How Important Is Pulse Pressure as a Predictor of Cardiovascular Risk?

To the Editor:

Miura and colleagues\(^1\) report that pulse pressure (PP) is of no added value to systolic blood pressure (SBP) in assessing long-term cardiovascular (CV) mortality in 60- to 74-year-old men and women volunteers from 84 cooperating Chicago-area companies and organizations.

In contrast, we published a Framingham Heart Study report that found coronary heart disease (CHD) risk in middle-aged and older individuals to be inversely related to diastolic blood pressure (DBP) at any given level of SBP $\geq$130 mm Hg (Franklin et al, 1999, Table 4),\(^2\) suggesting that PP may be superior to SBP as a predictor of risk in this older population. We would like to consider some of the explanations for the different results reported in our paper and that of Miura et al.

First, numerous longitudinal and cross-sectional studies of age-related changes in blood pressure have shown that mean DBP levels off by about age 50 years and begins to decrease by the age of 60 years.\(^3\)–\(^5\) Contrary to these findings, the Miura study shows a rise in DBP from age 40 to 59 versus age 60 to 74 in men (83.5 versus 85.8 mm Hg) and in women (79.5 versus 82.3 mm Hg), suggesting that the Chicago-area volunteer workers population may not be typical of many other populations in the United States and around the world.

Second, Miura et al state correctly that the proper approach in assessing the value of PP is to place both SBP and DBP in the same Cox model, and only if DBP has an inverse relation to CV mortality can PP be shown superior to SBP. This inverse relation of DBP to CV mortality was not observed in their study, largely because DBP increased rather than decreased after age 60. In contrast, the Framingham report,\(^2\) the Physicians Health Study,\(^6\) and the Medical Research Council mild hypertension trial\(^7\) all showed an inverse relation of DBP to CHD risk. Furthermore, there are 4 additional publications, including a total of 11 different population databases, that showed an inverse relation of DBP to total and CV mortality.\(^8\)–\(^11\) strongly suggesting that PP is superior to SBP in predicting risk in these elderly cohorts.

Thus, it would appear that not all elderly populations show the same relation of PP in predicting cardiovascular disease. The reasons for discrepancies between the Miura study and the majority of other studies in this age group are not entirely clear. The presence of a healthy cohort effect in the Miura study could well be the most important factor, especially because the oldest group (ages 60 to 74) had only a mean age of 63 years. The use of supine blood pressures in the Miura study instead of the more conventional sitting position also may have influenced results. Single blood pressure recordings in the Miura study (verses 2 in the Framingham study) undoubtedly reduced precision.

We also would like to correct the record on a few minor points made by Miura et al. They reported that 2 studies, both from Framingham, compared PP and SBP as predictors of CHD risk (Kannel, 2000, and Franklin et al, 1999)\(^2\)\(^,\)\(^12\) and stated that these 2 studies came to opposite conclusions. This is incorrect. Only Franklin et al, 1999,\(^2\) placed DBP and SBP in the same Cox model to assess PP. Kannel, 2000,\(^0\)\(^,\)\(^12\) was a historical review article that compared SBP and DBP separately as predictors of CHD risk and, therefore, did not come to different conclusions from Franklin et al, 1999.\(^2\)

Miura et al did show that DBP was superior to both PP and SBP in predicting CV risk, but only in middle-aged men. Indeed, our recent Framingham publication\(^13\) further clarified this issue by showing superiority of DBP to PP and SBP in both young men and women. This study showed that, with increasing age, there was a gradual shift from DBP to SBP and then to PP as predictors of CHD risk. In patients <50 years of age, DBP was the strongest predictor. The age-period 50 to 59 years was a transition period when all 3 blood pressure indices were comparable predictors, and from 60 years of age on, DBP was negatively related to CHD risk so that PP became superior to SBP. These findings were largely confirmed by a British study using 24-hour intra-arterial ambulatory blood pressure monitoring.\(^11\)

Finally, we also agree with the authors that PP cannot replace SBP as a single measure of cardiovascular risk. Indeed, of the 3 blood pressure indices, SBP is the best predictor for the majority of persons with hypertension. However, for older persons, the best clinical strategy for estimation of cardiovascular risk is to first determine the level of SBP elevation and then adjust the overall risk upward if there is wide PP, ie, discordantly low DBP.\(^14\)

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Response

We appreciate the interest of Franklin et al in our report on pulse pressure compared with other blood pressure indices, each considered singly, in predicting 25-year mortality from a large employed population of men and women in Chicago. As we pointed out in our paper, main findings from our study on coronary heart disease (CHD), cardiovascular disease (CVD), and all-cause mortality were that (1) relations of pulse pressure (PP) were less strong than were those of systolic blood pressure (SBP) for all end points in all age/gender groups studied; (2) relations of PP were less strong than were those of diastolic blood pressure (DBP) for all end points in middle-aged men and women and in older women; (3) among the 4 blood pressure (BP) indices we studied, the strongest relation was observed for either SBP or mean arterial pressure (MAP) in all age/gender groups; (4) relations of SBP to death tended to be stronger than or similar to those of DBP; and (5) with control for SBP, DBP was positively and significantly related to death in middle-age men and women, but not in younger men and older men and women. Thus, the major comments of Franklin et al were previously discussed in our paper.

In addition, we acknowledged that our results were based on a single measurement of BP. However, as we discussed, the consequence of this is that our results probably are underestimates of true associations because of regression dilution bias. We also recognized, and discussed, the possible role of the “healthy worker effect.” As we noted, however, it is a reasonable inference that our findings are generalizable to other “healthy” general population samples. We also discussed the age range in our study and noted previous reports emphasizing the possibility, remaining to be confirmed, that PP becomes more important physiologically and prognostically primarily (or exclusively) at ages ≥60 years. Given that most of our oldest participants were in their early 60s at entry, our findings may have limited implications for persons beyond the age of 63 years, as we also stated.

Nothing in our results, or those reviewed by Franklin et al, suggests that pulse pressure can replace an emphasis on SBP in older people, healthy or otherwise. DBP may take precedence over SBP in risk assessment in persons under age 60, but our results were not strong in favor of this approach. As pointed out in our paper and by Franklin et al, we did not confirm the results of Franklin et al as to the added value of PP after age 60. As we previously stated, for younger and middle-aged persons, the evidence is clear that an emphasis on PP should be avoided. There is no evidence, in a general population younger than age 60, that PP is superior to SBP in the prediction of CVD or all-cause mortality. Detection and evaluation of hypertension based mainly on SBP, considered together with DBP, per the sixth report of the Joint National Committee of Prevention, Detection, Evaluation, and Treatment of High Blood Pressure (JNC-VI) recommendations, should remain the most practical and easy approach in the general population for young adult, middle-aged, and older men and women (at least up to about age 60 years). PP may have added value in risk assessment, but, if so, apparently only in certain age groups or in certain populations.

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