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**Blood pressure, cardiac biomarkers and cognitive function in old age**  
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# Chapter 1

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**General introduction**



## Introduction

With the increase in life expectancy, the prevalence of cognitive disorders is expected to further rise the coming years.(1) The number of people suffering from dementia worldwide is estimated to almost double every 20 years, with prevalence numbers of 65.7 million in 2030 and 115.4 million in 2050.(1) Accumulating evidence of the last years highlights the role of cardiovascular risk factors in the pathogenesis of cognitive disorders.(2-4) Epidemiological, pathological and neuroimaging studies show that cardiovascular risk factors in middle age associate with an increased risk of brain aging and cognitive impairment in later life.(5, 6) In older people, however, the contribution of cardiovascular risk factors in the development of cognitive impairment is still a matter of debate.(7) Furthermore, although a variety of mechanisms have been proposed to explain the association of cardiovascular risk factors with cognitive disorders, the underlying pathways have not been fully understood.

An example of a cardiovascular risk factor in middle age that is associated with cognitive impairment in later life, is high blood pressure.(8) Numerous studies demonstrate that midlife high blood pressure is a risk factor for cardiovascular events, brain atrophy, and cognitive decline.(9-12) In addition, some randomized controlled trials show favorable effects of midlife antihypertensive treatment on risk of cognitive impairment.(13, 14) However, recent evidence shows that this association attenuates with increasing age and it has even been reported that in older age, low instead of high blood pressure relates with increased risk of cognitive disorders and cardiovascular events.(6, 15-17) In particular people who are biologically older seem to suffer from low blood pressure values.(18-20)

Besides blood pressure, cardiac disease is associated with increased risk of cognitive disorders and dementia. Patients with coronary artery disease, atrial fibrillation, and chronic heart failure have worse cognitive function and a higher risk of progression to dementia. (3, 21-23) A possible explanation behind this association is reduced cardiac output, leading to cerebral hypoperfusion and subsequently to impairment of delivery of oxygen and nutrients to the brain.(3) Concordantly, it has been shown that in patients with severe systolic heart failure, cognitive function significantly improved after a cardiac transplantation, or after implantation of a left ventricular assist device.(24, 25) However, whether people with early signs of cardiac disease are also at increased risk of cognitive impairment, has poorly been studied.

The aims of this thesis are 1) to further investigate whether blood pressure in older people is a risk factor for cardiovascular events and cognitive impairment; 2) to study whether early markers of cardiac disease are related with cognitive impairment; and 3) to evaluate the feasibility of home blood pressure monitoring using smartphone-assisted technology, which might eventually assist to prevent cognitive impairment.

## Outline of this thesis

This thesis is divided in three parts. The first part consists three studies evaluating the association of blood pressure and blood pressure variability with cardiovascular events and cognitive function in older age, respectively. **Chapter 2** evaluates whether the association between (diastolic) blood pressure and cardiovascular events differs in people with and without a history of cardiovascular disease. Besides average blood pressure, visit-to-visit blood pressure variability has been associated with cardiovascular events and cognitive impairment. In **chapter 3**, we therefore study the association of visit-to-visit blood pressure variability with cognitive function. Furthermore, we investigate potential explanations behind this association in a magnetic resonance substudy. **Chapter 4** further elaborates on this topic by studying how blood pressure lowering medication is related to both visit-to-visit blood pressure variability and cognitive function; and whether blood pressure lowering medication could explain the relation between visit-to-visit blood pressure variability and cognitive impairment.

The second part of this thesis consists of two studies addressing the association between early markers of cardiac disease and cognitive function. In **chapter 5**, we evaluate the relation of N-terminal pro-brain natriuretic peptide (NT-proBNP), a neurohormone that is commonly used in the diagnosis of clinical heart failure, with cognitive function and decline. Furthermore, **chapter 6** investigates whether cardiac troponin T (cTnT), routinely used in the diagnosis of acute myocardial infarction, associates with cognitive function.

Part three includes the translation of results of previous studies into an innovative method, focused on the prevention of cognitive impairment. The online research platform iVitality, that comprises a website, a smartphone-based application and health sensors, was designed to perform large-scale studies in an aging population at risk for cognitive impairment. **Chapter 7** describes the first results of a proof-of-principle study, in which we evaluated the feasibility of home blood pressure monitoring using iVitality.

In **chapter 8** the main conclusions of this thesis are summarized and discussed, and future perspectives are proposed.

## References

1. Prince M, Bryce R, Albanese E, Wimo A, Ribeiro W, Ferri CP. The global prevalence of dementia: a systematic review and metaanalysis. *Alzheimers Dement* 2013;9(1):63-75.
2. Abete P, Della-Morte D, Gargiulo G, Basile C, Langellotto A, Galizia G, Testa G, Canonico V, Bonaduce D, Cacciatore F. Cognitive impairment and cardiovascular diseases in the elderly. A heart-brain continuum hypothesis. *Ageing Res Rev* 2014;18:41-52.
3. Eggermont LH, de BK, Muller M, Jaschke AC, Kamp O, Scherder EJ. Cardiac disease and cognitive impairment: a systematic review. *Heart* 2012;98(18):1334-1340.
4. Gorelick PB, Scuteri A, Black SE, Decarli C, Greenberg SM, Iadecola C, Launer LJ, Laurent S, Lopez OL, Nyenhuis D, Petersen RC, Schneider JA, Tzourio C, Arnett DK, Bennett DA, Chui HC, Higashida RT, Lindquist R, Nilsson PM, Roman GC, Sellke FW, Seshadri S. Vascular contributions to cognitive impairment and dementia: a statement for healthcare professionals from the american heart association/american stroke association. *Stroke* 2011;42(9):2672-2713.
5. Debette S, Seshadri S, Beiser A, Au R, Himali JJ, Palumbo C, Wolf PA, Decarli C. Midlife vascular risk factor exposure accelerates structural brain aging and cognitive decline. *Neurology* 2011;77(5):461-468.
6. Lewington S, Clarke R, Qizilbash N, Peto R, Collins R. Age-specific relevance of usual blood pressure to vascular mortality: a meta-analysis of individual data for one million adults in 61 prospective studies. *Lancet* 2002;360(9349):1903-1913.
7. Qiu C, Winblad B, Fratiglioni L. The age-dependent relation of blood pressure to cognitive function and dementia. *Lancet Neurol* 2005;4(8):487-499.
8. Kennelly SP, Lawlor BA, Kenny RA. Blood pressure and the risk for dementia: a double edged sword. *Ageing Res Rev* 2009;8(2):61-70.
9. den Heijer T, Launer LJ, Prins ND, van Dijk EJ, Vermeer SE, Hofman A, Koudstaal PJ, Breteler MM. Association between blood pressure, white matter lesions, and atrophy of the medial temporal lobe. *Neurology* 2005;64(2):263-267.
10. Korf ES, White LR, Scheltens P, Launer LJ. Midlife blood pressure and the risk of hippocampal atrophy: the Honolulu Asia Aging Study. *Hypertension* 2004;44(1):29-34.
11. Kivipelto M, Helkala EL, Laakso MP, Hanninen T, Hallikainen M, Alhainen K, Soininen H, Tuomilehto J, Nissinen A. Midlife vascular risk factors and Alzheimer's disease in later life: longitudinal, population based study. *BMJ* 2001;322(7300):1447-1451.
12. Launer LJ, Ross GW, Petrovitch H, Masaki K, Foley D, White LR, Havlik RJ. Midlife blood pressure and dementia: the Honolulu-Asia aging study. *Neurobiol Aging* 2000;21(1):49-55.
13. Forette F, Seux ML, Staessen JA, Thijs L, Babarskiene MR, Babeau S, Bossini A, Fagard R, Gil-Extremera B, Laks T, Kobalava Z, Sarti C, Tuomilehto J, Vanhanen H, Webster J, Yodfat Y, Birkenhager WH. The prevention of dementia with antihypertensive treatment: new evidence from the Systolic Hypertension in Europe (Syst-Eur) study. *Arch Intern Med* 2002;162(18):2046-2052.
14. in't Veld BA, Ruitenberg A, Hofman A, Stricker BH, Breteler MM. Antihypertensive drugs and incidence of dementia: the Rotterdam Study. *Neurobiol Aging* 2001;22(3):407-412.
15. Boutitie F, Gueyffier F, Pocock S, Fagard R, Boissel JP. J-shaped relationship between blood pressure and mortality in hypertensive patients: new insights from a meta-analysis of individual-patient data. *Ann Intern Med* 2002;136(6):438-448.
16. Protogerou AD, Safar ME, Iaria P, Safar H, Le DK, Filipovsky J, Henry O, Ducimetiere P, Blacher J. Diastolic blood pressure and mortality in the elderly with cardiovascular disease. *Hypertension* 2007;50(1):172-180.
17. Voko Z, Bots ML, Hofman A, Koudstaal PJ, Wittteman JC, Breteler MM. J-shaped relation between blood pressure and stroke in treated hypertensives. *Hypertension* 1999;34(6):1181-1185.
18. Muller M, Maier AB, Smulders YM. [High blood pressure and mortality in the elderly: what does gait speed tell?]. *Ned Tijdschr Geneesk* 2013;157(7):A5801.

19. Post HG, Smulders YM, Maier AB, Deeg DJ, Muller M. Relation between blood pressure and mortality risk in an older population: role of chronological and biological age. *J Intern Med* 2014.
20. Odden MC, Peralta CA, Haan MN, Covinsky KE. Rethinking the association of high blood pressure with mortality in elderly adults: the impact of frailty. *Arch Intern Med* 2012;172(15):1162-1168.
21. Qiu C, Winblad B, Marengoni A, Klarin I, Fastbom J, Fratiglioni L. Heart failure and risk of dementia and Alzheimer disease: a population-based cohort study. *Arch Intern Med* 2006;166(9):1003-1008.
22. Vogels RL, Scheltens P, Schroeder-Tanka JM, Weinstein HC. Cognitive impairment in heart failure: a systematic review of the literature. *Eur J Heart Fail* 2007;9(5):440-449.
23. Zuccala G, Marzetti E, Cesari M, Lo Monaco MR, Antonica L, Cocchi A, Carbonin P, Bernabei R. Correlates of cognitive impairment among patients with heart failure: results of a multicenter survey. *Am J Med* 2005;118(5):496-502.
24. Zimpfer D, Wieselthaler G, Czerny M, Fakin R, Haider D, Zrunek P, Roethy W, Schima H, Wolner E, Grimm M. Neurocognitive function in patients with ventricular assist devices: a comparison of pulsatile and continuous blood flow devices. *ASAIO J* 2006;52(1):24-27.
25. Gruhn N, Larsen FS, Boesgaard S, Knudsen GM, Mortensen SA, Thomsen G, Aldershvile J. Cerebral blood flow in patients with chronic heart failure before and after heart transplantation. *Stroke* 2001;32(11):2530-2533.



