Glomerular Ultrafiltration Coefficient after Ischemic Renal Injury in Dogs

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SUMMARY. Micropuncture studies of acute renal failure after ischemic renal injury suggest that glomerular ultrafiltration coefficient may remain normal in the period immediately after ischemia and decline significantly during the following 18-24 hours. The present series of in vitro experiments was designed to evaluate glomerular ultrafiltration coefficient and glomerular oncometric and rheological properties in ischemic acute renal failure in dogs. To obtain glomeruli prior to ischemia, a right nephrectomy was performed and glomeruli were isolated for studies of filtration and cell and extracellular spaces. The left renal pedicle then was occluded for 90 minutes; glomeruli isolated from biopsies of this kidney were studied at intervals up to 48 hours after ischemia. Glomeruli were isolated by sieving renal cortical fragments, and filtration was induced by an oncotic gradient. The glomerular ultrafiltration coefficient remained near control levels for the first hour after ischemia, but declined significantly at 24 and 48 hours. Specifically, glomerular ultrafiltration coefficient of glomeruli isolated from normal kidneys was 16.5 ± 0.9 nl/min per mm Hg (n = 15). Immediately following ischemia, glomerular ultrafiltration coefficient remained essentially unchanged (15.9 ± 1.1 nl/min per mm Hg, n = 4). At 1 hour, there was a small decrease in glomerular ultrafiltration coefficient (14.4 ± 1.3 nl/min per mm Hg, n = 4). At 24 hours, glomerular ultrafiltration coefficient was significantly decreased (9.8 ± 0.5 nl/min per mm Hg, n = 9, P < 0.01) and remained at that level at 48 hours (9.5 ± 0.5 nl/min per mm Hg, n = 8, P < 0.001). In experimental glomeruli, the oncometric response was diminished and erythrocyte movement along glomerular capillaries was impaired. Total water and inulin spaces were measured in glomeruli from control and 48-hour postischemic periods, and glomerular morphology was studied by transmission and scanning electron microscopy at the same time. Intracellular water comprised a significantly larger portion of total glomerular water 48 hours after ischemia than during the control period. Concurrent morphological changes included a decrease in the diameter of endothelial fenestrae and widening of epithelial foot processes. These results are consistent with the view that one or more nonglomerular factors are responsible for profound oliguria during the early phase of acute renal failure after ischemia. However, reduction of glomerular ultrafiltration coefficient, probably secondary to altered glomerular cellular characteristics, may be an important determinant to decreased glomerular filtration rate in established acute renal failure. (Circ Res 53: 439-447, 1983)

Several difficulties are encountered in measuring glomerular function in acute renal failure (ARF) by classical micropuncture techniques. First, severe oliguria may make accurate clearance studies or estimation of single nephron filtration rates difficult or impossible. Second, only the surface glomeruli of Munich-Wistar rats may be studied by direct puncture, whereas superficial glomeruli from most other species must be studied by less direct stop-flow techniques, and deep glomeruli are inaccessible. Third, in states of markedly reduced perfusion, filtration equilibrium may prevail and a unique value for the ultrafiltration coefficient cannot be calculated. To overcome the problems associated with determination of glomerular ultrafiltration coefficient (Kf) by micropuncture techniques, we have studied filtration in dogs with ARF, using isolated glomeruli.

Methods

Studies were performed on mongrel dogs weighing from 14 to 24 kg. Dogs were fed laboratory chow ad libitum and allowed free access to water. The animals were anesthetized with intravenous sodium pentobarbital (30 mg/kg body weight) and intubated, and respiration...
was maintained with a Harvard respirator (Harvard Apparatus Co.) and room air.

Initially, six animals were studied without hemodynamic monitoring or clearance measurements. The right kidney was removed and the glomeruli isolated to determine control values for glomerular size and $K_f$. Renal failure was induced by stripping the left renal capsule to eliminate capsular blood supply and clamping the renal pedicle for 90 minutes, as described previously (Hermreck et al., 1975; Patak et al., 1979). Before the renal artery was clamped, the animals were given 1000 units of heparin intravenously to prevent clotting within the renal vessels. Five of the animals studied were killed, under pentobarbital anesthesia, 48 hours after surgery. In the sixth animal, biopsies of the superficial renal cortex were taken for glomerular isolation immediately after the release of the pedicle clamp, at 1 hour, and at 24 hours, as well as at 48 hours.

In nine additional dogs, arterial and venous catheters were inserted percutaneously for monitoring vascular pressures, sampling blood, and constant intravenous infusion of 2 g inulin/dl in Ringer's solution. In these experiments, pressure tracings were recorded on a Hewlett-Packard physiograph. A midline abdominal incision was made and the renal pedicles were exposed. Inulin clearance was measured from each kidney separately during the control period, as described previously (de Torrente et al., 1975; Patak et al., 1979). Before the renal artery was clamped, the animals were given 1000 units of heparin intravenously to prevent clotting within the renal vessels. Five of the animals studied were killed, under pentobarbital anesthesia, 48 hours after surgery. In the sixth animal, biopsies of the superficial renal cortex were taken for glomerular isolation immediately after the release of the pedicle clamp, at 1 hour, and at 24 hours, as well as at 48 hours.

Isolation of Glomeruli

Glomeruli were isolated by techniques reported previously from this laboratory (Savin and Terreros, 1981). Briefly, the renal cortex was minced and the resulting fragments were sieved through stainless steel screens. Glomeruli were suspended in isolation medium at room temperature. Medium consisted of isotonic salt solution containing, in millimoles per liter: sodium chloride, 115; potassium, 5; sodium acetate, 10; dibasic sodium phosphate, 1.2; sodium bicarbonate, 25; magnesium sulfate, 1.2; calcium chloride, 1.0; and glucose, 5.5. The pH was adjusted to 7.4 by equilibration with 5% carbon dioxide and 95% oxygen immediately before use. Bovine serum albumin (BSA; Sigma Chemical Co.) was added to medium to give a final concentration of 4–12 g/dl. The concentration of BSA was estimated by refractive index (American Optical Total Solids Meter), and colloid oncotic pressure was estimated by the Landis and Pappenheimer equation (Landis and Pappenheimer, 1963). Estimated colloid oncotic pressure corresponded well with colloid oncotic pressure measured by oncometer (Wescor 4100, Wescor Inc.) in the ranges studied.

Estimation of Glomerular Ultrafiltration Coefficient

Filtration was induced and ultrafiltration coefficient calculated as previously described (Savin and Terreros, 1981). For each determination, a glomerulus that had been isolated in 4 g/dl BSA was selected and held for observation. A video image of the glomerulus (final magnification 667x) was recorded while 4 g/dl BSA medium was replaced by 1 g/dl BSA medium. This medium change produced an oncotic gradient of about 12 mm Hg across the capillary wall. Fluid was filtered into the glomerular capillary, and total glomerular diameter increased, producing maximal distention 1–2 seconds after the beginning of the medium change. In control glomeruli, erythrocyte ejection began simultaneously with maximal distention, and continued filtration resulted in further erythrocyte ejection without increase in glomerular size. In glomeruli from ischemic kidneys, filtration also caused glomerular diameter to increase and achieve a maximum after 1–2 seconds, but, in some cases, erythrocyte ejection was reduced or absent. Glomerular diameter, measured at 1/60-second intervals, was used to calculate glomerular volume. $K_f$ was estimated, using the largest volume increment in a single interval during the first 100 msec of filtration, according to the formula $K_f = \Delta V/\Delta t - \Delta p$. In each case, the volume increment used to calculate $K_f$ occurred before erythrocyte movement or ejection. Average $K_f$ was calculated using 5–8 glomeruli.

Oncometric Behavior of Isolated Glomeruli

Oncometric behavior was studied in glomeruli as described previously (Savin and Terreros, 1981). Glomeruli from 15 dogs were isolated in 4 g/dl BSA and studied during filtration and expansion produced by a 12 mm Hg gradient. Maximal relative volume increase, $V_{max}/V_0$, was calculated for each glomerulus. To determine the oncometric properties of glomeruli over a wider range of oncotic gradients, glomeruli from four additional dogs were isolated in media with BSA concentrations of 4, 6, 8, and 12 g/dl before, and 48 hours after, renal ischemia. Replacement of these isolation media by 1 g/dl BSA medium produced gradients of 12, 23, 37, and 77 mm Hg, respectively.

Estimation of Gradient Required to Produce Erythrocyte Ejection

A semiquantitative scale was developed to evaluate the pattern of erythrocyte movement that occurred during filtration (Savin et al., 1982). Movement was graded from
Isotopic Estimation of Glomerular Water Space and Extracellular Space

In the initial six dogs, the total water space and extracellular space of glomeruli isolated during the control period and 48 hours after ischemia were estimated using $^2$H$_2$O and $^{14}$C-inulin (Savin and Terreros, 1981). All determinations were carried out in triplicate. To evaluate relative changes in cellular and extracellular water compartments, the ratio of cell water to total water, as well as the absolute values for the several isotope spaces, were compared.

Morphology

The control and experimental kidney 48 hours after ischemia were perfused-fixed with 1.25% glutaraldehyde in 0.125 M sodium phosphate (pH 7.4) at approximately the mean arterial pressure in each of two additional dogs. A portion (about 5 g) of renal cortex was placed in the same fixative for 24 hours and freeze fractured according to the method of Avashanti et al. (1979). Both epithelial and endothelial surfaces of segments of at least 10 glomeruli from control and 48-hour postischemic periods were examined and photographed with a scanning electron microscope (JOEL-JSM-35; SEM) at magnification of 6000 to 32,000×. Additional renal cortex was prepared for transmission electron microscopy and examined with a JEOL 100S electron microscope at 5000 to 20,000×.

Epithelial foot process width was estimated from photomicrographs of 10 control and nine ischemic glomeruli.

Statistical Analysis

Systemic and renal hemodynamic and clearance parameters, as well as $K_r$ and glomerular volume determinations and average erythrocyte ejection scores, were evaluated by paired $t$-tests, each dog being used as its own control. Distributions of erythrocyte ejection scores of control and injured glomeruli were compared by $\chi^2$ analysis.

Results

Documentation of Acute Renal Failure and Results of Hemodynamic Studies

Each dog developed renal failure after renal pedicle clamping. Average body weight, serum creatinine, hematocrit, and hemodynamic data are shown in Table 1. Serum creatinine rose and inulin clearance fell after ischemia. Five dogs were anuric. Mean arterial pressure was maintained near the control level throughout the study. Renal blood flow returned to control values after release of the pedicle clamp, decreased 1 hour after ischemia, and returned again to the preinjury level at 24 and 48 hours. In individual dogs, hematocrit at 24 and 48 hours varied depending upon the magnitude of blood loss and the adequacy of fluid replacement during the posts ischemic period. When values for all dogs were averaged, there was no significant change in weight or hematocrit.

Studies of Isolated Glomeruli

Glomerular Size

Geometric size and radioisotope spaces of isolated glomeruli are shown in Table 2. The geometric glomerular volume, calculated from optical measure-
TABLE 2
Geometric Size and Radioisotopic Spaces of Isolated Glomeruli

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n = 15
Mean: 3.95, 4.09, 4.60, 3.57
SD: 0.90, 0.64, 0.65, 1.05
SEM: 0.23, 0.33, 0.33, 0.37

* Differs from control, P < 0.01 by paired t-test.
† Relative cell volume calculated as $(^3$H$_2$O $- ^3$C-Inulin)/$^3$H$_2$O.

TABLE 3
Results of Filtration by Isolated Glomeruli

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n = 15
Mean: 1.043, 1.043, 1.049, 1.034, 1.032
SD: 0.012, 0.012, 0.014, 0.007, 0.007
SEM: 0.003, 0.003, 0.007, 0.002, 0.002

* Differs from control, P < 0.02 by paired t-test.
† Differs from control, P < 0.01 by paired t-test.
‡ Differs from control, P < 0.001 by paired t-test.
Savin et al. / Ultrafiltration Coefficient after Renal Ischemia

Sequential change in average $K_f$ during the 48 hours after ischemic injury. A significant decrease in $K_f$ was observed at 24 and 48 hours after ischemia ($P < 0.01$, $P < 0.001$ by paired t-test).

merits of the mean diameter of individual glomeruli in 4 g/dl medium before the filtration studies, did not change significantly from control values during the course of postischemic renal failure.

Neither glomerular water content ($^{3}H_2O$ space) nor extracellular water content ($^{14}$C-inulin space) was significantly altered 48 hours after ischemia. However, intracellular water ($^{3}H_2O$ space minus $^{14}$C-inulin space) was slightly increased at 48 hours, and the ratio of intracellular water to total water increased in each dog at 48 hours.

Studies of Filtration by Isolated Glomeruli

Results obtained from studies of filtration by isolated glomeruli in experiments in which the incubation medium was abruptly changed from 4 g/dl BSA to 1 g/dl BSA (oncotic gradient 12 mm Hg) are shown in Table 3.

Glomerular Ultrafiltration Coefficient. The mean $K_f$ in control glomeruli was 16.5 ± 0.9 nl/min per mm Hg ($n = 15$). Values obtained from glomeruli of four dogs isolated immediately after release of the renal pedicle clamp and 1 hour later were slightly, but not significantly, lower than their respective control values ($P > 0.10$ by paired t-test). In these dogs, $K_f$ at 1 hour after ischemia was slightly higher than that at 24 or 48 hours ($P < 0.10$ by paired t-test). $K_f$ was lower than control in seven of eight dogs studied at 24 hours and in all eight dogs studied at 48 hours after ischemia ($P < 0.01$ and $P < 0.001$, 24 and 48 hours, respectively). Thus, mean $K_f$ appeared to decline steadily after release of the pedicle clamp, although the changes were not statistically significant at 0 or 1-hour periods (Fig. 1).

Oncometric Behavior. During studies of reverse ultrafiltration, every glomerulus increased in size. In studies with an oncotic gradient of 12 mm Hg, relative volume increase of experimental glomeruli up to 1 hour after ischemia was not different from that of control glomeruli. Relative volume increase of experimental glomeruli at 24 or 48 hours was significantly decreased ($P < 0.02$, $n = 15$). Results of studies carried out with larger gradients in four dogs are shown in Figure 2. Relative volume increase averaged 1.05 ± 0.01, 1.11 ± 0.02, 1.13 ± 0.01, and 1.18 ± 0.01 for gradients of 12, 23, 37, and 77 mm Hg, respectively, in glomeruli from control kidneys and 1.05 ± 0.01, 1.07 ± 0.01, 1.12 ± 0.02, and 1.15 ± 0.02 for the same conditions in glomeruli obtained 48 hours after ischemia. In this study, a decreased oncometric response in ischemic glomeruli was evident when they were exposed to gradients greater than 12 mm Hg (paired t-test $P < 0.05$, $n = 16$).

Erythrocyte Ejection Studies. Mean ejection scores during filtration induced by a 12 mm Hg gradient averaged 3.2 ± 0.1 for the control period and were decreased at each experimental period ($P < 0.02$ by paired t-test at each period). Results of studies of ejection with larger transcapillary oncotic gradients are presented in Figure 3, A and B. Erythrocytes
were ejected from each control glomerulus, and vigorous ejection (scores 3 or 4) occurred in 60% of control glomeruli when a gradient of 12 mm Hg was used. Vigorous ejection was observed in every case in which larger gradients were applied. In contrast, ejection was absent in 18–35% of ischemic glomeruli when the oncotic gradient was 37 mm Hg or less. Vigorous ejection occurred in most ischemic glomeruli only when the gradient used to produce filtration was greater than or equal to 37 mm Hg. Significant differences in the distribution of erythrocyte ejection scores of control and 48 hour postischemic glomeruli were evident at gradients of 12 and 23 mm Hg (P < 0.05 and P < 0.005, respectively). Distribution of ejection scores at gradients of 37 and 77 mm Hg were not altered from control.

Scanning and Transmission Electron Microscopic Studies

Scanning electron micrographs of glomeruli 48 hours after ischemia showed a marked reduction in the diameter of endothelial fenestrae (Fig. 4, A and B). Endothelial cytoplasmic folds and blebs were more prominent than in control glomeruli. Epithelial surfaces appeared normal by scanning electron microscopy, whereas transmission electron micrographs of glomeruli 48 hours after ischemia showed a minimal increase in the width of epithelial cell foot processes.

Discussion

The study of filtration in vitro has several unique advantages over micropuncture techniques. It permits the estimation of Kf even in severe oliguria. Glomeruli from any species may be studied and, in some cases, as in the present series of experiments,
Serial biopsies may be obtained and each animal used as its own control. A unique value for $K_f$ may be calculated, regardless of the variations of renal perfusion rate or the presence of filtration equilibrium in vivo. Additionally, glomerular function may be studied in isolation from local influences of renal tubules or interstitium, and from local or systemic hormonal variations during the study. Using isolated glomeruli, we were also able to estimate glomerular size, cell and extracellular water, and glomerular capillary oncometric and rheological properties.

To calculate $K_f$ in vitro, we assumed that the initial oncotic pressure of the fluid contained within the glomerular capillaries had equilibrated with that of the bathing medium during isolation and initial incubation, that the oncotic gradient between the initial and the new bathing medium was the principal driving force for filtration, that there was no significant hydrostatic force within the capillary during the first 0.1 second or filtration, that the entire filtering surface of the glomerulus was uniformly bathed by the new medium, that unstirred layers adjacent to the epithelial or endothelial surfaces were inconsequential, and that no fluid ejection occurred prior to erythrocyte movement. Errors arising from any of the above assumptions would tend to decrease the calculated value for $K_f$. We have used the largest change in volume during a single interval to estimate $K_f$. This convention may cause overestimation of the average $K_f$ of both control and experimental glomeruli. The values for $K_f$ reported here must be regarded as estimations of the actual $K_f$; nonetheless, relative changes produced by experimental manipulations reflect changes in the hydraulic permeability of the glomerular capillaries.

We have previously reported values of $K_f$ for normal rats, rabbits, dogs (Savin and Terreros, 1981), and humans (Savin et al., 1981) using this oncometric technique. $K_f$ of rat glomeruli averaged about 6 nl/min per mm Hg and is comparable to values derived by direct glomerular capillary puncture [2–6 nl/min per mm Hg (Daugherty et al., 1974; Arendshorst and Gottschalk, 1980)]. Under the experimental conditions we have used, $K_f$ of normal glomeruli from anesthetized dogs averaged 16.5 ± 0.9 nl/min per mm Hg, a higher value than reported from stop-flow studies (Navar et al., 1977; Oswald et al., 1979; Williams et al., 1981). The difference between our values for $K_f$ of canine glomeruli and those previously reported from in vivo estimates may be explained in several ways. First, there may be considerable variation among animals, as has been shown in comparisons of inbred rats from different colonies (Arendshorst and Gottschalk, 1980). Second, one of several differences in technique may explain the discrepancy. As noted above, we may have overestimated $K_f$ by considering only the largest single-interval volume increase. Alternatively, under the conditions of reduced renal artery pressure used for many stop-flow studies, $K_f$ may be reduced by humoral or other mechanisms. Finally, technical problems may cause overestimation of capillary hydraulic pressure and underestimation of $K_f$ during stop-flow studies (Ichikawa and Troy, 1981). The basis for the difference in absolute values for $K_f$ determined in vivo and in vitro is of considerable interest. However, the precise value for $K_f$ is not crucial to the documentation of glomerular abnormalities in the present study, since we have compared normal and injured glomeruli of each dog.

Glomerular ultrafiltration coefficient, $K_f$, remained near control values for the first hour after ischemia and then declined, averaging about 50% of control values 48 hours after injury. The decline in $K_f$ was temporally unrelated to altered hemodynamics. Specifically, $K_f$ was nearly normal, both immediately after the release of the renal artery clamp, when renal blood flow was normal, and 1 hour later, when renal blood flow was decreased. $K_f$ declined at 24 and 48 hours while renal blood flow returned to control levels. No significant correlation between $K_f$ and systemic or renal hemodynamic parameters was observed.

Previous reports suggest that $K_f$ remains normal or nearly normal in the early period following renal ischemia. Daugherty et al. (1974) calculated $K_f$ using pressure measurements derived from direct glomerular puncture in Munich-Wistar rats 2 hours after the release of 80% renal artery occlusion. At that time, plasma flow and glomerular filtration rate were decreased, while $K_f$ could not be determined explicitly because of filtration pressure equilibrium. The authors concluded that decreased filtration rate was dependent on decreased plasma flow, rather than altered $K_f$. Conger et al. (1981), studying rats in which renal injury was induced by norepinephrine infusion, also documented impaired renal perfusion following ischemia. However, they found that GFR remained low even after renal blood flow had been restored by infusion of acetylcholine. Intratubular pressure was elevated and appeared to be an important determinant of decreased GFR. Our documentation of normal or nearly normal $K_f$ of isolated glomeruli immediately after ischemia is consistent with these in vivo studies, and we concur that decreased glomerular filtration in the early period after ischemia is probably the result of one or more nonglomerular factors.

During established ARF, 18–48 hours after injury, $K_f$ appears to play a more important role in determining glomerular filtration rate. Williams et al. (1981) have recently performed micropuncture studies 18 hours after renal ischemia in dogs. In these studies, GFR, single nephron GFR, and $K_f$ were each decreased by about 50%, compared with control values. Filtration equilibrium was not present and $K_f$ appeared to be an important determinant of decreased glomerular filtration. Our findings are very similar to those of Williams et al., and we agree that $K_f$ probably contributes to decreased GFR in estab-
lished ARF following ischemia.

Abnormalities in glomerular cell volume and morphology accompanied decreased $K_f$ in our studies. Forty-eight hours after severe ischemic injury, total glomerular size, as reflected by glomerular diameter and $^3$H$_2$O space, remained constant, while the ratio of cell water to total glomerular water was slightly increased. These findings suggest an increase in cell volume and a concurrent decrease in capillary volume. The morphological abnormalities that we documented, including foot processes widening and decreased endothelial fenestral size, may also reflect increased cell volume. Similar morphological abnormalities have been documented by others (Cox et al., 1974; Williams et al., 1981; Barnes et al., 1981; Solez et al., 1981), and structural and functional abnormalities may occur together (Williams et al., 1981).

Although the precise roles of the endothelial and epithelial cells in determining $K_f$ remain undefined, the possible effects of several structural alterations may be considered. Since $K_f$ represents the product of the hydraulic conductivity ($L_p$) of the capillary wall and the total capillary filtering area ($A$), any decrease in either $L_p$ or $A$ will diminish $K_f$. $L_p$ is determined by the characteristics of the paracellular pathway for fluid movement and may be altered by modifying this pathway. Paracellular barriers to filtration include the endothelial fenestrae and the slit diaphragms between adjacent epithelial foot processes. Total area of fenestrae and $K_f$ each decrease in toxic ARF caused by heavy metals in rats (Blantz, 1975; Cachia, 1981) and by gentamicin in rats and rabbits (Baylis et al., 1977; Avasthi, 1979; Chonko, 1979), as well as in ischemic ARF (Williams et al., 1981). We have found similar alterations in fenestrae in the present study. Endothelial cell swelling or separation of endothelial cells from the basement membrane have been observed in acute glomerulonephritis and may decrease $L_p$ by increasing filtration path length (Blantz and Wilson, 1976). The slit diaphragm is the next major barrier to filtration, and has been proposed as the primary determinant of $L_p$ (Rodewald and Karnovsky, 1976). Swelling of epithelial cells and foot process fusion have been documented in ARF (Solez et al., 1981; Barnes et al., 1982) and may diminish $L_p$ by decreasing the area available for filtration or increasing the length of the filtration path. We have also observed epithelial cell abnormalities in the present study.

Loss of effective capillary filtering area ($A$) may also decrease $K_f$. Total capillary area may be reduced by glomerular sclerosis. Occlusion of capillaries by inflammatory cells or debris (Maddox et al., 1975) or segmental narrowing of capillaries with resulting segmental hypoperfusion (Savin et al., 1982) may also decrease the effective filtering area. $K_f$ also declines during salt depletion (Steiner et al., 1979; Schor et al., 1980; Ridge et al., 1981). It has been proposed that mesangial contraction and conse-

quent functional decrease in filtering area may effect this decrease (Schor and Brenner, 1980; Ichikawa and Schor, 1981). Mesangial contraction may occur in ARF and may diminish both the filtering area and $K_f$.

In the present studies, we have documented two additional alterations in glomerular characteristics. The glomerular oncometric response to changes in the BSA concentration of the isolation medium 24–48 hours after ischemia was decreased relative to that of normal glomeruli. This impaired oncometric response may reflect decreased compliance of the glomerular capillary after ischemia; its significance in determining glomerular filtration is not known. Rheological properties of the injured glomerular capillary were also altered. Since the net hydraulic pressure within the glomerular capillary may approach, but not exceed, the oncotic gradient used to produce filtration, the finding that an increased gradient was required to produce vigorous erythrocyte ejection from injured glomeruli suggests an increased resistance to perfusion. Capillary perfusion is essential for filtration, and increased intraglomerular resistance may contribute to decreased single nephron GFR in established ARF. We have reported a similar finding in proliferative glomerulonephritis (Savin et al., 1982).

In summary, $K_f$ remains normal or nearly normal in the early period after ischemic injury, but is markedly decreased 24–48 hours later. $K_f$ may be decreased because of changes in cell configuration which lead to decreased hydraulic conductivity or because of decreased effective filtering area. Altered glomerular rheological properties may cause relative underperfusion of some capillary segments and may contribute to impaired GFR in vivo. Decreased GFR in the early period after ischemia appears to be due to alterations in one or more nonglomerular factors. In contrast, decreased $K_f$ may be an important determinant of decreased single nephron GFR in established postischemic ARF in the dog. Additional studies are needed to determine the relative contributions of cellular and humoral factors to the decrease in $K_f$ and of $K_f$ to decreased glomerular filtration in acute renal failure.

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References


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