High blood pressure at old age : The Leiden 85 plus study

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Chapter 9

Summary

Chapter 1

This chapter contains a short review of the history of high blood pressure. The changing perspective in time of the hazardous effect of high blood pressure is highlighted. In the last 3 decades there has been an explosion in knowledge about high blood pressure. As a result of that treatment goals have been stricter and goal populations have been broader. However, the evidence of a hazardous effect of high blood pressure in the elderly is not robust and even contradictory compared to middle-aged people. To explore this possible contradiction this thesis has two aims. First it contributes to observational evidence between high blood pressure at older age and adverse outcomes, including cardiovascular mortality, renal failure and cognitive decline. Secondly, it tries to disentangle the association between blood pressure and cardiac function at older age.

Chapter 2

The aim of chapter 2 is to study the impact of a history of hypertension and current blood pressure on mortality in the most elderly. This study was part of the Leiden 85-plus Study, an observational population-based cohort study in the community city of Leiden, the Netherlands. Five hundred and ninety-nine inhabitants of the birth-cohort 1912-1914 were enrolled on their 85th birthday. There were no selection criteria related to health or demographic characteristics. The mean follow-up was 4.2 years. Five hundred and seventy-one participants were included, 39 % had a history of hypertension. During follow-up 290 participants died, 119 due to cardiovascular causes. Compared to participants without a history of hypertension, those with a history of hypertension had a 60% increased mortality risk from cardiovascular causes, but equal mortality risks from all causes. High blood pressure at age 85 years was not a risk factor for mortality irrespective of a history of hypertension. However, blood pressure values below 140/70 mmHg (n=48) at age 85 years were associated with excess mortality, predominantly in participants with a history of hypertension. Thus, in the most elderly, high blood pressure is not a risk factor for mortality, irrespective of a history of hypertension. Blood pressure values below 140/70 are associated with excess mortality.

Chapter 3

The aim of chapter 3 is to study the effect of blood pressure on creatinine clearance over time in very old participants. High blood pressure is associated with a decline in renal function. Whether this is true for very old people is largely unknown. This study was part of the Leiden 85-plus Study. For this study 550 subjects (34% men) were enrolled at their 85th birthday and followed until death or age 90. Blood pressure was measured twice at baseline and at age 90 years. Creatinine clearance was estimated annually (Cockcroft-Gault formula). The mean creatinine clearance at baseline was 45 ml/min. Systolic blood pressure was not associated with changes in creatinine clearance during follow-up. Those with diastolic blood pressure below 70 mmHg had a significant accelerated decline of creatinine clearance compared with those with higher diastolic blood pressure. Participants with a decline in systolic blood pressure during follow-up had a significant accelerated decline of creatinine clearance compared with those with stable blood pressures. Similar results were found for a decline in diastolic blood. Thus, in this study high blood pressure at older age is not associated with renal function. In contrast, low diastolic blood pressure is associated with an accelerated decline of renal function.

Chapter 4

The aim of this chapter is to determine the prospective relationship between blood pressure and cognitive function across a wide age range. This study was part of the Rotterdam Study and the Leiden 85-plus Study, both prospective population-based cohort studies.

Three thousand seventy-eight men and women, initial age 55 to 84 years from the Rotterdam Study and 276 men and women, initial age 85 years, from the Leiden 85-plus Study were included. Systolic blood pressure and diastolic blood pressure were measured at baseline; cognitive function was assessed at the end of follow-up using a dedicated neuropsychological test battery. In the youngest participants (<65 years), systolic and diastolic blood pressure were not associated with cognitive function 11 years later. For persons aged 65 to 74 years, higher baseline systolic and diastolic blood pressures were related to worse cognitive function 11 years later. In contrast, in older age (≥75 years), higher systolic and diastolic blood pressure seemed to be related to better cognitive function at the

end of follow-up. This effect appeared strongest in the highest age group (85 years). Thus, high blood pressure was associated with greater risk of cognitive impairment in persons younger than 75 but with better cognitive function in older persons.

Chapter 5

The aim of this study is to elucidate the underlying mechanism of the observational findings that low blood pressure in the very old is associated with organ dysfunction and excess mortality. We hypothesized that cardiac dysfunction contributes to low blood pressure in the very old. A sample of 82 participants all aged 90 years from the Leiden 85-plus Study, were invited. Blood pressure was measured twice and all but one underwent echocardiography to assess cardiac dimensions and functional cardiac parameters. Some 47 participants were free from hemodynamically significant valvular disease and were included in the present analyses. There were low values for mean cardiac output (2.0 l/min/m2) and mean stroke volume (31 ml/m2). For every 10-mmHg decrease in systolic blood pressure, cardiac output and stroke volume were significantly lower. Mean left ventricular ejection fraction was normal and higher for each 10-mmHg decrease in systolic blood pressure. Mean left ventricular dimensions were normal but the E/A ratio was 0.68 indicating diastolic dysfunction. In conclusion, among the most elderly, low systolic blood pressure correlates with low cardiac output while systolic ventricular function is not impaired.

Chapter 6

This study evaluates the prevalence of significant left-sided valvular heart disease in community dwelling nonagenarians. In addition, we evaluated the impact of valvular heart disease on the ability to perform activities of daily living. Nested within the Leiden 85-plus Study a sample of 81 nonagenarians was recruited. The left ventricular (LV) dimensions, function and the presence and severity of heart valvular disease were evaluated by echocardiography. Daily life activities were assessed using the Groningen Activity Restriction Scale (GARS). LV cavity diameters and systolic LV function were within normal for the majority of the participants. Significant valvular disease was present in 57 (70%) individuals, with mitral regurgitation and aortic regurgitation being mostly affected (73%

and 47% respectively). The GARS score between individuals with and without significant valvular heart disease was similar. In conclusion, the majority of the nonagenarians from the general population have significant valvular heart disease that does not affect the ability to perform activities of daily living.

Chapter 7

This study investigated markers of autonomic tone on a standard electrocardiogram in relation to mortality in old age. This study was part of the Leiden 85-plus Study. A total of 599 inhabitants were enrolled in a population-based follow up study at their 85th birthday. Electrocardiograms were taken on entry and annually thereafter. Electrocardiograms were analysed automatically to determine four markers of autonomic tone, i.e. heart rate, the occurrence of ventricular extrasystoles and two time domain measures of heart rate variability. All participants were followed up for mortality. For those participants with a heart rate in the highest quartile the total mortality risk was 1.8-fold increased. However, they had not an increased cardiovascular mortality risk. The occurrence of at least one ventricular extrasystole was related with a 2.3-fold increased total mortality risk and a 3.6-fold increased cardiovascular mortality risk. In stratified analyses, the prognostic effect was confined to males. Both measures of heart rate variability were not related to mortality. Thus, on a standard 10 sec. Electrocardiogram, high heart rate and the occurrence of a ventricular extrasystole, both markers of sympathetic dominance, were predictive for mortality in old age. Two short-term measures of heart rate variability as measured on a standard 10 sec. electrocardiogram were not related to mortality, and hence may not reflect autonomic tone in old age.

Chapter 8

This chapter reveals a general discussion about the hazardous effect of high blood pressure in the elderly. The population-based reports indicating lower mortality and morbidity risks in association with high blood pressure in the very old are robust and should not be ignored. However, the results of the only randomised double blind interventional trial done, is solid too. Possibly, high blood pressure concordant with a low cardiac output is a different entity compared with high blood pressure concordant with a normal/high cardiac output. This might explain that elderly with a limited amount of atherosclerosis / vascular disease will have

benefit from treatment of high blood pressure. In contrast, those with a huge amount of atherosclerosis / vascular disease might not benefit from treatment, due to decreased perfusion, especially in those persons with a decreased cardiac output. Clinicians have to make a decision whether the blood pressure in a particular patient is appropriate or not. Our hypothesis is that high blood pressure concordant with a low cardiac output should not be treated in contrast with high blood pressure concordant with a normal/high cardiac output. Therefore, at present, we propose that treatment of high blood pressure in the very old is not withheld but highly individualized. In our opinion, future research should focus on the relation between blood pressure and cardiac output.