Intrarenal Haemodynamics During Hypothermic Perfusion of Cadaver Kidneys

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The preservation of potential renal allografts by continuous pulsatile perfusion has increased the margin of time available for matching cadaver donors with recipients by histocompatibility tests. It has also provided time for assessment of the viability of kidneys before implantation. During perfusion, measurements of perfusion pressure, flow, pH and LDH levels are used as guides in determining the functional integrity of the kidney. Although these parameters are valuable, it is still difficult to adequately judge the viability of a kidney during preservation procedures.

Within the past ten years, the presence and functional significance of separate relatively independent circulatory pathways within the kidney has attracted much attention. Indirect evidence in man suggests that the intrarenal distribution of blood flow is an important determinant of renal function (Hollenberg et al, 1972). Because there is a relationship between renal function and the intrarenal distribution of blood flow, we felt it necessary to investigate this relationship during organ preservation. The purpose of our study was twofold.

First we wanted to determine the intrarenal distribution of plasma flow in human cadaver kidneys during hypothermic perfusion by means of the xenon washout technique. Secondly, we wanted to correlate the intrarenal distribution of plasma flow during organ preservation with kidney viability.

Forty one human kidneys were recovered through the North Eastern Ohio cadaver Kidney Procurement Program (participating hospitals: Akron City, Cleveland Metropolitan General, Mount Sinai, University Hospitals, Veterans Administration of Cleveland, and the Cleveland Clinic). These kidneys were placed on the Belzer L1-400 preservation unit and perfused with cryoprecipitated plasma at 10°C. Mean perfusion pressure was 40 ± 2 mm and total plasma flow measured directly was 100 ± 5 ml/min for the 41 kidneys. After one hour of pulsatile perfusion, the intrarenal distribution of plasma flow was determined by the xenon washout technique.
Scintillation probes (Picker Tri Probe) were arranged over the kidneys on the Belzer unit to record the washout of $^{133}$Xenon. Approximately 1 mCi of xenon dissolved in saline was injected simultaneously into the arterial supply of each kidney and the rate of disappearance of $^{133}$Xenon was monitored for 45 minutes. The number of components in each washout curve was determined graphically by plotting the logarithm of the counts against time and using the curve peeling method described by Thorburn and colleagues (1963). Total renal blood flow was also measured directly before and after each $^{133}$Xenon washout.

The number of components as determined by the exponential analysis of each washout curve for the 41 kidneys are presented in Table I.

<table>
<thead>
<tr>
<th>Number of kidneys</th>
<th>Clearance rate $T^{1/2}_c$ for each component</th>
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<tbody>
<tr>
<td>21</td>
<td>$35^\pm 4$ 171$^\pm 16$ 1239$^\pm 120$</td>
</tr>
<tr>
<td>19</td>
<td>52$^\pm 5$ 1005$^\pm 135$</td>
</tr>
<tr>
<td>1</td>
<td>126</td>
</tr>
</tbody>
</table>

* $T^{1/2}_c$ (sec) determined from exponential analysis of $^{133}$Xenon washout curves
+ Values represent mean $^\pm$ SEM

The components are presented in terms of the half time clearance rate ($T^{1/2}_c$) for each component as determined from the washout curves. $T^{1/2}_c$ represents the time in seconds which is required for the radioactivity in the component to decrease by half its original value.

In 21 kidneys the washout curve was described as the sum of three exponentials as illustrated by the three components, having a $T^{1/2}_c$ of 35, 171, and 1239 seconds respectively. In 19 of the kidneys, the washout curve was described as the sum of two exponentials, a fast component represented by a $T^{1/2}_c$ of 52 seconds and a slow component of 1005 seconds. In one kidney, the washout of xenon was described by a single exponential by a $T^{1/2}_c$ of 126 seconds.

The important observation in Table I is that human kidneys perfused at $10^\circ$C are not perfused in a homogeneous manner. Rather there is a heterogeneous distribution of plasma flow in most of the kidney as indicated by the observance of more than one component in the washout curves of the 41 kidneys. Translation of these rates of disappearance into more meaningful flow rates and areas of distribution is presented in Table II. The flow is represented as millilitres per minute per 100 grams of tissue corresponding to the anatomical compartment for each component. From autoradiographs made from human kidneys the fastest component I, represents the mid-cortical area whereas component II represents the juxtamedullary area, and III, the renal fat which is not considered since it is so small.
Table II. Plasma flow rate and distribution in isolated human kidneys as determined by a three component washout curve*

<table>
<thead>
<tr>
<th>Components</th>
<th>I</th>
<th>II</th>
<th>III†</th>
</tr>
</thead>
<tbody>
<tr>
<td>% xenon to compartment</td>
<td>43± 5</td>
<td>54± 3</td>
<td>very small</td>
</tr>
<tr>
<td>Flow rate ml/min/100 g</td>
<td>52± 5</td>
<td>17± 2</td>
<td>very small</td>
</tr>
<tr>
<td>compartment</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

* Values represent Mean± SEM as determined from exponential analysis of xenon washout curves in 21 kidneys
† Since $T_{1/2}$ for this component was very long 1239± 120 sec, this compartment was not considered

Rosen et al (1968) reported that approximately 70% of the total renal blood flow in humans goes to the cortical compartment at a rate of 375 - 400 ml/min/100 g. In the isolated kidney (Table II) only 43% of the total plasma flow goes to the cortical compartment at a rate of 52 ml/min/100 g or at a flow approximately 1/8 that of normal. Thus, there is not only an alteration in the distribution of flow in these kidneys, but the percentage of flow going to the cortex and its flow rate is greatly decreased.

Since the pressure flow relationship has been used as one criterion of kidney viability during preservation (Belzer et al, 1970), we were anxious to know if there was any correlation between the intrarenal distribution of plasma flow as determined by $^{133}$Xenon and the resistance or pressure flow relationship of the kidneys. Accordingly, in the kidneys characterised by three flow components we plotted the percentage of total blood flow going to the mid-cortical compartment against the resistance of each kidney (Figure 1). Even though we were working with a fairly homogeneous group of kidneys in terms of weight, flow, and perfusion pressure, there was a great difference

![Graph of percentage of total renal plasma flow going to component I versus the kidney perfusion resistance. Data plotted from those kidneys in which $^{133}$Xenon washout was described by three components](image)

Figure 1. Graph of percentage of total renal plasma flow going to component I versus the kidney perfusion resistance. Data plotted from those kidneys in which $^{133}$Xenon washout was described by three components
between individual kidneys in regard to the percentage of total flow going to the mid-cortical compartment. At approximately the same resistance, either practically none of the cortex or almost all of it could be perfused. This inability to predict the vascular filling and perfusion pattern within a kidney from the pressure flow relationship, is further emphasized by Figures 2 and 3 which are pictures of silicon rubber casts of the renal cortical vasculature. These casts were made by pumping silicon rubber (Microfil) into each kidney on the Belzer unit at the same pressure at which the kidney was perfused with plasma. Figure 2 shows complete filling of the cortical compartment. The vasculature is evenly filled all the way to the capsule. In contrast to the kidney shown in Figure 2, the cortical compartment (Figure 3) is barely filled; only the major blood vessels are filled in this kidney. Both of these kidneys had approximately the same resistance during perfusion but the percentage of total flow going to the cortex in each case was vastly different.

In conclusion, these data show first that human kidneys maintained by hypothermic pulsatile perfusion do have an altered heterogeneous intrarenal

Figure 2. Vascular pattern of human kidney visualized by silicon rubber injected into renal artery after perfusion on the Belzer unit X40. Good filling pattern
distribution of plasma flow. In contrast to the normal distribution, and the flow patterns observed in vivo, the percentage of total plasma flow going to the cortex is greatly reduced. Less of the cortex is perfused during preservation procedures. Moreover, one cannot predict the vascular filling and perfusion patterns within a kidney from the pressure-flow relationship: the cortex of one kidney may be better perfused than the cortex of another kidney for the same resistance. Alfidi and Magnusson (1972) using angiographic criteria in dog kidneys reported a similar disparity between uniform angiographic perfusion and renal perfusion resistance.

Thus, prediction of the functional viability of kidneys during preservation by the pressure-flow relationship alone can be misleading. Kidneys judged to have good total flow at a low perfusion pressure may have incomplete patchy cortical filling and poor function subsequent to implantation.

Finally, because the problems involved in transplantation are legion, it
has not been easy to correlate the intrarenal distribution of plasma flow
determined during preservation with the viability of the kidney after trans-
plantation. Kidneys with good cortical filling appear to function better
immediately after transplantation than kidneys with poor cortical filling.
Clearly better documentation is needed and this information may ultimately
only come from transplantation studies in dogs where one can deliberately
transplant a kidney with a poor cortical perfusion and flow as illustrated
in Figure 3.

This approach has been useful to us in practice for the assessment of
kidney viability during perfusion preservation on the Belzer unit. We feel
that this is a promising approach to a very complex problem.

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OPEN DISCUSSION

A SCHWARZBECK (Mannheim): Is it possible that the variation in your
material resulted from different positions of the collimator? In your
diagram (figure 1 in text), there was no correlation between component
volume and intrarenal resistance.

STOWE: Yes, I said that the percentage of total flow going into the cortex as
determined from the washout curves was not correlated with resistance.
With regard to your question about the placing of the collimators affecting
the type of wash out curves we obtained, the answer is that it did not.

H LOKKEGAARD (Varlose): How long after the start of the infusion did you
make your measurements? Have you attempted to compare measurements
at the commencement and perhaps six hours later to see whether the control
compartment changed during perfusion?
STOWE: Yes. First of all we routinely do this about one hour after the kidney has been placed on the Belzer unit. We have had the opportunity to determine the blood flow distribution 12 hours later in some kidneys. Interestingly enough, the distribution does not seem to change - that is if it is a good distribution at the beginning of the perfusion it seems to be maintained. Likewise, if it is a poor distribution the percentage of flow going to the cortex does not seem to be improved with time.

E KEMP (Odense, Denmark): Has it not been a difficult problem, particularly with cadaver kidneys to decide on the value of the curves? Did you find any relationship between autoradiography and your results?

STOWE: In the kidneys we graphically plotted the logarithm of the counts versus time and manually determined the number of exponents in each curve. We have been working on a computer programme since when you get more than three components it becomes very time consuming.

With regard to the verification of the components we have approached the problem in three ways:
1. Silicone injection
2. Krypton autoradiographs
3. We have been able to use the gamma counter and this seems to correlate with the curve. We have also done some studies with angiography, but Magnusson and Alfidi showed a year ago that there was no correlation between angiographic data and the resistance of the kidneys.