Circulation Journal
Official Journal of the Japanese Circulation Society
http://www.j-circ.or.jp

Some Caution When Conducting Long-Term Follow-up Study of Cardiovascular Mortality – Reply –

We thank Dr Kawada for his suggestions to improve understanding of our study[1] and for encouraging us to do further research with the interesting data from the Seven Countries Studies. We performed a number of additional analyses for cardiovascular disease mortality and the results are shown in the **Table**. We have now adjusted for body mass index at baseline instead of height and weight (**Table**, Model 1), which yielded similar associations. We did not include the serum cholesterol level in our multivariable models because we did not consider it a confounder. Adjustment for serum cholesterol (**Table**, Model 2) yielded a slight attenuation of the observed hazard ratio (HR) in the mid category of systolic blood pressure (BP) in Tanushimaru. Findings for Ushibuka did not change. Adjustment for both body mass index and serum cholesterol (**Table**, Model 3) did not essentially change these results. In our different models, we included a maximum of 10 independent variables, including 2 categories of BP, which is acceptable in relation to the number of cardiovascular events (total of 118 in Tanushimaru and 130 in Ushibuka).

In our paper,[1] we did not present the results for the different confounders or place of residence in relation to cardiovascular outcomes because it was not the aim of the study. We agree that repeated BP measurements would have increased the precision of our study, resulting in smaller confidence intervals (CI). The lack of precision, however, cannot form an explanation for the differential associations between systolic BP and cardiovascular endpoints that we found between the 2 areas. Also, the fact that the mortalities of stroke and coronary heart disease in Japan have substantially changed during the past decades cannot explain our findings. Regrettably, our data did not allow separate analyses for hemorrhagic stroke and cerebral infarction, although we agree that it would be worthwhile examining these different types of stroke. We did examine coronary heart disease mortality, but the number of events was very small and HRs were unstable. In Tanushimaru, the HRs for coronary heart disease mortality were 1.68 (95%CI, 0.64–4.42) in the mid category and 1.76 (95%CI, 0.60–5.20) in the upper category of systolic BP, compared to the lower category. In Ushibuka, these HRs were 0.80 (95%CI, 0.24–2.62) and 1.32 (95%CI, 0.42–4.20), respectively.

Reference

1. Hirai Y, Geleijnse JM, Adachi H, Imaizumi T, Kromhout D. Systolic blood pressure predicts cardiovascular mortality in a farming but not in a fishing community: A 40-year follow up of the Japanese cohorts of the seven countries study. *Circ J* 2011; **75:** 1890–1896.

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(Released online December 14, 2011)

Table. SBP and 40-Year Risk of Mortality From Cardiovascular Diseases in Tanushimaru and Ushibuka

	Baseline SBP (mmHg)		
	<120	120–139	≥140
Tanushimaru			
No. of subjects/events	158/18	188/43	162/57
HR, original model*	1	1.78 (1.00–3.14)	3.05 (1.73–5.40)
HR, model 1**	1	1.77 (1.00–3.14)	3.05 (1.72–5.41)
HR, model 2†	1	1.68 (0.92–3.06)	3.08 (1.69–5.60)
HR, model 3††	1	1.67 (0.91–3.04)	3.07 (1.68–5.59)
Ushibuka			
No. of subjects/events	122/26	186/38	190/66
HR, original model*	1	1.00 (0.58–1.71)	1.66 (1.01–2.75)
HR, model 1**	1	0.99 (0.58–1.70)	1.61 (0.97–2.66)
HR, model 2†	1	0.98 (0.57–1.68)	1.67 (1.01–2.77)
HR, model 3††	1	0.97 (0.57–1.67)	1.60 (0.97–2.65)

SBP, systolic blood pressure; HR, hazard ratio, obtained by Cox proportional hazard analysis, with 95% confidence interval.
*Model as presented in our original paper: HR adjusted for age (continuous), height (continuous), weight (continuous), smoking status (1 dummy), physical activity (2 dummies) and occupation (2 dummies); **HR adjusted for age, body mass index, smoking status, physical activity and occupation; †HR adjusted for age, height, weight, smoking status, physical activity, occupation and serum total cholesterol level; ††HR adjusted for age, body mass index, smoking status, physical activity, occupation and serum total cholesterol level.