Blood pressure, ageing and mortality

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In this issue, Hakala and co-workers report on the relationship between mortality and blood pressure in 521 subjects, aged 75 to 85 years, who had been followed for up to 5 years in the context of the Helsinki Ageing Study\(^\text{[1]}\). Confirming a previous work of Mattila et al.\(^\text{[2]}\), it was shown that an inverse relationship linked systolic or diastolic blood pressure and mortality. It was also shown, however, that in the 75-year-old subgroup this association had a J-shape.

Furthermore, after controlling for age, gender and for the occurrence of clinically significant diseases, baseline blood pressure was positively related to 5 year survival.

The existence of a J curve relating blood pressure and mortality is a debated issue, however. Strong arguments have been raised against the relevance of this phenomenon within the blood pressure range usually found in a clinical setting. MacMahon and co-workers, in a meta-analysis which included data from a total of 420,000 individuals below 70 years of age, did not find evidence of any ‘threshold’ or J-shape in the relation between diastolic blood pressure and the risk of stroke and coronary artery disease: in the large majority of subjects, a lower blood pressure was associated with a lower risk\(^\text{[3]}\). Similarly, in the SHEP study, patients with isolated systolic hypertension who underwent active treatment did not display any J-shape relationship between their systolic blood pressure and stroke or coronary artery disease. This was also the case for patients aged 80 years and above\(^\text{[4]}\). Further evidence against the occurrence of a J-shape phenomenon was provided by other major trials on elderly hypertensives, such as the STOP\(^\text{[5]}\) and the MRC trial in the Elderly\(^\text{[6]}\), which showed that a drug-induced blood pressure reduction reduces cardiovascular morbidity and mortality in these subjects. In the STOP trial, the benefit was detectable in subjects aged up to 84 years\(^\text{[5]}\).

The belief that a J-shaped relationship between blood pressure and mortality is unusual is further supported by data obtained in older subjects through routine use of ambulatory blood pressure monitoring in a clinical setting. In this age group, the low blood pressure which is frequently recorded at night is not associated with a higher rate of events, as compared to the more elevated blood pressure recorded during the day. The inverse association between mortality and blood pressure reported by Hakala et al. in people older than 80 years\(^\text{[1]}\) is therefore unlikely to indicate that a lower blood pressure was associated per se with a higher risk. Their observations might rather have reflected the effects of co-morbidity. In other words, among very elderly subjects, a lower blood pressure could have been just the marker of an overall frail health condition in those individuals who were approaching death. On the other hand, the higher blood pressure levels found in the elderly subjects with a better survival might have reflected the persistence of a good left ventricular function as well as the continued ability of these subjects to live an active life, due to better general health. This interpretation is supported by the outcome of a subgroup analysis on the results of the EWPHE trial\(^\text{[7]}\).

According to this analysis, a U curve between mortality and diastolic blood pressure was observed not only in patients under active treatment, but also in patients taking placebo. This may indicate that the increased mortality observed in the treated elderly hypertensives with lower blood pressure was not drug-induced, but it just depended on some deterioration in general health, as suggested by the concomitant decrease in body weight and in haemoglobin concentration.

Admittedly, Hakala and co-workers have tried to exclude subjects with any clinically important disease from their analysis. This, however, may not have been enough to guarantee adequate protection from the confounding role of subclinical pathological conditions frequently associated with ageing. Moreover, the elderly subjects of this study were followed up for 5 years only, and over such a short follow-up period co-morbidity and the occurrence of low blood pressures in frail individuals approaching death might indeed have represented very important confounders. In a recent study by Glynn et al.\(^\text{[8]}\) which included subjects with an average age of 75 years, over the first 3 years of follow-up, participants with the lowest blood pressure did have the highest death rates. However, after exclusion of this initial period from the analysis, high and low blood pressure levels predicted the increase in cardiovascular mortality.

Notwithstanding this, however, it has to be acknowledged that the relationship between blood pressure and mortality in the very old has not yet been adequately clarified. Indeed most data available on this issue come from subgroup analysis, i.e. from an approach which is not devoid of methodological limitations. Moreover, in all the studies carried out so far, including the EWPHE, the SHEP, and the HOT trials, the number of individuals older than 80 years...
was unsatisfactorily low. This means that more trials are still needed to define the actual prognostic value of blood pressure in the very old. It is likely that only the results of randomized controlled trials of adequate size, aimed at assessing the risks and benefits of lowering blood pressure in hypertensive subjects over the age of 80, will provide us with convincing evidence on whether very old subjects with elevated blood pressure should or should not be treated.

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References


Primary ventricular fibrillation: a reason to be cautious

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It has been stated that the prognosis of ventricular fibrillation in the initial stages of acute infarction is always favourable [1,2]. This lethal arrhythmia was estimated to occur (in the pre-thrombolytic era) in about 5% of all infarctions after admission [3]. Because immediate treatment with defibrillation resulted in a short-term favourable prognosis in the resuscitated patient, strategies were developed to create a safer environment for patients in the early stages of the infarction. The establishment of coronary care units offered continuous ECG monitoring and availability of defibrillators. As most deaths due to ventricular fibrillation occur before admission to hospital, efforts were undertaken to reduce the delay to admission after the onset of chest pain. Mobile units, capable of defibrillating when necessary, were to be used to transport the patient to hospital.

It is now evident that early reperfusion by thrombolytic agents reduces early death and the probability of in-hospital fibrillation, as demonstrated by several multicentre trials on thrombolytic therapy [4]. Therefore, early thrombolytic therapy or angioplasty are important next steps, even when this does not necessarily reduce the incidence of primary ventricular fibrillation [4].

This takes us to the question, why do patients with acute infarction have ventricular fibrillation in the early stage? Ventricular fibrillation, generally considered the result of random reentry, has no obvious other reason in this condition than the acute infarction, and occurs not as a result of shock or heart failure [5]. The electrical environment that favours this arrhythmia is created by the dynamics of