Blood pressure variability measurements

Sir,

The recent article by Tozawa et al. examines the effect of increased variability of systolic blood pressure (SBP) on cardiovascular and all-cause mortality in chronic haemodialysis patients in Japan. The authors report that there was increased all-cause (but not cardiovascular) mortality with higher BP variability [1].

The methods used to measure SBP variation were co-efficient of variation (SD-SBP/Mean SBP × 100) and a ‘maximum minus minimum’ SBP value. All BP values were obtained by one measurement 5 min before a standard HD session.

BP variability is a complex series of phenomena [2,3]. Variation can be described over decades (the effect of ageing), over seasons, diurnally, and, on a shorter time-scale, over minutes or even with cardiac systole (LV function and aortic compliance). It is not surprising that comprehensive analysis of these BP variations is notable for its complexity. Using as an index of BP variation a derivative comprising the subtraction of just two BP readings (from a dataset of about 150 readings for each patient taken over a 1 year period) has the merit of simplicity but may not be robust enough for a study of only 150 patients.

What the authors have shown is that patients whose predialysis SBP is more variable (when assessed over 12 months) have a greater all-cause mortality. In their Table 2 it is clear that a greater proportion of the patients with greater-than-median SBP variability were older diabetics with lower predialysis BP and plasma creatinine levels. Mortality numbers were really very small—one more patient was withdrawn from dialysis in the higher BP variability group than from the lower group, and one patient died from infection. It is very hard to see how these modes of death are relevant to BP variation, and we suspect that the analysis is only valuable with respect to cardiovascular mortality, and here, once corrected for age, diabetes etc., there was not a significant association.

Both uraemia [4] and diabetes [5] are associated with autonomic neuropathy, one of whose manifestations is systolic BP variation with posture. In the discussion the authors state that there was no difference between the higher and lower BP variability cohorts with respect to a disordered autonomic nervous system—but we have failed to spot these data in the paper. Cardiac dysautonomia is a well-recognized marker for cardiovascular mortality [6].

Important supportive evidence would bolster the hypothesis—did the patients with greater SBP variability exhibit greater pre-to post-dialysis BP variability, or greater intradialytic BP variability?

It was interesting to see that the three cases of fatal congestive cardiac failure were all in the increased BP variation cohort. In our cross-sectional study of the impact of disordered BP variation on cardiac function in haemodialysis patients, we found that the lower the BP variability the larger the left ventricular internal diameter and the worse the LV function [7].

We believe that disordered BP variation is very relevant to patients with all stages of renal disease [8]. A recent paper suggests that abnormal BP variation may arise from inhibited endothelial nitric oxide synthase activity [9] as well as from disordered autonomic function. It is premature we think though to conclude that this has a malign influence on patient survival.

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Reply

Sir,

We wish to provide the following reply to the letter by Dr Goldsmith.

There were 194 dialysis patients in our dialysis unit at the start of 1994. Among them, some patients were transferred to other units or died (annual mortality rate was about 10% in all dialysis patients in Okinawa) or transplanted during 1994. After all, complete blood pressure records of a full year of sessions were obtained in only 144 patients (74%). Therefore this study certainly has a bias for survival of patients as mentioned in the last part of discussion [1].

We showed that the difference between the maximum and minimum systolic blood pressure in 1994 (ΔSBP) correlated with the coefficient of variation in systolic blood pressure (SBPCV) calculated from 1-year records (about 156 records in each patient) and was an independent predictor for all-causes mortality. We believe ΔSBP is a reliable index of survival as much as SBPCV.

Age, sex, presence of diabetes mellitus, diastolic blood pressure, and serum creatinine were significantly different between the smaller and the larger SBPCV groups (Table 1 in [1]). Therefore, we adjusted the crude hazard ratios by above clinical variables. Nevertheless, the adjusted hazard ratio of SBPCV and ΔSBP were statistically significant.

The number of deaths was 13 (9.0%) among the studied patients. This was similar to that of the patients in Okinawa, Japan (about 10%). If one includes other dialysis units to increase the number of study patients, the bias resulting from inter-dialysis unit data should be taken into account. The hazard ratio of cardiovascular death was not significant. Certainly, we need a longer time of experience to strengthen the evidence or a larger scale investigation.

Seasonal variation of blood pressure has been reported in haemodialysis patients [2,3]. We may need to take into account the seasonal variation when evaluating blood pressure variability. The range of seasonal SBP variation was very small (within 2 mmHg) in our study subjects [3]. Also in this study, we used a complete set of blood pressure records throughout the year of 1994 for all the patients. Therefore, the seasonal influence would be negligible in the present study.

Dr Goldsmith pointed out that ‘In the discussion, the authors state that there was no difference between the higher and lower BP variability cohorts with respect to a disordered autonomic nervous system.’ In this study, we did not examine the autonomic function of the patients. We only raised the possibility of autonomic disorder with respect to the mechanisms by which blood pressure variability increased the risk of mortality.

In our study, we used only pre-haemodialysis BP. Therefore, analyses of pre- to post-dialysis BP variability, or intra-dialytic BP variability have not been done.

It is clinically relevant that the mortality from all causes was predicted by the SBPCV or ΔSBP in this study. Reasons why deaths due to cardiovascular events were not predicted by blood pressure variability remain to be examined in a future study.

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