

Clinical hypertension
From early prediction to prevalence, treatment
adherence and outcome of resistant hypertension

Akademisk avhandling

Som för avläggande av medicine doktorsexamen vid Sahlgrenska akademien, Göteborgs universitet kommer att offentligens försvaras i hörsal Hjärtats aula, Vita Stråket 12, Sahlgrenska universitetssjukhuset/S, Göteborg

Fredagen den 10 februari 2017 klockan 09:00

av

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Fakultetsopponent:

Professor Peter M Nilsson

Enheten för internmedicin/Medicinska fakulteten

Lunds universitet

Lund

Avhandlingen baseras på följande delarbeten:

- I L Holmqvist, L Mortensen, C Kanckos, C Ljungman, K Mehlig, K Manhem. Exercise blood pressure and the risk of future hypertension. *J Hum Hypertens* 2012; 26:691-695.
- II L Holmqvist, K Bengtsson Boström, T Kahan, L Schiöler, J Hasselström, P Hjerpe, B Wettermark, K Manhem. Prevalence of treatment-resistant hypertension and important associated factors - results from the Swedish Primary Care Cardiovascular Database. *J Am Soc Hypertens* 2016; 10(11):838-846.
- III L Holmqvist, K Bengtsson Boström, T Kahan, L Schiöler, J Hasselström, P Hjerpe, B Wettermark, K Manhem. Cardiovascular outcome in treatment resistant hypertension - results from the Swedish Primary Care Cardiovascular Database. *Submitted*
- IV L Holmqvist, K Bengtsson Boström, T Kahan, L Schiöler, M Qvarnström, J Hasselström, P Hjerpe, B Wettermark, K Manhem. Drug adherence in treatment resistant and in controlled hypertension - results from the Swedish Primary Care Cardiovascular Database. *Manuscript*

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Clinical hypertension From early prediction to prevalence, treatment adherence and outcome of resistant hypertension

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Abstract

Aims The four studies in this thesis highlight both undetected hypertension and hypertension in patients receiving extensive blood pressure treatment. The aim of the first study was to investigate whether, and by which blood pressure measurements, one can predict the probability of future hypertension by analyzing the blood pressure response during exercise testing. The second study aimed to investigate the prevalence of treatment resistant hypertension (TRH) i.e. patients who do not reach target blood pressure despite treatment with three or more antihypertensive drugs. The aim was further in the third study to describe cardiovascular outcomes in a TRH population. The fourth study compared the two-year medication adherence to antihypertensive treatment in patients with controlled and uncontrolled hypertension. The overall aim of this thesis was to give rise to increased knowledge regarding hypertension in clinical practice.

Methods In study I, a cohort of patients without known hypertension or cardiovascular disease who performed exercise testing for various reasons during 1996-1997 was investigated. Blood pressure data from the exercise test were used to predict hypertension. Ten years after the exercise test, a questionnaire evaluating development of hypertension was carried out. In study II-IV, data from the Swedish Primary Care Cardiovascular Database (SPCCD) were used. In the SPCCD, data from medical records of hypertensive patients aged ≥ 30 from 48 primary health care centres in two regions in Sweden, collected between 2001 and 2008, are linked to five Swedish population based registers. In study II the prevalence of TRH according to the different prevailing TRH-definitions from the treated hypertensive population was evaluated. Study III analysed the association between TRH and cardiovascular events with adjustment for important confounders in the SPCCD from 2006 and with follow-up in the population based registers until 2012. Patients with known cardiovascular co-morbidity were excluded. Data on antihypertensive drug dispenses were derived from the Prescribed drug registry. In study IV the change in medication adherence, measured by proportion of days covered (PDC), over two years was evaluated for patients with both controlled and uncontrolled hypertension, dispensed three or more antihypertensive drugs. In studies II-IV high medication adherence was defined as $PDC \geq 80\%$.

Results Higher blood pressure before the exercise test and a rapid rise in blood pressure during the test resulted in an increased risk of hypertension ten years post exercise testing. Treatment resistant hypertension is present in 8-17% of hypertensive patients in Swedish primary care. The increased risk of cardiovascular events in this population is mainly associated with an increased risk of heart failure. Antihypertensive medication adherence does not seem to differ between patients achieving target blood pressure and patients with treatment resistant hypertension.

Conclusions Modified blood pressure screening during an exercise test can help identify patients with increased risk of developing hypertension. Treatment resistance to antihypertensive treatment is not a negligible problem, and these patients have an increased risk of heart failure despite adherence to antihypertensive treatment. Awareness of high blood pressure and adherence to antihypertensive treatment must be increased in order to reduce the burden of disease caused by high blood pressure.

ISBN 978-91-629-0041-0 (print)
ISBN 978-91-629-0042-7 (pdf)

<http://hdl.handle.net/2077/49483>