

# Current Research in Hypertension — the Swedish Experience

## Badania dotyczące nadciśnienia tętniczego — doświadczenia szwedzkie

### Streszczenie

Nadciśnienie tętnicze stanowi istotny problem zdrowotny w wielu populacjach, ponieważ zwiększa zagrożenie powikłaniami sercowo-naczyniowymi, i co za tym idzie, koszty opieki medycznej. Nadciśnienie tętnicze bądź izolowane nadciśnienie skurczowe stwierdza się u znacznego odsetka dorosłej populacji zarówno w Polsce, jak i w Szwecji. U wielu chorych nie osiąga się jednak odpowiedniej kontroli ciśnienia tętniczego z powodu niewłaściwej terapii. Niniejsze doniesienie, które stanowi krótki przegląd szwedz-

kich badań nadciśnienia tętniczego, ma się przyczynić do dalszego rozwoju wzajemnych stosunków pomiędzy naszymi krajami, a zwłaszcza pomiędzy obydwooma towarzystwami nadciśnieniowymi. Temat ten jest tym bardziej aktualny, że coraz więcej lekarzy z Polski podejmuje pracę w Szwecji i ma do czynienia z chorymi na nadciśnienie tętnicze.

**słowa kluczowe:** nadciśnienie tętnicze, badania, praktyka kliniczna

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### Introduction

In Sweden, hypertension and its complications represents one of the major public health problems with wide implications for health care. It has been estimated that about 20% of the adult population is diagnosed with essential hypertension ( $\geq 140/90$  mm Hg), showing increasing prevalence rates with increasing age. Many of the patients also suffer from the combined effects of hypertension and metabolic disturbances, e.g. dyslipidaemia and glucose intolerance/type 2 diabetes, as well as end-organ damage such as left ventricular hypertrophy. In a nation-wide survey on the management of high blood pressure in Sweden during the early 1990's, organised by Lars H. Lindholm, it was estimated that about 600 000 hypertensive patients are currently being treated with various anti-hypertensive drugs, and even more patients with lifestyle inter-

ventions alone, or in combination with drug therapy [1]. It has also been shown that the cardio-vascular risk of hypertensives is normally not effectively controlled by common blood pressure treatment, and that many patients do not feel well due to adverse drug reactions, or to the subjectively felt burden of risk factors. Therefore it is necessary to further develop research efforts to improve both the understanding and clinical management of essential hypertension. This is also the goal for the Swedish Hypertension Society, an organisation with currently around 2200 members, both physicians and trained nurses.

### Epidemiology

New data on trends in hypertension reveals that the incidence of malignant hypertension has decreased since the 1960's, as has the mean blood pressure level of the male population in Gothenburg according to one trend analysis [2]. In spite of treatment the proportion of well-controlled hypertensives is not impressive, only 40% of all patients in a national survey (1993), based on data from 128 health centres, had a mean blood pressure below 140/90 mm Hg [3]. It now seems as if this

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proportion has improved somewhat according to a more recent analysis of blood pressure control in Swedish primary health care patients (Project Q-Heart, abstract presented at the ESH meeting 2000).

Defects in cognitive function has been found to be prevalent in many elderly cardiovascular patients, and is often preceded by a blood pressure elevation several years before. In a population-based study in Gothenburg it was shown that increased blood pressure at the age of 70 years predicts dementia, both vascular and of Alzheimer type, after a long-term follow-up [4]. Similar findings have also been presented based on study results in hypertensive men living in Uppsala [5]. This is of substantial public health importance as the treatment of systolic hypertension has now been proved to reduce the risk of dementia [6]. A previous cross-sectional Swedish study, based in primary health care, showed no deterioration of cognitive function in treated hypertensives compared to matched normotensive controls [7].

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### Patophysiology of hypertension

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Some of the many aspects of hypertensive mechanisms have been subject to research based in Sweden. In Gothenburg a long tradition has produced many important papers on the patophysiology of essential hypertension. Starting with outstanding research by the group headed by Björn Folkow [8] current research efforts focus on vascular structure and remodelling. Another group, headed by Mattias Aurell, has focused on renal mechanisms, including studies regarding the role of medullipin in the regulation of blood pressure [9]. There are also a couple of recent important studies investigating for example endothelial function [10], stress reactions in relation to blood pressure regulation in females [11], and defects of the fibrinolytic system [12]. Of special importance are the studies revealing how the genetic polymorphisms of tissue plasminogen activator (tPA) influence fibrinolytic function, carried out by a research group led by Sverker Jern [13]. Another group, headed by Thomas Hedner, has mostly worked with clinical pharmacology, e.g. investigating new substances such as the endothelin (ET-1) antagonists [14].

In Uppsala, studies on the association between hypertension, dyslipidaemia, diabetes and insulin resistance has been ongoing since the early 1970's, organised today by Hans Lithell and his co-workers. They have described in depth the interplay between blood pressure regulation [15, 16], glucose and insulin metabolism [15], as well as blood flow regulation in hypertensive patients [17].

In Stockholm and Malmö research efforts have recently focused on borderline hypertension [18], insulin resistance in therapy-resistant hypertension [19], and metabolic disturbances in young relatives to hypertensive parents [20].

In Northern Sweden, current research based in epidemiology has described the relationship between hypertension, treated or untreated, and fibrinolysis [21].

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### Foetal factors in hypertension

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During the last few years reports from Uppsala, in co-operation with British and Czech researchers, have described the association between low birth weight, post-natal weight increase and adult hypertension [22, 23]. One epidemiological study has focused on blood pressure in young male conscripts in relation to birth weight based on register data [24]. Other studies have described the importance of genetic factors in the interplay between low birth weight and adult blood pressure elevation [25, 26].

In the Hypertension in Pregnancy Offspring Study it was shown that children born after hypertensive pregnancies have higher blood pressure compared to children born after normotensive pregnancies [27], indicating that the blood pressure of pregnant women is an important factor in foetal programming.

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### Clinical management

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During the 1990's Sweden has been the scene of several landmark clinical studies of drug treatment in hypertension, most of them inspired by Lennart Hansson. Among them are the STOP-1 [28] and STOP-2 [29] studies, the CAPPP study [30], and the NORDIL study [31]. The two latter studies have included patients in both Sweden and Finland, and the NORDIL study also patients from Norway. In addition, Swedish patients with hypertension have contributed data to the HOT study [32], as well as to some on-going international, multicenter hypertension treatment studies (e.g. ASCOT, ELSA, LIFE, SCOPE).

Another aspect of clinical management is how to deal with the consultation in a favourable way. This has recently been studied by Karin Kjellgren in a thesis which included an evaluation of video-taped consultations, asking questions about the quality and mutual understanding in the patient-doctor relationship [33].

That an ambitious blood pressure reduction is associated with an improved, not worse, quality of life has been described by Ingela Wiklund in a substudy of HOT [34]. This is important as some critics have

suggested that such treatment could not easily be tolerated. It should however also be kept in mind that the tolerance of blood pressure reductions could well be age-related, as it was recently reported in the STOP-2 study that a total of 25% of elderly hypertensive patients experienced dizziness [29], not a life-threatening symptom but nevertheless sometimes a nuisance to orthostatic elderly subjects.

A multiple-riskfactor approach in the treatment of hypertensive patients has been developed in Gothenburg by Björn Fagerberg et al. and proved very successful to reduce risk factors and to prevent cardiovascular events [35]. The conclusion to be made is that blood pressure control in itself is important, but this must be combined with smoking cessation and an improved lifestyle, as well as drug treatment of diabetes and hyperlipidaemia in many patients.

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### **Quality control in clinical practice**

If the quality of care should increase for common hypertensive patients, not only for the well-cared patients of big clinical studies, it takes new initiatives. Therefore it has been hoped for that the introduction of computer-based support for clinical decision-making in hypertension care should improve the situation. This has been developed by some Swedish researchers [36], but the results are so far not based on a large number of patients from several health centres, thus precluding firm conclusions to be drawn, however the process is continuing.

It is also very important to work for a shared care model in the treatment of hypertensive patients in order to optimise the quality of care. One way to do this is to enhance co-operation and educational efforts based on studies of clinical practice, both in primary health care (PHC) and at the hospital level, as carried out by Mats Ribacke [37].

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### **The National Diabetes Register of Sweden**

This is an ongoing nation-wide registration of diabetes patients since 1995 with annual data collection and reports, useful as indicators of the quality of risk factor management. The National Diabetes Register is organised by the Swedish Association for Diabetology. The register reports both hospital and PHC data, the latter including a total of 6072 men and 5653 women with diabetes (1996), 77% of whom with debut after age 60 years which implies type 2 diabetes in most subjects. In all, 4699 hypertensive diabetics were registered the first year. It was shown that only 21% of

the patients were well controlled with a blood pressure equal or below 140/85 mm Hg, leaving the majority of patients with a less favourable and potentially deleterious blood pressure control. This deserves clinical action in view of the great advantage of a strict blood pressure control [32], which is also cost-effective according to findings in the UKPDS [38].

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### **Hypertension research based in general practice**

Research on hypertension in Swedish primary health care (PHC), published in international journals, has been ongoing since more than 15 years. The first reports dealt with the evaluation of screening programmes for hypertension [39], or the remaining high cardiovascular risk in spite of treatment [40]. Other studies have reported on hypertensive patients' satisfaction in PHC [41], health economic aspects of treatment of hypertension [42, 43], or PHC practice evaluation [37, 44, 45]. The most recent studies have focused on patients' knowledge of hypertension [46], and perceived symptoms of hypertensive patient in routine clinical practice [47]. Taken together, these studies have substantially increased the knowledge of hypertension management in the PHC of Sweden. General practitioner have also taken a very active part in many of the large-scale, multi-centre, randomised hypertension studies of Scandinavia reported in international medical journals during the 1990's [28–31]. The impressive results of these studies have provoked a debate on treatment recommendations (e.g. first-line drugs) and intervention goals that is still on-going.

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### **Conclusions**

Hypertension research in Sweden is ongoing and active in many scientific areas. Ever since the late Bertil Hood started drug treatment of malignant hypertension in the early 1950's [48], it has been an ambition to improve the standards of clinical care for the hypertensive patients. Such an ambition must however be based on a more developed understanding of the pathophysiology behind perturbances in blood pressure regulation. In the near future new findings in cardiovascular genetics, including the genetics of hypertension, may hopefully expand our knowledge to improve the proper targeting of risk patients and to tailor antihypertensive treatment to the needs of the individual [49, 50]. The continuing research in hypertension is truly an ongoing story, in Sweden as well as in the other Nordic countries.

## Summary

Clinical hypertension is a matter of great concern in many populations due to the high risk of cardiovascular disease and increasing health care costs. Both in Poland and Sweden a large proportion of the adult population has now been diagnosed with combined hypertension or isolated systolic hypertension. Not all patients are however effectively treated and thus do not have a satisfactory blood pressure control. In order to further develop the bilateral contacts between our two countries and hypertension societies this short review of Swedish research in hypertension has been written. It is also timely to write about this topic as more and more Polish physicians are coming to work in Sweden for clinical work and will get in contact with hypertensive patients and their treatment.

**key words: hypertension, research, clinical practice, Sweden**  
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## References

1. Treatment of mild hypertension. The Swedish National Agency for the Evaluation of Medical Technologies. *J. Internal Med.* 1995 (supl.).
2. Ribacke M., Tibblin G., Rosengren A., Eriksson H.: Is hypertension changing? Blood pressure development in cohorts of 50-year-old men between 1963 and 1993. *Blood Pressure* 1996, 5, 134–138.
3. Nilsson P., Andersson P.E., Schwan Å., Östlund B., Malmberg R., Lithell H. et al.: Cardiovascular risk factors in treated hypertensives — a nation-wide, cross-sectional study in Sweden. *J. Internal Med.* 1993, 233, 239–245.
4. Skoog I., Lernfelt B., Landahl S., Palmertz B., Andersson L.A., Nilsson L. et al.: 15-year longitudinal study of blood pressure and dementia. *Lancet* 1996, 347, 1141–1145.
5. Kilander L., Nyman H., Boberg M., Hansson L., Lithell H.: Hypertension is related to cognitive impairment: a 20-year follow-up of 999 men. *Hypertension* 1998, 31, 780–786.
6. Staessen J.A., Fagard R., Thijs L. et al.: Randomised double-blind comparison of placebo and active treatment for older patients with isolated systolic hypertension. *Lancet* 1997, 350, 757–764 (correction: *Lancet* 1997, 350, 1636).
7. Nilsson P., Gullberg G., Ekesho R., von Schenck H., Gustafson L.: No impaired cognitive function in treated patients with mild-moderate hypertension, compared to matched normotensive controls. *Blood Pressure* 1998, 7, 209–213.
8. Folkow B.: Structure and function of the arteries in hypertension. *Am. Heart J.* 1987, 114, 938–948.
9. Bergström G., Göthberg G., Karlström G., Rudenstam J.: Renal medullary blood flow and renal medullary antihypertensive mechanisms. *Clin. Exp. Hypertens.* 1998, 20, 1–26.
10. Feng Q., Hedner T.: Endothelium-derived relaxing factor (EDRF) and nitric oxide (NO). II. Physiology, pharmacology and pathophysiological implications. *Clin. Physiol.* 1990, 10, 503–526.
11. Manhem K., Jern C., Pihall M., Hansson L., Jern S.: Cardiovascular responses to stress in young hypertensive women. *J. Hypertens.* 1992, 10, 861–867.
12. Jern S., Wall U., Bergbrant A., Selin-Sjögren L., Jern C.: Endothelium-dependent vasodilation and tissue-type plasminogen activator release in borderline hypertension. *Arterioscler. Thromb. Vasc. Biol.* 1997, 17, 3376–3383.
13. Jern C., Ladenvall P., Wall U., Jern S.: Gene polymorphism of t-PA is associated with forearm vascular release rate of t-PA. *Arterioscler. Thromb. Vasc. Biol.* 1999, 19, 454–459.
14. Sun X.Y., Hedner T., Feng Q., Edvinsson L.: Inhibition of endothelin (ET-1) induced pressor responses by the endothelin (ETA) receptor antagonist FR39317 in the pithed rat. *Blood Pressure* 1992, 1, 108–112.
15. Pollare T., Lithell H., Berne C.: Insulin resistance is a characteristic feature of primary hypertension independent of obesity. *Metabolism* 1990, 39, 167–174.
16. Nilsson P., Lind L., Andersson P.E., Hänni A., Berne C., Baron J., Lithell H.: On the use of ambulatory blood pressure recordings and insulin sensitivity in support of the insulin-hypertension hypothesis. *J. Hypertens.* 1994, 12, 965–969.
17. Lind L., Andersson P.E., Fugmann A., Hänni A., Reneland R., Linde T., Lithell H.: The haemodynamic response to hyperinsulinaemia in hypertensive subjects. *J. Hum. Hypertens.* 1999, 13, 41–45.
18. Lemne C.E.: Increased blood pressure reactivity in children of borderline hypertensive fathers. *J. Hypertens.* 1998, 16, 1243–1248.
19. Isaksson H., Cederholm T., Jansson E., Nygren A., Östergren J.: Therapy-resistant hypertension associated with central obesity, insulin resistance, and large muscle fibre area. *Blood Pressure* 1993, 2, 46–52.
20. Hulthén U.L., Endre T., Mattiasson I., Berglund G.: Insulin and forearm vasodilation in hypertension-prone men. *Hypertension* 1995, 25, 214–218.
21. Eliasson M., Nilsson P., Jansson J.H.: Increased levels of tissue plasminogen activator antigen in essential hypertension — A population-based study in Sweden. *J. Hypertens.* 1997, 15, 349–356.
22. Leon D.A., Kuopilöva I., Lithell H.O., Berglund L., Mohsen R., Vågerö D. et al.: Failure to realise growth potential in utero and adult obesity in relation to blood pressure in 50 year old Swedish men. *BMJ* 1996, 312, 401–406.
23. Kuopilöva I., Leon D.A., McKeigue P.M., Lithell H.O.: Is the effect of low birth weight on cardiovascular mortality mediated through high blood pressure? *J. Hypertens.* 1999, 17, 19–26.
24. Nilsson P., Söderström M., Ericson A., Östergren P.O., Allebeck P.: Low birth weight is associated with elevated systolic blood pressure in adolescence: a prospective study of a birth cohort of 149 378 Swedish boys. *J. Hypertens.* 1997, 15, 1627–1631.
25. Nilsson P.: Increased weight and blood pressure in adolescent male offspring to mothers with pre-pregnancy diabetes — a genetic link? *J. Hum. Hypertens.* 2000, 13, 793–795.
26. Melander O., Mattiasson I., Marsal K., Groop L., Hulthén U.L.: Heredity for hypertension induces intra-uterine growth and the relation between fetal growth and adult blood pressure. *J. Hypertens.* 1999, 17, 1557–1561.
27. Himmelmann A., Svensson A., Hansson L.: Relation of maternal blood pressure during pregnancy to birth weight and blood pressure in children. The Hypertension in Pregnancy Offspring Study. *J. Internal Med.* 1994, 235, 347–352.
28. Dahlöf B. et al.: Morbidity and mortality in the Swedish Trial in Old Patients with hypertension (STOP-Hypertension). *Lancet* 1991, 338, 1281–1285.
29. Hansson L. et al.: A randomized trial of old and new anti-hypertensive drugs in elderly patients: cardiovascular mortality and morbidity in the Swedish Trial in Old Patients with hypertension-2. *Lancet* 1999, 354, 1751–1756.

30. Hansson L., Lindholm L.H., Niskanen L., Lanke J., Hedner T., Niklason A. et al.: Effect of angiotensin-converting-enzyme inhibition compared with conventional therapy on cardiovascular morbidity and mortality in hypertension: the Captopril Prevention Project (CAPPP). *Lancet* 1999, 353, 611–616.
31. Hansson L.H., Hedner T., Lund-Johansen P., Kjeldsen S.E., Lindholm L.H., Syvertsen J.O. et al.: Randomised trial of effect of calcium antagonists compared with diuretics and b-blockers on cardiovascular morbidity and mortality in hypertension: the Nordic Diltiazem (NORDIL) Study. *Lancet* 2000, 356, 359–365.
32. Hansson L., Zanchetti A., Carruthers S.G. et al.: Effects of intensive blood-pressure lowering and low-dose aspirin in patients with hypertension: principal results of the Hypertension Optimal Treatment (HOT) randomised trial. *Lancet* 1998, 351, 1755–1762.
33. Kjellgren K.I., Svensson S., Ahlner J., Sälsjö R.: Antihypertensive medication in clinical encounters. *Int. J. Cardiol.* 1998, 64, 161–169.
34. Wiklund I., Halling K., Ryden-Bergsten T., Fletcher A.: Does lowering the blood pressure improve the mood? Quality-of-life results from the Hypertension Optimal Treatment (HOT) study. *Blood Pressure* 1997, 6, 357–364.
35. Fagerberg B., Wikstrand J., Berglund G., Samuelsson O., Agewall S.: Mortality rates in treated hypertensive men with additional risk factors are high but can be reduced: a randomized intervention study. *Am. J. Hypertens.* 1998, 11 (1 Pt 1), 14–22.
36. Linnarsson R.: Medical audit based on computer-stored patient records exemplified with an audit of hypertension care. *Scand. J. Prim. Health Care* 1993, 11, 74–80.
37. Ribacke M.: Treatment preferences, return to visit planning and factors affecting hypertension practice amongst general practitioners and internal medicine specialists. *J. Intern. Med.* 1995, 237, 473–478.
38. UK Prospective Diabetes Study Group. Cost effectiveness analysis of improved blood pressure control in hypertensive patients with type 2 diabetes: UKPDS 40. *BMJ* 1998, 317, 720–726.
39. Råstam L., Eckerlund I., Rydén L.: Hypertension case-finding in primary health care. Experience from the Skaraborg Hypertension Study. *Scand. J. Prim. Health Care* 1987, 5, 9–12.
40. Lindholm L., Ejlertsson G., Scherstén B.: High risk of cerebro-vascular morbidity in well treated male hypertensives. A retrospective study of 40–59-year-old hypertensives in Swedish primary health care. *Acta. Med. Scand.* 1984, 216, 251–259.
41. Carlberg A., Tibblin G.: Patient satisfaction in primary health care. A comparative study of two modes of treatment in hypertension. *Fam. Pract.* 1992, 9, 304–310.
42. Johannesson M., Borgqvist L., Jönsson B.: The cost of treating hypertension in Sweden. An empirical investigation in primary health care. *Scand. J. Prim. Health Care* 1991, 9, 155–160.
43. Nilsson P., Kandell-Collén A., Lindholm L.H., Scherstén B.: Care of hypertensives in Dalby: organisation and health economic aspects. *J. Hum. Hypertens.* 1993, 7, 551–554.
44. Ribacke M.: The concept of individualized hypertension care in general practice and outpatients clinics. The general practitioner hypertension practice study (III). *Scand. J. Prim. Health Care* 1995, 13, 112–117.
45. Troein M., Gardell B., Selander S., Råstam L.: Guidelines and reported practice for the treatment of hypertension and hypercholesterolaemia. *J. Intern. Med.* 1997, 242, 173–178.
46. Kjellgren K.I., Svensson S., Ahlner J., Saljo R.: Hypertensive patients' knowledge of high blood pressure. *Scand. J. Prim. Health Care* 1997, 15, 188–192.
47. Kjellgren K.I., Ahlner J., Dahlöf B., Gill H., Hedner T., Saljo R.: Perceived symptoms amongst hypertensive patients in routine clinical practice — a population-based study. *J. Intern. Med.* 1998, 244, 325–332.
48. Hood B., Björk S.: The diagnosis essential hypertension. *Acta. Med. Scand.* 1967, 181, 63–70.
49. Pratt R.E., Dzau V.: Genomics and hypertension: concepts, potentials, and opportunities. *Hypertension* 1999, 33, 238–247.
50. Sanders R.: Mining the Swedish clinical archives to develop pharmacogenomic test. *Mol. Diagn.* 1999, 4, 319–325.

