Ahead of the Curve
Waveform Analysis of Blood Pressure, Reflection Magnitude, and Outcomes

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The history of blood pressure (BP) waveform analysis is almost as undulatory as the waveform itself. The development of the sphygmograph in the mid-19th century led to a relatively brief, albeit intense, interest in the interpretation of the BP waveform. This was perhaps more an art than a science, and interest in the sphygmograph and the waveform declined after the introduction of the cuff-based sphygmonanometer. More recently, interest in pulse waveform analysis has re-emerged, and the relative merits of estimated aortic (central) as opposed to brachial systolic and pulse pressure have been widely discussed. Although some issues remain unresolved, evidence from systematic reviews suggests that central pulse pressure may be a better predictor of cardiovascular events than peripheral BP. However, whatever the merits of measurement of central systolic or pulse pressure, a single number is unlikely to be an adequate descriptor of the morphology of a waveform, and the waveform may contain additional valuable and quantifiable information.

In this issue, Zamani et al report the results from 6000 participants in the Multi-Ethnic Study of Atherosclerosis (MESA). BP waveforms were recorded using a noninvasive radial tonometric device and analyzed using a technique that separates them into forward (Pf) and backward (Pb) components. Reflection magnitude (RM) was calculated as the ratio of peak Pf/peak Pb. RM and Pb were found to predict all-cause mortality, cardiovascular mortality, and noncardiovascular mortality in unadjusted models. Notably, the association with mortality, cardiovascular mortality, and noncardiovascular mortality was independent of a wide range of measures of subclinical atherosclerosis.

These findings extend previous data from MESA where RM predicted cardiovascular end points and was strongly predictive of new-onset chronic heart failure. Associations between cardiovascular events and RM and Pb have also been observed in a study of 725 patients (55–72 years) undergoing coronary angiography and between reflection index (RM/[1+RM]) and Pb in another study of 1272 individuals (30–79 years) drawn from a community-based survey in Taiwan. The results of these studies seem reasonably consistent (Figure).

Some technical considerations regarding the approach used by Zamani et al and in other studies are worth consideration. Strictly, pressure separation requires measurement of both pressure and flow waveforms at a given location. Zamani et al circumvented the requirement for flow measurement by using a scaled representative average aortic velocity waveform derived from the Asklepios population-based study. Other studies have used an estimate of aortic flow based on a Windkessel model or have assumed a triangular shape for aortic flow. Whichever assumption is used will introduce some uncertainty into the estimates of Pb and Pf. A previous study by Kips et al suggests that the correlation between RM calculated using average and measured waveforms is good ($r^2=0.74$) but not perfect. Zamani et al also used a generalized transfer function to approximate the aortic BP waveform. This is a widely accepted approach, and most published transfer functions are similar; nevertheless, the use of a generalized transfer function will introduce further variability into the reconstructed aortic BP waveform.

Imprecision in the pressure and flow waveform estimates should not introduce systematic bias, but will tend to weaken associations seen, so it is likely that the estimates of association between RM or Pb and outcomes are underestimates of true relationships. Together, the limited published studies so far suggest that these indices are likely to add to the predictive information obtained by BP measurement. In their earlier study, Chirinos et al reported that adding RM to a model containing age, sex, body mass index, diabetes mellitus, and BP resulted in a category-free net reclassification index of 0.38 and achieved a 48% relative increase in the discrimination slope. It would be valuable to know to what extent measurement of RM and Pb improves reclassification of risk in other populations.

As yet, estimates of RM and Pb in relation to mortality or cardiovascular events have been performed using radial or carotid tonometry; however, these indices can be calculated by cuff-based oscillometric devices. The extent of agreement between different devices and locations has not been studied for RM and Pb, but there is evidence that estimates of central BP differ depending on the device or location used. This issue merits further study. Undoubtedly, there are clear advantages in using cuff-based devices in terms of familiarity and convenience in clinical practice. All oscillometric devices
Figure. Meta-analysis of published studies examining the association between (A) reflection magnitude (RM) and (B) peak backward pressure (Pb) and cardiovascular events (unadjusted). To allow pooling of data for meta-analysis with Zamani et al,4 data from Weber et al6 and Wang et al7 were converted from hazard ratios (HRs) per 1 SD increase to HR per 10% increase
RM, using either the published SD or by assuming that ±1 SD was approximated by the interquartile range. CI indicates confidence interval. For Wang et al,7 data for men and women were pooled using fixed-effects meta-analysis before pooling with other data. Meta-analysis was performed in Stata 13.1 using the metan command and using a random-effects model.

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References

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