Intrarenal Hemodynamics in Patients With Essential Hypertension

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Intrarenal hemodynamics were estimated clinically in essential hypertension. Two-week studies were performed in 30 patients with essential hypertension who were given a regular sodium diet in the first week and a sodium-restricted diet in the second week. Intrarenal hemodynamic parameters such as afferent arteriolar (preglomerular) resistance, efferent arteriolar resistance, and glomerular hydrostatic pressure were calculated from renal clearances and plasma total protein concentration measured on the last day of the regular sodium diet. Calculations were based on Gomez’s equations with the assumption that the gross filtration coefficient of glomerular capillaries was normal. The increase in afferent arteriolar resistance \( (8,100±500 \text{ dyne-sec-cm}^{-5}) \) was significantly correlated with an elevation in mean arterial pressure \( (120±2 \text{ mm Hg}) \), whereas glomerular pressure \( (56±1 \text{ mm Hg}) \) and efferent arteriolar resistance \( (2,500±100 \text{ dyne-sec-cm}^{-5}) \) remained normal.

The renal function curve (pressure–natriuresis relation) was drawn by plotting urinary sodium excretion on the y axis as a function of mean arterial pressure on the x axis, both of which were measured on the last 3 days of each week. The extrapolated x intercept \( (107±2 \text{ mm Hg}) \) of the renal function curve was strongly correlated in a 1:1 fashion with the sum of the arterial pressure drop from the aorta to the renal glomeruli plus the opposing pressures against glomerular filtration at glomeruli \( (r=0.7, p<0.001) \) on the regular sodium diet, suggesting that the difference between mean arterial pressure on the regular sodium diet and the extrapolated x intercept represented the effective filtration pressure across the glomerular capillaries on the regular sodium diet. The gross filtration coefficient of glomerular capillaries was estimated as \( 0.154±0.018 \text{ ml/sec/mm Hg} \), suggesting that the filtration coefficient was not affected in essential hypertension. Our results indicate that Gomez’s equations can be applied to patients with essential hypertension. Furthermore, it is suggested that intrarenal hemodynamics can be estimated independently of Gomez’s equations by analyzing the renal function curve. (Circulation Research 1991;69:421–428)

On the basis of animal experiments, Brenner et al1–3 recently proposed that an abnormality of intrarenal hemodynamics plays a key role in the progression of renal failure. However, intrarenal hemodynamics such as afferent and efferent arteriolar resistances and glomerular hydrostatic pressure cannot be evaluated clinically except by Gomez’s equations,4,5 where the gross filtration coefficient of glomerular capillaries must be assumed to be normal. Thus, it is impossible to examine whether Brenner’s hypothesis1–3 can also be applied to clinical settings, since the gross filtration coefficient should be reduced in renal failure.6,7 In the present study, we estimated intrarenal hemodynamics in patients with essential hypertension by Gomez’s equations and by analyzing their interrelation with the renal function curve (pressure–natriuresis relation).8,9

Materials and Methods

Patients

Thirty inpatients with essential hypertension (17 men and 13 women; 40–69 years old [average, 52±1 years]; body weight, 63.0±2.0 kg; height, 160.0±1.4 cm), who had given their informed consent, were studied in the Hypertension Unit of the National Cardiovascular Center Hospital in Osaka, Japan. The administration of antihypertensive drugs was discontinued at least 2 weeks before hospitalization. During the initial hospi-
talization, a routine examination of hypertensive patients was performed to exclude secondary hypertension and to evaluate the severity of the hypertensive state. None had evidence of detectable cause for hypertension or malignant hypertension.

**Study Protocol**

After the initial 1–2-week hospitalization, during which blood pressures had been stabilized, the patients were studied in the following two stages. First, they were fed a regular sodium diet containing 12–15 g NaCl (205–256 meq sodium)/day for 1 week (stage I). Then, they were fed a low sodium diet containing 1–3 g NaCl (17–51 meq sodium)/day for the next week (stage II). During these 2 weeks, no antihypertensive drugs were administered.

The blood pressures and urinary sodium excretion rates ($U_{NaV}$) were measured on the last 3 days of each stage. Blood pressure in the supine position was measured by nurses three times each day at about 10:00 AM after the patients rested for at least 30 minutes, and the lowest value was adopted. The mean arterial pressure (MAP) was calculated by adding one third of the pulse pressure to the diastolic pressure, both of which were the averages of the last 3 days of measurements.

On the last day of stage I, blood hematocrit value (Hct) and plasma total protein concentration (TP) were measured. The renal plasma flow rate (RPF) and glomerular filtration rate (GFR) were calculated by standard clearance techniques using para-aminomhippurate and endogenous creatinine as markers, respectively. Patients fasted overnight and rested in the supine position during measurements of renal clearances. A bolus intravenous injection of 5 ml of 10% para-aminomhippurate was given at about 8:30 AM followed by the continuous infusion at a rate of 5 ml/hr. After a 30-minute equilibration period, two 30-minute urine collections were performed. Venous blood sampling for plasma para-aminomhippurate and creatinine determinations was drawn at the beginning and end of each urine collection period. The renal clearance data, obtained by averaging the above two 30-minute clearances, were standardized for a body surface area of 1.73 m². The renal blood flow rate (RBF) was calculated from RPF and Hct.

Intrarenal hemodynamics were calculated based on Gomez’s equations using clinical data such as MAP, RPF, GFR, Hct, and TP. The renal function curve (pressure–natriuresis relationship) was drawn by plotting $U_{NaV}$ on the y axis as a function of MAP on the x axis; both variables were measured after a steady-state sodium balance had been achieved on regular and low sodium diets. The interrelation between intrarenal hemodynamics and the renal function curve was studied. The theoretical background of the interrelation is described in detail in “Appendix.” Finally, intrarenal hemodynamics were calculated also by analyzing the renal function curve and were compared with those obtained by Gomez’s equations.

### Table 1. Blood Pressures and Urinary Sodium Excretion in 30 Patients With Essential Hypertension on Regular and Low Sodium Diets

<table>
<thead>
<tr>
<th>Measurements</th>
<th>Regular sodium diet (stage I)</th>
<th>Low sodium diet (stage II)</th>
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</thead>
<tbody>
<tr>
<td>$U_{NaV}$ (meq/day)</td>
<td>223±10</td>
<td>30±3</td>
</tr>
<tr>
<td>SBP (mm Hg)</td>
<td>163±2</td>
<td>143±3</td>
</tr>
<tr>
<td>DBP (mm Hg)</td>
<td>98±2</td>
<td>92±2</td>
</tr>
<tr>
<td>MAP (mm Hg)</td>
<td>120±2</td>
<td>109±2</td>
</tr>
</tbody>
</table>

Values are mean±SEM. $U_{NaV}$, urinary sodium excretion rate; SBP, DBP, MAP, systolic, diastolic, and mean blood pressure of systemic circulation, respectively.

### Statistical Analysis

Results are expressed as mean±SEM. The significance of difference was tested by Student’s t test for paired samples, and the correlation coefficient was obtained by the least-squares method. The significance of difference from 1 in the slope of the regression line and from 0 in the y intercept was tested by SAS/STAT Statistical Software Package (SAS Institute Inc., Cary, N.C.).

### Results

**Urinary Sodium Excretion and Blood Pressure**

$U_{NaV}$ and blood pressures were measured during regular (stage I) and low (stage II) sodium diets in 30 patients with essential hypertension, and the results are summarized in Table 1. When sodium intake was restricted from the regular to low sodium diet, $U_{NaV}$ was decreased from 223±10 to 30±3 meq/day, reflecting the amount of sodium intake in each stage and indicating that a steady state of sodium balance had been achieved. Systolic blood pressure, diastolic blood pressure, and MAP of systemic circulation were all lowered significantly by sodium restriction.

**Renal Clearances, Hematocrit, and Plasma Protein**

GFR, RPF, RBF, Hct in systemic blood, and TP in systemic plasma were measured on the regular sodium diet (stage I), and the results are summarized in Table 2.

### Renal Function Curve

The renal function curve (arterial pressure–$U_{NaV}$ relation) was obtained by plotting $U_{NaV}$ (meq/day) in stages I and II on the y axis as a function of MAP (mm Hg) on the x axis (Figure 1). The extrapolated x intercept (A) and the slope (B) of the renal function curve were 107±2 mm Hg and 23.4±2.4 (meq/day)/

### Table 2. Renal Clearances, Hematocrit, and Plasma Total Protein Concentration on Regular Sodium Diet

<table>
<thead>
<tr>
<th>GFR (ml/min)</th>
<th>RPF (ml/min)</th>
<th>RBF (ml/min)</th>
<th>Hct (%)</th>
<th>TP (g/dl)</th>
</tr>
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<tbody>
<tr>
<td>85±3</td>
<td>377±15</td>
<td>666±27</td>
<td>43.2±0.7</td>
<td>6.8±0.1</td>
</tr>
</tbody>
</table>

Values are mean±SEM (n=30). GFR, glomerular filtration rate; RPF, renal plasma flow rate; RBF, renal blood flow rate; Hct, hematocrit value of systemic blood; TP, total protein concentration in systemic plasma.
mm Hg, respectively, indicating a theoretical $U_N V$ of zero when systemic MAP was lowered to approximately 107 mm Hg and a change in systemic MAP (1/B) of 4 mm Hg per 100 meq/day change in the sodium intake.

**Intrarenal Hemodynamics**

According to Gomez’s equations (see “Appendix”), the intrarenal hemodynamic parameters in 30 patients with essential hypertension on the regular sodium diet (stage I) were calculated using clinical data such as MAP, renal clearances, and TP, which have been summarized in Tables 1 and 2. The gross filtration coefficient of glomerular capillaries ($K_{gO}$) was assumed to be normal (0.0812 [ml/sec/mm Hg]).

Total renal vascular resistance ($R_A$), afferent arteriolar resistance ($R_A$), and efferent arteriolar resistance ($R_E$) were calculated as $13,900±700, 8,100±500,$ and $2,500±100$ dyne-sec-cm$^{-5}$, respectively (Table 3). The mean glomerular pressure ($P_G$) was $56±1$ mm Hg, which is similar to the normal value of 60 mm Hg. These results were comparable with those of the original works by Gomez.

Relations between segmental renal vascular resistances ($R_A$ or $R_E$) and renal clearances (RPF, GFR, or filtration fraction that is equal to GFR/RPF) were examined. RPF was reduced with increases in both $R_A$ ($r=−0.852, p<0.001$) and $R_E$ ($r=−0.680, p<0.01$). On the other hand, GFR decreased with the increase in $R_A$ ($r=−0.479, p<0.01$), while it increased with the increase in $R_E$ ($r=0.370, p<0.05$). Thus, filtration fraction was increased with increases in both $R_A$ ($r=0.551, p<0.01$) and $R_E$ ($r=0.939, p<0.001$). It was notable that $R_A$ correlated strongly with RPF, and $R_E$ correlated strongly with filtration fraction.

Relations between segmental renal vascular resistances and systemic arterial pressure were also examined. $R_A$ was increased even in patients whose blood pressure was normal, and the increase in $R_A$ was positively correlated with an elevation in MAP ($r=0.6, p<0.01$), while $R_E$ remained normal and had no significant relation with MAP ($r=0.3, NS$). Similarly, $P_G$ remained normal and was not correlated with MAP ($r=0.02, NS$). Thus, autoregulatory mechanisms seemed almost intact in these essential hypertensive patients; the increases in $R_A$ and MAP were parallel, and therefore, $P_G$ remained normal.

**Interrelation Between Intrarenal Hemodynamics and Renal Function Curve**

Since the x intercept of the renal function curve (A) is the theoretically critical blood pressure level at which urinary sodium excretion stops with the reduction in MAP, the difference between MAP on the regular sodium diet and A (MAP−A) may correspond to the effective filtration pressure across the glomerular capillaries on the regular sodium diet. In other words, when urinary sodium excretion stops with the reduction in MAP, MAP should be lowered to A, and at the same time, glomerular filtration must stop because of the zero effective filtration pressure. Thus, A may correspond to the sum of the arterial pressure drop from the aorta to the renal glomeruli plus the pressures opposing glomerular filtration at the glomerulus on the regular sodium diet, as shown by Equation A15 in “Appendix”:

$$A = R_A \times RBF/1,328 + (H_T + \Pi_G)$$

<table>
<thead>
<tr>
<th>Table 3. Intrarenal Hemodynamics Estimated by Gomez’s Equations and by Analyzing Renal Function Curve</th>
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<tbody>
<tr>
<td><strong>By Gomez’s equations</strong></td>
</tr>
<tr>
<td>$R_A$ (dyne-sec-cm$^{-2}$)</td>
</tr>
<tr>
<td>$R_E$ (dyne-sec-cm$^{-2}$)</td>
</tr>
<tr>
<td>$R_E'$ (dyne-sec-cm$^{-2}$)</td>
</tr>
<tr>
<td>$P_G$ (mm Hg)</td>
</tr>
<tr>
<td>$K_{gO}$ (ml/sec/mm Hg)</td>
</tr>
</tbody>
</table>

Values are mean±SEM (n=30). $R_A$, afferent arteriolar resistance; $R_E$, efferent arteriolar resistance; $R_E'$, an approximate of $R_E$ obtained as the difference between total renal vascular resistance and $R_A$; $P_G$, glomerular hydrostatic pressure; $K_{gO}$, gross filtration coefficient of glomerular capillaries.
where $H_t$ is the hydrostatic pressure in Bowman’s space (assumed to be 10 mm Hg) and $I_G$ is the mean oncotic pressure within glomerular capillaries (estimated in each patient as 28.9±0.4 mm Hg based on the mass conservation law of plasma protein across the glomerular capillaries using TP, RPF, and GFR as shown by Equations A3 and A4 in “Appendix”). In Figure 2, the left side of this equation (A) was plotted on the ordinate as a function of the right side of the equation ($R_A\times RBF/1,328+[H_t+I_G]$) calculated by Gomez’s equations$^4,5$ on the x axis. The slope of this regression line (0.818±0.151) was not significantly different from 1 ($p>0.238$), nor was its y intercept (23.0±15.5 mm Hg) different from 0 mm Hg ($p>0.149$). Although A was obtained independently of the other parameters, such as $R_A$ and RBF, there was a strong 1:1 relation between these two ($r=0.72$, $p<0.001$), suggesting the validity of the arbitrary assumption that the difference between MAP on the regular sodium diet and A corresponded to the effective filtration pressure across the glomerular capillaries on the regular sodium diet. However, there was a small but significant difference (4.5±1.4 mm Hg, $p<0.005$) between A (107±2 mm Hg) and $R_A\times RBF/1,328+[H_t+I_G]$ (102±2 mm Hg).

Once it has been established that MAP–A corresponds approximately to the effective filtration pressure, the $K_{FG}$ of glomerular capillary walls may be estimated from its definition by using Equation A1 in “Appendix.” The estimated $K_{FG}$ was 0.154±0.018 (ml/sec/mm Hg), which was nearly twice as great as the assumed value of 0.0812.5 This is because A was significantly greater than $R_A\times RBF/1,328+(H_t+I_G)$ by 4.5±1.4 mm Hg and MAP–A seemed smaller than the true value of effective filtration pressure by this magnitude. These results indicate that $K_{FG}$ is not decreased in essential hypertension and that Gomez’s equations$^4,5$ can be applied to patients with essential hypertension.

Estimation of Intrarenal Hemodynamics by Analyzing Renal Function Curve

Once it has been established that MAP–A corresponds approximately to the effective filtration pressure across the glomerular capillaries on the regular sodium diet, as shown in Figure 2, $R_A$ can be estimated by analyzing the renal function curve by rearranging Equation A15 in “Appendix.” Thus, an approximate ($R_E'$) of the efferent arteriolar resistance can be obtained as the difference between the total renal vascular resistance and $R_A$. The glomerular hydrostatic pressure ($P_G$) can be estimated as the difference between systemic arterial pressure and the pressure drop across afferent arteriole from aorta to glomeruli, which corresponds to $R_A\times RBF/1,328$. Table 3 compares the intrarenal hemodynamic parameters estimated by analyzing the renal function curve with those by Gomez’s equations. Since the $R_A$ estimate was significantly higher by the renal function curve than by Gomez’s equations, the $R_E'$ and $P_G$ estimates were lower. Figure 3 shows the correlations in $R_A$, $R_E'$, and $P_G$ between these two methods of estimation. The slopes of these regression lines, 0.930±0.075 in $R_A$ ($p>0.358$) and 0.798±0.143 in $R_E'$ ($p>0.170$) were not significantly different from 1, nor were the y intercepts, 1.120±0.639 dynes-sec-cm$^{-2}$ in $R_A$ ($p>0.090$) and 622±856 dynes-sec-cm$^{-2}$ in $R_E'$ ($p>0.474$), different from 0 dynes-sec-cm$^{-2}$. There were highly significant 1:1 correlations in $R_A$ and $R_E'$ between these two methods of estimation, and thus, no correlation in $P_G$. Therefore, it seemed possible to estimate $R_A$ and $R_E'$ clinically by analyzing the renal function curve. Of course, there was a significant correlation ($r=0.512$, $p<0.01$) between $R_E'$ estimated by the renal function curve and $R_E$ by Gomez’s equations ($R_E'=2.100+1.25\times R_E$). No correlation in $P_G$ should be ascribed to the fact that $P_G$ is autoregulated within a narrow range. Furthermore, it should be emphasized here that if we assume $K_{FG}$ to be 0.154±0.018 instead of 0.0812 (ml/sec/mm Hg in each patient, then we get exactly the same results by Gomez’s equations as by analyzing the renal function curve (see Figure 4). The observed difference (Table 3) between results obtained by Gomez’s equations and by analyzing the renal function curve is ascribed only to the difference in $K_{FG}$.

Discussion

By relating intrarenal hemodynamics with the renal function curve (pressure–natriuresis relation),
the validity of the underlying assumptions in Gomez’s equations\(^4,5\) for calculating intrarenal hemodynamics using clinical data has been clarified. Furthermore, it is suggested that intrarenal hemodynamics can be estimated clinically by analyzing the renal function curve without assuming a normal and constant gross filtration coefficient of glomerular capillaries.

Our results on intrarenal hemodynamics in 30 patients with essential hypertension were consistent with those of the original works by Gomez.\(^4\) Among total renal vascular resistances, the preglomerular (afferent) arteriolar resistance was prominently elevated, and thus, the glomerular pressure remained normal. Reasonable relations between segmental renal vascular resistances, afferent or efferent (postglomerular), and renal clearances observed in the present study, although they are all interdependent, may also suggest the validity of Gomez’s equations\(^4,5\) as well as of our data concerning intrarenal hemodynamics. RPF was reduced by both afferent and efferent arteriolar vasoconstriction, whereas GFR was decreased with the increase in the afferent arteriolar resistance and was increased with the increase in the efferent resistance. Estimation of intrarenal hemodynamics by Gomez’s equations\(^4,5\) requires two major assumptions, as summarized in “Appendix.” First, in the estimation of glomerular hydrostatic pressure by Gomez’s equations, \(K_{FG}\) must be assumed. Here, we assumed normal value of \(K_{FG}\) in patients with essential hypertension. In spontaneously hypertensive rats, which is a model of human essential hypertension, the filtration coefficient of single nephron was reported as normal, and afferent arteriolar resistance was prominently increased with an elevation in systemic blood pressure, resulting in normal glomerular pressure.\(^17,18\) These data were also comparable with those observed in essential
hypertensive patients in the present study. Recently, we used Gomez's equations to analyze intrarenal hemodynamics in patients with unilateral renovascular hypertension11 and found them completely comparable with those reported in the Goldblatt rat model.19,20 Second, filtration disequilibrium is assumed in Gomez's equations. However, it is not known yet whether filtration equilibrium is achieved at the end of the human glomerular capillaries. Therefore, as far as we know, there are no exact formulas to calculate intrarenal hemodynamics in humans. Fortunately, in dogs and rats there were no significant differences between conclusions derived by Gomez's disequilibrium model and by the filtration equilibrium model.12-14 Using dextran sieving data, Shemesh et al7 and Tomlanovich et al7 attempted to assess glomerular hemodynamics in humans. They concluded that \( K_{FG} \) is reduced in both membranous nephropathy and diabetic glomerulopathy.7 In their assessment, however, the effective filtration pressure must be assumed.6,7 Therefore, it seems difficult to quantitatively assess intrarenal hemodynamics such as glomerular pressure, afferent arteriolar resistance, and efferent arteriolar resistance calculated in the present study.

Furthermore, interrelations between intrarenal hemodynamics and the renal function curve were studied. Since the x intercept (A) of the renal function curve represents the theoretically critical blood pressure level at which urinary sodium excretion stops with the decrease in systemic arterial pressure,8,9 MAP–A seems to be the effective filtration pressure across the glomerular capillary walls on the regular sodium diet. Therefore, A may be expressed as the sum of the arterial pressure drop from the aorta to the renal glomeruli, mainly in the afferent arteriole, plus opposing pressures against glomerular filtration at the glomerulus as shown by Equation A15 in “Appendix.” Figure 2 revealed that there was a 1:1 relation between A and the sum, both of which were estimated independently of each other by the renal function curve and by Gomez's equations, respectively, although A was slightly greater than the other. This small difference (4.5 ± 1.4 mm Hg, \( p<0.005 \)) may be ascribed to the fact that the renal function curve is not truly linear. Linking two data points, where the steady-state MAP and \( U_{Na} \) under two different amounts of sodium intake were plotted on the x and y axes, respectively, and calculating the extrapolated A might give us a value greater than the true value. However, we still believe that the renal function curve can be regarded as linear in clinical practice as we have discussed in detail elsewhere.15 Since there was a strong 1:1 relation between A and the sum of the arterial pressure drop from the aorta to glomeruli plus opposing pressures against glomerular filtration despite the small difference, we believe that A can be used to estimate approximately the effective filtration pressure across the glomerular capillary walls in clinical studies. In the present study, we tested the validity of the above relation, Equation A15 in “Appendix,” under the conditions in which afferent arteriolar resistance mainly varied. It is reported that the relation holds when the oncotic pressure within glomerular capillaries primarily varies.21,22 The renal function curve was shifted leftward (A was decreased) when the oncotic pressure was reduced,21 while it was shifted rightward (A was increased) by increasing the oncotic pressure.22

Once it has been established that MAP–A corresponds approximately to the effective filtration pressure across the glomerular capillaries on the regular sodium diet, the \( K_{FG} \) of glomerular capillary walls can be estimated from its definition using the estimated effective filtration pressure, MAP–A, and GFR. The estimated \( K_{FG} \), 0.154 ± 0.018 (ml/sec)/mm Hg, was nearly twice the assumed value of 0.0812,5 reflecting the small difference between MAP–A and the true value of the effective filtration pressure, discussed above. It seems that \( K_{FG} \) is not affected, at least not decreased, in essential hypertension as assumed by Gomez.4 Thus, it is suggested that Gomez's equations can be applied to calculating intrarenal hemodynamics in patients with essential hypertension. If \( K_{FG} \) is known to be 0.154 ± 0.018 (ml/sec)/mm Hg from analysis of the renal function curve, then intrarenal hemodynamic parameters can be calculated. Intrarenal hemodynamics calculated by analyzing the renal function curve were comparable with those obtained by Gomez's equations (Table 3), indicating that they can be estimated without assuming \( K_{FG} \).

In animal experiments, Brenner et al1-3 recently showed the importance of intrarenal hemodynamics in the progression of renal failure. However, there is no way to evaluate intrarenal hemodynamics in clinical settings except by Gomez's equations.4,5 Thus, Gomez's original report itself has not been reevaluated until now. Furthermore, \( K_{FG} \) is assumed normal in Gomez's equations,4,5 making it even more difficult to apply them to the disease processes of renal failure. The renal function curve may be useful to estimate intrarenal hemodynamics quantitatively in clinical settings, especially when we want to see mainly the changes in intrarenal hemodynamics instead of the absolute values.10 The present study may enable us to examine whether intrarenal hemodynamics play an important role in the progression of renal failure in humans, as Brenner proposed in animal models, by analyzing the renal function curve. For example, the relatively infrequent occurrence of renal failure despite systemic hypertension in essential hypertension as seen in spontaneously hypertensive rats3,17,18 may be ascribed to the normal glomerular pressure due to afferent vasoconstriction. Since direct measurements of intrarenal hemodynamics are impossible in humans at present, there is no direct way to clarify the validity of our indirect estimation. Further studies are clearly required before our method can be applied to clinical practice. We hope that our present approach will stimulate further studies to analyze intrarenal hemodynamics in clinical settings.
Appendix
Summary of Gomez’s Equations

Gomez reported in detail how to estimate quantitatively intrarenal hemodynamics using clinical data such as systemic MAP, GFR, RPF, RBF, and TP. Introduced by Smith, Gomez’s equations are summarized briefly here to make it easier to understand their underlying principles as well as the present study.

First, in Gomez’s equations, the intrarenal vascular resistances are functionally divided into three components: preglomerular (afferent, \( R_a \)), postglomerular (efferent, \( R_e \)), and venular. Second, the hydrostatic pressures in venules, interstitium, renal tubules, and Bowman’s space within kidneys are considered to be in equilibrium and are given a value of 10 mm Hg. Third, the \( K_{FG} \) of glomerular capillaries is assumed normal (0.0812 [ml/sec/mm Hg]). From the above assumptions, the following equations are derived:

\[
GFR = K_{FG} \times \Delta P_F \quad \text{(A1)}
\]

\[
\Delta P_F = P_G - (H_T + \Pi_G) \quad \text{(A2)}
\]

where \( \Delta P_F, P_G, H_T, \) and \( \Pi_G \) (mm Hg) are the effective filtration pressure across the glomerular capillaries, glomerular hydrostatic pressure, hydrostatic pressure in Bowman’s space (assumed to be 10 mm Hg), and oncotic pressure within glomerular capillaries, respectively. GFR is expressed in milliliters per second per 1.73 m\(^2\). \( \Pi_G \) can be obtained knowing the mean concentration (\( C_M \)) of plasma protein within glomerular capillaries:

\[
\Pi_G = 5 \times (C_M - 2) \quad \text{(A3)}
\]

\( C_M \) can be calculated on the basis of mass conservation law of plasma protein during glomerular ultrafiltration using TP in systemic plasma and filtration fraction, FF (=GFR/RPF).

\[
C_M = \frac{TP}{FF} \times \log_e \frac{1}{1 - FF} \quad \text{(A4)}
\]

Solving Equations A1–A4, \( P_G \) can be estimated as

\[
P_G = \frac{GFR}{K_{FG}} + H_T + 5 \times \left( \frac{TP}{FF} \times \log_e \frac{1}{1 - FF} \right)^2 \quad \text{(A5)}
\]

Once \( P_G \) is known, the following equation can be derived from Ohm’s law:

\[
\text{MAP} - P_G = \frac{R_A \times \text{RBF}}{1,328} \quad \text{(A6)}
\]

Here, the number 1,328 is the conversion factor. Finally, the afferent arteriolar resistance can be calculated as

\[
R_A = \frac{\text{MAP} - P_G \times 1,328}{\text{RBF}} \quad \text{(A7)}
\]

Similarly, the efferent arteriolar resistance can be obtained as

\[
R_E = \frac{\text{GFR}}{K_{FG} \times (\text{RBF} - \text{GFR})} \times 1,328 \quad \text{(A8)}
\]

Since \( K_{FG} \) must be assumed in Gomez’s equations, the effects of the errors in \( K_{FG} \) on the estimation of intrarenal hemodynamics were analyzed using Equations A5, A7, and A8 (Figure 4). Here, the measured values such as GFR, RBF, and MAP were kept constant. When \( K_{FG} \) is increased, \( P_G \) and \( R_E \) are reduced and \( R_A \) is increased.

Determination of the Renal Function Curve

Assuming that the relation between arterial pressure and urinary sodium excretion rate is linear, the renal function (pressure–natriuresis) curve was drawn by linking two data points obtained in a steady state under two different amounts of sodium intake (regular and low) in each patient, where MAP (mm Hg) and \( U_{NaV} \) (meq/day) were plotted on the x and y axes, respectively. The extrapolated x intercept, \( A \) (mm Hg), and the slope, \( B \) ([meq/day]/mm Hg), were calculated as follows:

\[
A = \frac{U_{NaV}(I) \times \text{MAP}(I) - U_{NaV}(II) \times \text{MAP}(I)}{U_{NaV}(I) - U_{NaV}(II)} \quad \text{(A9)}
\]

\[
B = \frac{U_{NaV}(I) - U_{NaV}(II)}{\text{MAP}(I) - \text{MAP}(II)} \quad \text{(A10)}
\]

where I and II refer to the data obtained in a steady state under regular (stage I) and low (stage II) sodium diets, respectively. Using \( A \) and \( B \), \( U_{NaV} \) can now be expressed as a function of MAP:

\[
U_{NaV} = B \times (\text{MAP} - A) \quad \text{(A11)}
\]

Interrelation Between Intrarenal Hemodynamics and Renal Function Curve

The renal function curve, expressed as Equation A11, shows that when MAP is lowered to \( A \), urinary output stops. That is, the x intercept of the renal function curve, \( A \), is the theoretically critical blood pressure level at which urinary sodium excretion stops with the decrease in MAP. The mechanisms of the stop of urinary sodium excretion with the reduction in MAP to \( A \) should be ascribed to the stop of glomerular ultrafiltration. Therefore, when MAP is lowered to \( A \), the \( \Delta P_F \) across the glomerular capillaries must be reduced to zero, resulting in the stop of glomerular filtration. Thus, MAP − A seems to correspond to \( \Delta P_F \) on the regular sodium diet:

\[
\Delta P_F = \text{MAP} - A \quad \text{(A12)}
\]

Since \( \Delta P_F \) can be expressed as Equation A2, from Equations A2 and A12 we get

\[
P_G - (H_T + \Pi_G) = \text{MAP} - A \quad \text{(A13)}
\]
Furthermore, by rearranging Equation A6, the glomerular hydrostatic pressure can be expressed as

$$ P_G = \frac{R_A \times RBF}{1,328} - MAP $$

(A14)

Finally, by comparing Equations A13 and A14, we get the following important relation:

$$ A = -\frac{R_A \times RBF}{1,328} + (H_T + \Pi_G) $$

(A15)

This equation means that the x intercept of the renal function curve may be expressed as the sum of the pressure drop from aorta to glomeruli along afferent arteriole plus the opposing pressures against glomerular filtration at the glomerulus on the regular sodium diet. It must be noted that the values of $A$, $R_A$, RBF, and $\Pi_G$ are all obtained on the regular sodium diet. Since $A$ and $R_A$ vary with systemic arterial pressure, all parameters must be measured on the same conditions. The above calculation is a form of the functional stop-flow method and seems similar to the original stop-flow method by which the glomerular hydrostatic pressure was first estimated by Gerz.\(^{23}\)

References


**Key Words** • renal hemodynamics • renal circulation • renal vascular resistance • filtration coefficient • glomerular hypertension • arterial pressure–natriuresis relation • essential hypertension
Intrarenal hemodynamics in patients with essential hypertension.
G Kimura, M Imanishi, T Sanai, Y Kawano, S Kojima, K Yoshida, H Abe, T Ashida, H Yoshimi and M Kawamura

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