methods generally applied for the viability testing of machine perfused kidneys.

Most of these procedures refer to the cellular (parenchymal) viability, not taking into account alterations of the renal vascular system. It must be recognized, however, that even if tests of cellular viability might indicate parenchymal survival after organ storage, lesions of the renal vascular system would prevent the reestablishment of blood flow after transplantation resulting in graft failure due to cortical necrosis.

According to Belzer the most common cause of post transplant renal failure, unless it is due directly to technical factors, is persisten vasoconstriction which occurs during the agonal period of many cadaver donors and may persist during isolated perfusion as well as after transplantation. In view of the fact that in many experimental preservation studies insufficient perfusion and severe cortical perfusion defects may be present in spite of normal flow rates, it was the purpose of these studies to examine the alterations of the renal vessels in order to find out if angiographic criteria might be valuable for the evaluation of machine perfused kidneys.

## Material and Method

Canine kidneys and potentially transplantable human cadaver kidneys were examined by angiography.

Unilateral nephrectomy was carried out on healthy mongrel dogs and the kidneys were placed on a Gambro perfusion system. The perfusate consisted of a 5% albumin solution with the addition of penicillin, magnesium sulphate, hydrocortisone and insulin. Systolic perfusion pressure was adjusted to 60 mmHg, the temperature of the perfusate was kept at 8°-10°C, the pH of the perfusate at 7.2-7.4.

The original organ chamber of the disposable Gambro perfusion set was modified (Fig. 1) in order to perform renal arteriograms under sterile conditions, without removing the kidney from the perfusion apparatus. The contrast medium consisted of two parts (10 ml) of an electrolyte solution blended with one part (5 ml)

Table 1. Viability tests of machine perfused kidneys

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|---|
| 1. Flow/pressure relationship (Belzer) |
| 2. Release of cellular enzymes and electrolytes into the perfusate (Ashby, Bauditz) |
| 3. Weight gain during perfusion (Liebau) |
| 4. pH alterations of the perfusate (Magnusson) |
| 5. Tetrazolium bromide test (Smith, Terasaki) |

Table 2. Electrolyte concentration of the diluted contrast medium

| | |
|---|---|
| Sodium | 130 mEq/l |
| Potassium | 10 mEq/l |
| Magnesium | 2 mEq/l |
| Calcium | 5 mEq/l |
| Chloride | 107 mEq/l |
| Lactate | 40 mEq/l |
| pH | 7.2 |

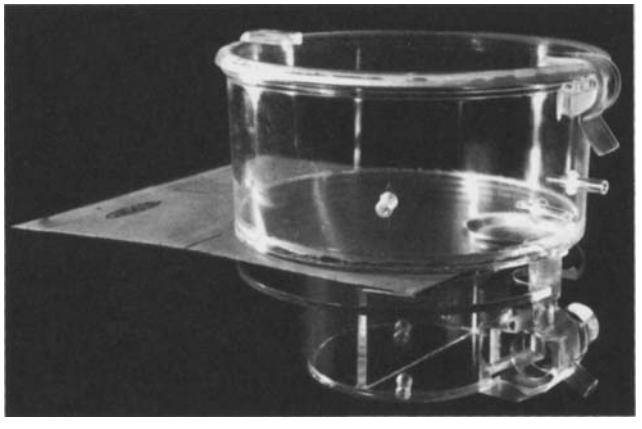


Fig. 1. Modified organ chamber with x-ray film

of Urografin$^{R}$ 76% thus imitating the electrolyte concentration of the perfusate.

Table 2 shows the electrolyte concentration of the diluted contrast medium.

For angiographic examination 10-15 ml of the cooled contrast medium was injected into the renal artery by gravity flow at perfusion pressure (60 mmHg). Industrial films were placed beneath the organ chamber and exposed by means of a simple X-ray apparatus (Nanodor II, Siemens).

The contrast medium was led out of the organ chamber immediately after having passed through the kidney in order to avoid mixing of the contrast medium with the perfusate. After renal angiography was completed, the organ chamber was flushed by an additional 100 ml of perfusate which was also discarded. Perfusion then continued normally.

Physical perfusion parameters (flow, pressure), pH of the perfusate and LDH concentrations in the perfusate were measured.

Group I. 5 dogs were unilaterally nephrectomized, the kidneys were placed on the perfusion apparatus and angiography was performed.

Group II. 5 dogs were submitted to haemorrhagic shock prior to nephrectomy with systolic blood pressures ranging between 30-40 mmHg for 45 minutes. The kidneys were removed, placed on the perfusion apparatus and angiography was performed. After an additional 60 minutes of perfusion angiography was repeated.

Group III. 5 kidneys were subjected to 60 minutes of warm ischaemia, placed on the perfusion apparatus and angiography was performed.

Group IV. 6 dogs were unilaterally nephrectomized, the kidneys were placed in the perfusion apparatus. Angiograms were performed after 48-52 hrs of perfusion and the kidneys were autotransplanted.

Group V. 5 human cadaver kidneys which were thought to be potentially transplantable were studied by angiography. These kidneys were not transplanted because of lack of suitable recipients.

## Results

Group I. The angiograms of the kidneys examined immediately after placement on the perfusion apparatus showed complete perfusion of the kidneys with dense and even filling of the arteriae interlobulares (Fig. 2).

Group II. The angiograms of the kidneys submitted to severe haemorrhagic shock prior to

nephrectomy showed marked medullary and corticalshut down when examined immediately after placement on the perfusion system (Fig. 3 a). After one hour of additional perfusion, a nearly normal medullary and cortical vascular perfusion pattern had been reestablished (Fig. 3 b).

Group III. The angiograms of the kidneys submitted to 60 minutes of warm ischaemia showed extreme medullary and cortical shut down (Fig. 4).

Group IV. 4 kidneys on which angiographic examination was performed after 48-52 hrs of perfusion showed normal angiograms with dense and even filling of the renal vessels including those of the cortex. There was spontaneous urine production after transplantation. The dogs survived immediate contralateral nephrectomy and the serum creatinine rapidly returned to normal values.

2 kidneys of this group showed extreme medullary and cortical perfusion defects (Fig. 5).

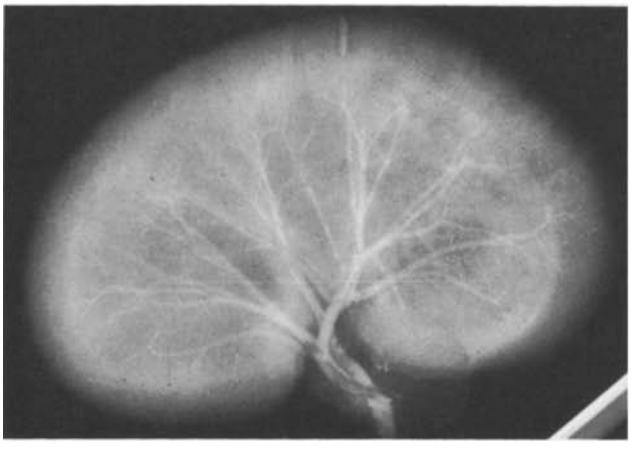


Fig. 2. Normal angiography of a canine kidney immediately after removal

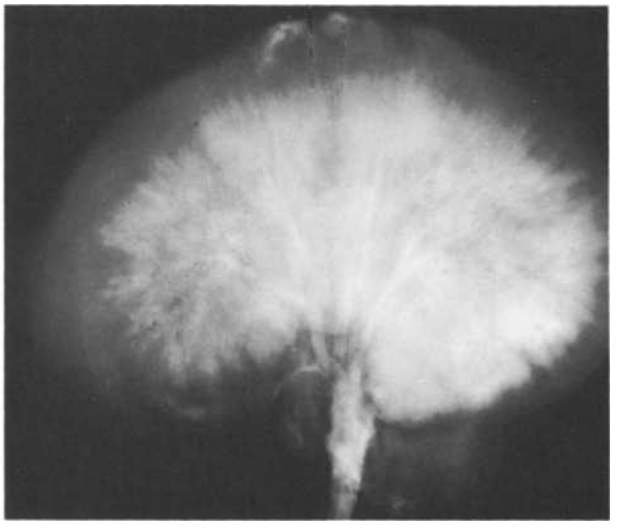
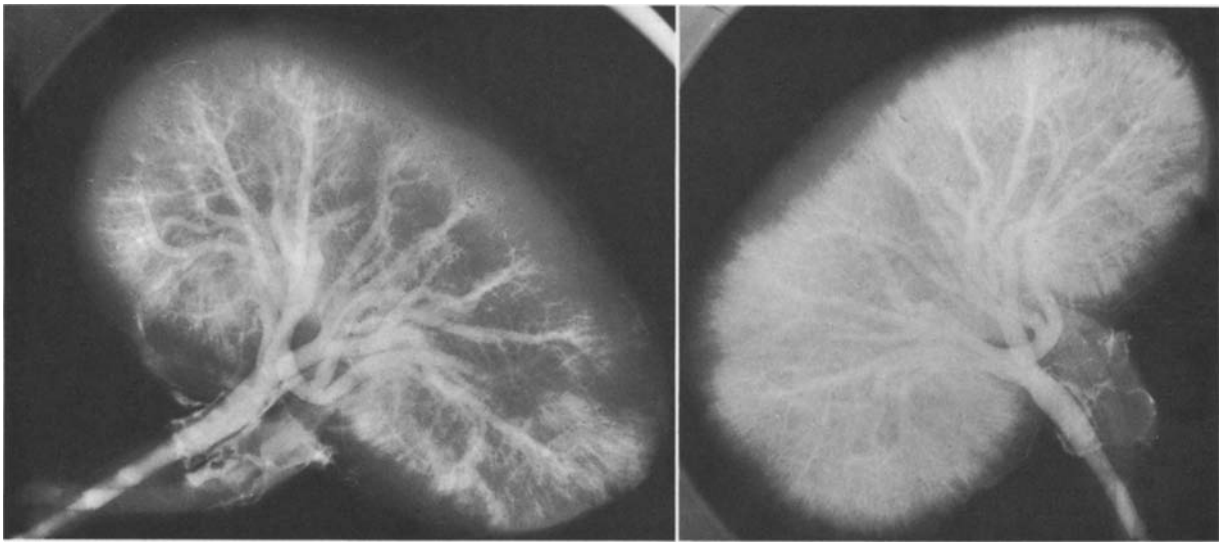


Fig. 4. Angiogram of a dog kidney after 60 min of warm ischaemia. Severe cortical perfusion defects



a b

Fig. 3 a and b. a) Angiography after 45 min of haemorrhagic shock. b) The same kidney after 60 min of perfusion

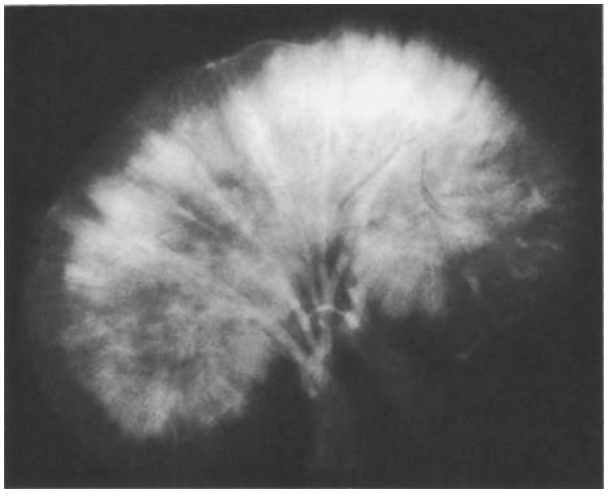
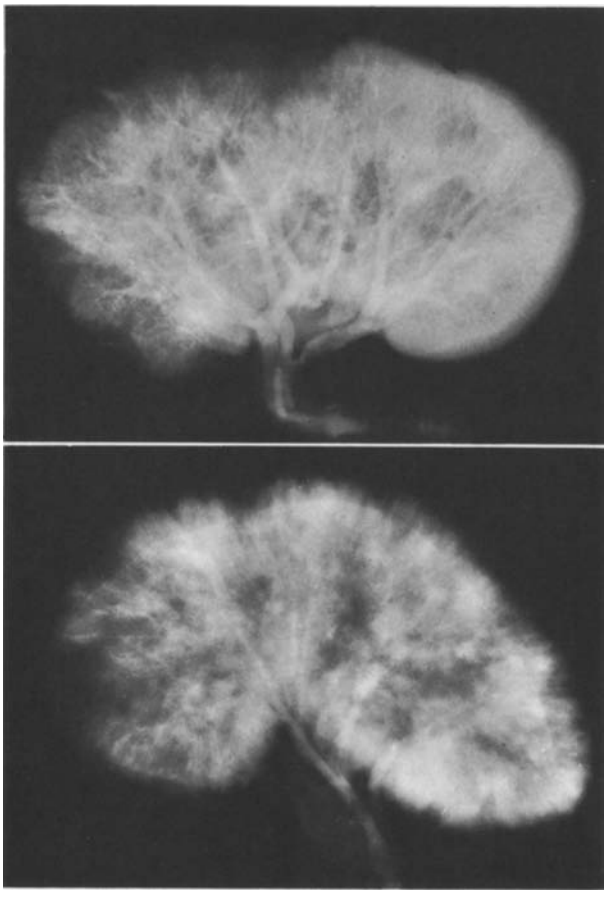


Fig. 5. Severe perfusion defects after 48 hrs of perfusion



a

b

Fig. 6a and b. Human cadaver kidneys after 24 hrs of perfusion: Cortical vascular shut down

Fig. 6b shows another human kidney after 24 hrs of perfusion. The kidney was thought to be transplantable. Angiography revealed severe perfusion defects.

The kidneys were soft and cyanotic after transplantation. There was no spontaneous urine production. After contralateral nephrectomy the dogs died in uraemia.

Perfusion parameters of all kidneys in this group were similar. Flow rates were 1.5-2 ml/min/g kidney weight, perfusion pressure and pH were constant, LDH release into the perfusate was less than 110 mU/ml at the end of the perfusion.

Group V. Fig. 6 a shows the cortical vascular shut down of human cadaver kidney after 24 hours of perfusion. The kidney was macroscopically normal after removal. Perfusion parameters did not indicate reduced viability. The angiogram, however, shows incomplete filling of the lower pole.

## Discussion

The increasing use of cadaver kidneys for renal transplantation, including many transplants which have undergone various degrees of ischaemic damage, often deriving from donors with premortal hypotension, necessitates reliable in vitro assays that can predict the functional state and prospective capacity of the organs preserved in order to evaluate borderline kidneys and eliminate non viable organs.

According to a report of the EDTA[1] (5) the transplantation of non viable kidneys was the cause of 7.8% of persistent transplant failures.

The procedures generally used for the viability testing of machine perfused kidneys (Table 1) probably do not always prevent the transplantation of non-viable kidneys and in many cases the evaluation is extremely difficult.

The common tests of cellular viability (Tetrazolium bromide test, LDH release into the perfusate, pH alterations of the perfusate) do not take into account possible lesions of the vascular system. Reduced flow during machine preservation may indicate increased vascular resistance but does not reveal its cause. Magnusson has shown that the flow/pressure relationship does not necessarily predict the functional capability of preserved kidneys. Complete and even perfusion during machine preservation is, however, a prerequisite for successful storage and an intact and patent vascular system is necessary for the reestablishment of renal blood flow after transplantation.

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1 European Dialysis and Transplant Association

Our studies show that haemorrhagic shock prior to nephrectomy causes marked medullary and cortical perfusion defects due to persisting vasoconstriction which, according to Belzer, is the most frequent cause of post-transplant failure. The studies show that perfusion may be improved by machine preservation suggesting wash out of vasoconstrictive substances during continuous perfusion resulting in reduced vascular resistance.

High flow rates during machine preservation are no guarantee of complete and even perfusion. Even when high flow rates are observed cortical vascular shut down may be present. This was also shown by Carrière and his co-workers in Boston by autoradiographic measurements of the renal blood flow after hemorrhagic shock. They demonstrated that with hypotension the blood flow in the cortex is progressively reduced due to an increase of vascular resistance in the outer cortex by up to 100%.

In contrast the vascular resistance in the medullary region and inner cortex is reduced by approximately 50% explaining maintenance of the total flow rate.

Angiographic examination of machine preserved kidneys is a simple means of demonstrating "normal" or "pathological" perfusion patterns and evaluating the degree and reversibility of vasospasm. Borderline kidneys can easily be examined.

From our experience in both experimental and clinical preservation it seems difficult to evaluate kidneys by determination of enzyme release into the perfusate. High enzyme levels are compatible with organ recovery from tubular necrosis. On the other hand no enzymes can be released into the perfusate from non perfused areas. Thus enzyme levels in the perfusate may be low even if the kidney is severely damaged and unsuitable for transplantation due to vascular lesions.

In order to avoid possible toxic effects of the contrast medium we suggest the use of a modified, diluted and buffered contrast medium which is not allowed to mix with the perfusate. Autografted dog kidneys funtioned well after repeated angiographic examinations.

Angiographic examination of machine preserved kidneys is a simple procedure and allows reliable assessment of the vascular state of a kidney which cannot always be obtained by the viability tests described so far.

It must be admitted, however, that a normal angiogram is no guarantee of viability of a kidney as it may be unsuitable for transplantation because of severe cellular damage. Nevertheless angiographic examination may be useful in addition to the tests of cellular viability in order to evaluate borderline kidneys prior to transplantation.

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