Brief Review

Renal Resistive Index
A Case of Mistaken Identity

W. Charles O’Neill

Of all the measured parameters in nephrology, none is more misunderstood and misused than the renal resistive index (RI). Although it is used widely as a marker of renal pathology based on the assumption that structural changes in the kidney alter renal vascular resistance, the sensitivity and specificity of RI for this purpose are questionable, and its clinical use remains uncertain. Both theoretical and experimental analyses of the RI can explain why this is the case.

RI is typically measured by Doppler sonography in an intrarenal artery and is the difference between the peak systolic and end-diastolic blood velocities divided by the peak systolic velocity.

\[
RI = \frac{V_{\text{syst}} - V_{\text{diast}}}{V_{\text{syst}}} \quad (1)
\]

It was first introduced in the 1950s and its naming was unfortunate because it is actually a measure of pulsatility. In fact, the closely related index in which the denominator is the mean velocity rather than the peak systolic velocity is termed the pulsatility index. Ironically, renal vascular resistance is the 1 hemodynamic parameter that has the least if any influence on RI.

A little mathematics will illustrate this point. Rearranging Equation 1 gives

\[
RI = 1 - \frac{V_{\text{diast}}}{V_{\text{syst}}} \quad (2)
\]

In the simplest analysis, velocity equals flow divided by lumen area (LA), and flow equals the difference in blood pressure (ΔP) divided by vascular resistance (R), yielding

\[
V = \frac{\Delta P}{R \times LA} \quad (3)
\]

Equation 2 then becomes

\[
RI = 1 - \left[ \frac{\Delta P_{\text{diast}}}{\Delta P_{\text{syst}}} \right] \frac{LA}{LA_{\text{diast}}} \quad (4)
\]

Although pressure and lumen area clearly change during systole and diastole, resistance should not. Changes in pressure and flow can alter renal vascular resistance through the myogenic response and flow-mediated vasodilation, respectively, but the time constants for these responses are far greater than the duration of the cardiac cycle. Thus, renal vascular resistance does not vary between consecutive systoles and diastoles and Equation 4 becomes

\[
RI = 1 - \left[ \frac{\Delta P_{\text{diast}}}{\Delta P_{\text{syst}}} \right] \frac{LA}{LA_{\text{diast}}} \quad \text{or} \quad 1 - \left[ \frac{\Delta P_{\text{diast}}}{\Delta P_{\text{syst}}} \right] \frac{LA}{LA_{\text{diast}}} \quad (5)
\]

and RI is independent of vascular resistance. Stated more simply, the proportional effect of resistance on blood flow should not vary with pressure and should be the same in systole and diastole. This independence of RI on resistance has been demonstrated in simple artificial circuits.

However, this basic analysis does not account for nonuniformity of blood velocity and, more importantly, downstream vascular properties such as compliance or capacitance. The more compliant the distal arteries are, the more flow they can accommodate during systole compared with diastole. When the arterial wall recoils during diastole, resistance determines how much of the extra blood they contain will move forward. Thus, when downstream properties (representing vascular impedance) are incorporated into mathematical or physical models, blood flow can become dependent on resistance.

Although this has been corroborated during postischemic hyperemia in the brachial artery and hypercapnea in neonatal cerebral arteries, the dependence of RI on vascular resistance varies considerably among vascular beds. In rabbit kidneys perfused ex vivo with increasing concentrations of phenylephrine, there was only a slight increase in RI despite a broad range of resistance not observed in vivo (Figure 1) and the inability of vasconstrictors or vasodilators to appropriately alter RI has also been observed in the uterine, carotid, and retinal circulations. In the latter 2, vasconstriction actually lowered RI and a negative correlation between RI and renal vascular resistance has also been demonstrated in transplanted kidneys.

The inconsistent relationship between RI and vascular resistance is undoubtedly attributable to the other factors that determine RI, which becomes clear on rearrangement of Equation 5:

\[
RI = 1 - \left[ \frac{\Delta P_{\text{diast}}}{\Delta P_{\text{syst}}} \right] \frac{LA_{\text{syst}}}{LA_{\text{diast}}} \quad \text{or} \quad 1 - \left[ \frac{\Delta P_{\text{diast}}}{\Delta P_{\text{syst}}} \right] \frac{LA_{\text{syst}}}{LA_{\text{diast}}} \quad (6)
\]
Equation 6 identifies 3 parameters that determine $RI$: (1) the ratio of diastolic to systolic blood pressure, which is an inverse function of pulse pressure; (2) $P_0$, a combination of interstitial pressure and venous pressure, essentially representing the renal capillary wedge pressure; and (3) the ratio of lumen area in systole and diastole at the site of insonation, a function of vascular compliance. Because downstream compliance also affects pulsatile flow, impedance also becomes a determinant as well, according to Equation 7:

$$\begin{bmatrix}
\text{Pulse flow} \\
\text{Mean flow}
\end{bmatrix} \approx \begin{bmatrix}
\text{Pulse pressure} \\
\text{Mean pressure}
\end{bmatrix} \times \begin{bmatrix}
\text{Resistance} \\
\text{Impedance}
\end{bmatrix}$$

Because essentially all the pressure drop in the kidney occurs at the afferent arterioles and beyond, central pressures are transmitted undampened to the renal arteries unless there is disease in the renal artery (see below). Thus, $P_{\text{syst}}$ and $P_{\text{diast}}$ represent systolic and diastolic blood pressure with the ratio being an indication of pulsatility or pulse pressure. The effect of tissue and venous pressure ($P_0$) is well described, as $RI$ was originally applied to the diagnosis of urinary obstruction. Experimentally, hydronephrosis increases $RI$ as does a compressing hematoma and even direct pressure from the ultrasound probe. Increased $P_0$ is the likely explanation for the increased $RI$ that can be observed in renal vein thrombosis and in acute inflammation or injury. In most cases, $P_0$ is not elevated and $RI$ is determined primarily by the other parameters.

Thus, $RI$ varies directly with pulse pressure and inversely with vascular compliance (or directly with vascular stiffness or impedance). Pulse pressure is the principal determinant and is influenced primarily by extrarenal factors, specifically cardiac function and systemic arterial compliance. Again, clinical and experimental data support the theoretical analysis. In the aforementioned study of rabbit kidneys perfused with pulsatile flow ex vivo, there was an essentially perfect correlation between $RI$ and pulse pressure, indicating that almost all the variability in $RI$ was explained by pulse pressure. Hypotension was noted to increase $RI$ in auto-transplanted kidneys in dogs, presumably because of increased pulse pressure. In a study of 133 subjects with hypertension, highly significant and strong correlations were found between renal $RI$ and aortic pulse pressure ($r=0.62$), incident pressure wave ($r=0.55$), augmented pressure ($r=0.49$), and aortic pulse wave velocity ($r=0.51$). Heart rate can also affect $RI$ independent of other hemodynamics, because of differences in diastolic duration, and this inverse relationship was nicely demonstrated in a study of 8 patients with cardiac pacemakers in whom heart rate could be varied directly.

Disease in the renal arteries can also alter $RI$ by virtue of decreasing pulse pressure. Furthermore, distal vascular disease that often coexists in these patients could reduce compliance and also increase $RI$. This is supported by a biopsy study showing that only arteriolosclerosis out of all histological parameters independently correlated with $RI$.

Figure 1. Effect of renal vascular resistance on resistive index in rabbit kidneys perfused ex vivo. Each set of symbols and line represents a different kidney. Adapted from Tublin et al with permission of the publisher. Copyright © 1999, Radiological Society of North America.

Figure 2. Mortality of renal transplant recipients with renal or splenic resistive indices (RIs) above or below the median. Adapted from Seiler et al with permission of the publisher. Copyright © 2012, Oxford University Press.
This potential confounding is avoided in studies in recipients of kidney transplants, which are particularly illustrative. Pulse pressure, the major determinant of \( R_I \), is clearly recipient specific and although the interlobular arteries are clearly donor specific, their compliance is likely influenced by systemic hemodynamics. In a study of 110 recipients of kidney transplants, \( R_I \) correlated with the age of the recipient but not the donor, again consistent with the dependence of \( R_I \) on systemic rather than intrarenal factors.

Furthermore, \( R_I \) correlated with pulse pressure but not parameters of allograft function. A subsequent study of 105 patients found correlations between allograft \( R_I \) and carotid intimal-media thickness or ankle-brachial index in the recipient but not allograft function. A recent study of 321 transplant recipients confirmed that \( R_I \) correlates with recipient age, but not donor age, and with recipient pulse pressure. There was also no correlation between \( R_I \) and histopathology obtained from protocol biopsies. A high \( R_I \) correlated with recipient death but not with allograft outcomes, which was also observed in a previous study.

These results in transplant recipients are all entirely consistent with \( R_I \) being a reflection primarily of the properties of the systemic vasculature rather than intrinsic renal disease. If this is indeed the case, then renal \( R_I \) should correlate with \( R_I \) measured in other organs and the clinical significance should be similar. This has been examined in patients with chronic kidney disease and in transplant recipients (Figure 2), in whom renal \( R_I \) correlated with splenic \( R_I \). In patients with chronic kidney disease, renal and splenic \( R_I \) showed similar correlations with a host of cardiovascular parameters including carotid intimal-medial thickness and left ventricular hypertrophy. The authors proposed the difference between renal and splenic \( R_I \) as a more specific marker of renal disease by accounting for systemic effects on renal \( R_I \), but the correlation with estimated glomerular filtration rate was weak (0.19).

The dependence on systemic vascular parameters explains the poor correlation with renal histology but at the same time explains how \( R_I \) can predict clinical outcomes. Although this prognostication could be directly related to the renal vasculature independent of systemic risk factors, the tight correlation between \( R_I \) and systemic hemodynamics and the fact that renal and splenic \( R_I \) showed similar correlations with mortality and allograft outcomes in transplant recipients suggest that it is explained mostly by extrarenal hemodynamics.

Both theoretical considerations and data from experimental and clinical studies clearly demonstrate that renal \( R_I \) is a misnomer and is instead an index of pulsatility and vascular compliance that, as suggested by others, might be more appropriately termed impedance index. Even if there were some effects of renal pathology on \( R_I \), the strong influence of extrarenal factors precludes it from ever being a specific test of renal disease. Although \( R_I \) may provide prognostic information, this is related to vascular disease that is often systemic and assessable by studying other arterial beds.

Disclosures

None.

References

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Hypertension. 2014;64:915-917; originally published online August 25, 2014;
doi: 10.1161/HYPERTENSIONAHA.114.04183

Hypertension is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
Copyright © 2014 American Heart Association, Inc. All rights reserved.
Print ISSN: 0194-911X. Online ISSN: 1524-4563

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World Wide Web at:
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On page 915, equations 5 and 6 were presented incorrectly. The correct equations are shown below.

\[
RI = 1 - \frac{\Delta P}{LA_{\text{diast}}} \quad \text{or} \quad 1 - \frac{\Delta P}{LA_{\text{syst}}} \times \frac{LA_{\text{syst}}}{\Delta P} \quad (5)
\]

\[
RI = 1 - \left( \frac{\Delta P_{\text{diast}}}{\Delta P_{\text{syst}}} \times \frac{LA_{\text{syst}}}{LA_{\text{diast}}} \right) \quad \text{or} \quad 1 - \left( \frac{P_{\text{diast}} - P_0}{P_{\text{syst}} - P_0} \times \frac{LA_{\text{syst}}}{LA_{\text{diast}}} \right) \quad (6)
\]

We apologize for these errors.

These corrections have been made to the current online version of the article, which is available at http://hyper.ahajournals.org/content/64/5/915.