Is the Aldosterone:Renin Ratio Truly Reproducible?

To the Editor:
Rossi et al recently concluded that the aldosterone:renin ratio (ARR) is reproducible. However, we think that several common errors were performed in their data interpretation, as described below.

In the Bland-Altman plot B (Figure 1 in Reference 1), the large differences in repeat measurements are overlooked on the basis that only 7% of points lay outside of the between-test “95% CIs,” by which they imply the Bland-Altman “limits of agreement.” These are constructed using the mean difference /deviation/ and so by definition alone, will always contain ~95% of the data and should certainly not, therefore, be regarded as evidence for good reproducibility. The latter should instead be qualitatively assessed by a careful clinical consideration of the magnitude of the 2 calculated limits. This step is often omitted, as was the case here.

The upper of the 2 “limits of agreement” in plot B is 2.1. This equates to a ratio of 8.2 between the 2 measures because, \[ \log(e)ARR1 - \log(e)ARR2 = \log(e)(ARR1/ARR2), \]
and \[ \exp(2.1) = 8.2. \] Therefore, the ratio of repeat measurements may differ by as much as 8.2. Had the authors drawn confidence limits for the limits of agreement, sometimes termed “tolerance limits,” the ratios of repeat measures would be as high as ~10. This follows from the formula for the SE for the limits of agreement of \( \sqrt{(3s^2/n)} = 0.097, \) where “s” is the SD of the differences \( \approx 0.92, \) ie, \( 2.1 - 0.3/1.96, \) and “n” is the sample size (268). The upper confidence limit for the upper limit of agreement is then calculated as \exp[2.1+(1.96*0.097)] = 9.9. In plot B, ratios of this magnitude are observed across the low to midrange of (log)ARR values, reflecting absolute ARR differences (as well as ratios) that are far too large in clinical terms to provide any convincing evidence for good reproducibility.

In plot D, absolute differences of ~30 and +30 occur around the 10th and 85th percentiles, indicating that approximately one fourth of subjects had differences \( \approx 30, \) the mean ARR value itself among primary hypertensive subjects, the majority of those studied.

The second Bland-Altman plot (plot C) confirms the large differences of plot B, because several points have ratios >8. However, this is distorted by constructing limits of agreement of ~1.4 and 3.7 that incorrectly assume a normal data distribution (by applying \( \pm 1.96 \) SDs to the mean difference). Although the use of ratios rather than differences may sometimes normalize skewed data, this is clearly not the case here, and only plot B should be used for Bland-Altman purposes.

Finally, the Pearson correlation coefficient is not useful to assess reproducibility. Bland-Altman methodology arose partly to dissuade researchers from presenting these statistics, because it would be a surprise if there were not a high degree of correlation between 2 repeat tests of the same measure.²

Disclosures

None.

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Hypertension. 2010;55:e18; originally published online March 8, 2010;
doi: 10.1161/HYPERTENSIONAHA.110.149799
Hypertension is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
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Print ISSN: 0194-911X. Online ISSN: 1524-4563

The online version of this article, along with updated information and services, is located on the
World Wide Web at:
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