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Skaraborg hypertension and diabetes project

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Aim: To examine the prevalence and characteristics of uncontrolled hypertension (HT).
Methods: A cross-sectional community-based study (1992–93) was carried out in Skara, Sweden, including 894 patients who consecutively underwent an annual follow-up at the hypertension outpatient clinic in primary care. Controlled HT was defined as diastolic blood pressure (DBP) $\leq$90 mmHg and systolic blood pressure (SBP) $\leq$160 mmHg and was used as reference. Uncontrolled DBP was defined as DBP >90 mmHg regardless of SBP level, and isolated uncontrolled SBP was defined as SBP >160 mmHg and DBP $\leq$90 mmHg. Proportions were age-standardized using the Skara population as reference.
Results: The prevalence of uncontrolled HT was 43% (isolated uncontrolled SBP 18% and uncontrolled DBP 25%). Both men and women with isolated uncontrolled SBP were older (73 years, CI: 70–75; and 73 years; CI: 72–75) than patients with controlled HT (64 years, CI: 63–66; and 65 years, CI: 64–66). Men and women with known cardiovascular disease (CVD) less often had isolated uncontrolled SBP (OR: 0.4, CI: 0.2–0.9; and OR: 0.5, CI: 0.3–0.9), whereas men and women with known diabetes more often had uncontrolled DBP (OR: 2.3, CI: 1.3–4.1; and OR: 3.3, CI: 1.9–5.7). Men with known CVD less often had uncontrolled DBP (OR: 0.5, CI: 0.3–1.0, $p = 0.04$), and men with fasting blood glucose >5.5 mmol/l more often had isolated uncontrolled SBP (OR: 1.9, CI: 1.0–3.5, $p = 0.04$). In women, the following high risk factor levels were associated with uncontrolled DBP: fasting blood glucose >5.5 mmol/l (OR: 1.4, CI: 1.1–1.8), fasting triglycerides $\geq$1.7 mmol/l (OR: 1.4, CI: 1.1–1.8), body mass index (BMI) >30 kg/m^2 (OR: 1.5, CI: 1.1–1.9), waist/hip ratio (WHR) >0.85 cm/cm (OR: 1.7, CI: 1.3–2.2), insulin resistance (homeostasis model assessment (HOMA) >third quartile) (OR: 1.4, CI: 1.1–1.9) and microalbuminuria (OR: 3.2, CI: 1.7–6.2).
Conclusion: Uncontrolled DBP is in both sexes related to type 2 diabetes, whereas isolated uncontrolled SBP is related to older age. In women, uncontrolled DBP, furthermore, is related to several other CVD risk factors of the metabolic syndrome. Patients with uncontrolled DBP should be carefully evaluated for metabolic disorders.

Keywords: cardiovascular disease risk factors, primary care, type 2 diabetes, uncontrolled hypertension
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Introduction

Hypertension (HT) is an important risk factor for cardiovascular morbidity and mortality [1]. Although pharmacological treatment of HT has been shown to reduce the risk of stroke [2,3], hypertensive-treated individuals are still at a considerable risk of cardiovascular disease (CVD) and the risk increases with the blood pressure level [4,5].

In spite of existing guidelines and recommendations, goals for blood pressure treatment are often not fulfilled

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[6,7]. Also, cardiovascular risk factors are known to cluster [8] and the effects of several risk factors coexisting in one individual are not only additive but also synergistic [9,10]. It is, therefore, important to know the risk factor profile of hypertensive patients, especially those that have not fulfilled treatment goals. In order to find more specific treatments, it is important to understand the underlying causes of blood pressure not being controlled.

The aim of this study was to describe the prevalence of uncontrolled HT and to examine the characteristics of the subgroups of patients with uncontrolled HT, using patients with controlled HT as reference.

Subjects and Methods

Skaraborg Hypertension Project

The Skaraborg hypertension project was launched in 1977 in the county of Skaraborg, Sweden, aiming to improve the control of HT in the population. Special outpatient clinics with educated nurses were established in the primary care settings including the community of Skara. The limits for diagnosis of HT in patients aged 40–60 years were >170/>105 mmHg and above 60 years >180/>110 mmHg.

During the following years, the hypertension outpatient clinic in Skara was preserved, and in 1986, it was combined with the diabetes outpatient clinic into one joint clinic. The criteria for diagnosis of HT followed the principles of the Skaraborg hypertension project until 1987, when routines were changed. According to the new national guidelines, definition of HT was based only on diastolic blood pressure (DBP) ≥90 mmHg [10]. In Skara, DBP ≤90 mmHg has been used as target goal in accordance with clinical praxis at the health care centre. In 1993 again, new national guidelines for diagnosis and treatment of HT in patients ≥70 years were authorized [11]. Limits for diagnosis were either DBP ≥90 mmHg or systolic blood pressure (SBP) ≥160 mmHg. Through all years, HT was defined as ongoing treatment, or in new cases, by the contemporary limits for diagnosis, which exceeded at three consecutive blood pressure readings. From 1977 through 1981, all patients visiting the health care centre in Skara were screened for HT. This procedure created a routine of frequent blood pressure measurements in patients visiting the centre during the following years. Diabetes was defined according to World Health Organization (WHO) criteria [12].

Skaraborg Hypertension and Diabetes Project

From June 1992 through September 1993, all patients who participated in an annual control at the hypertension and diabetes outpatient clinic in Skara were surveyed for cardiovascular risk factors [13]. Medical history included registration of acute myocardial infarction, angina pectoris, heart failure, acute stroke, intermittent claudication and diabetes mellitus. Fasting laboratory tests included blood glucose, serum cholesterol, low-density lipoprotein-cholesterol, high-density lipoprotein (HDL) cholesterol, serum triglycerides and serum insulin. Morning urine was tested for microalbuminuria using Micral® test [14].

Supine (5 min rest) systolic and diastolic (phase V) right brachial arterial pressures were recorded to the nearest 2 mmHg using Tricuff® for automatic adjustment of cuff size to arm circumference [15], and the heart rate was registered simultaneously. Height (to the nearest cm) and weight (to the nearest 0.1 kg) were also recorded as were the waist and hip circumferences (both to the nearest cm). Body mass index (BMI) was calculated by the formula weight (kg)/length^2 (m^2) and waist/hip ratio (WHR) by dividing the waist circumference (cm) by the hip circumference (cm). A questionnaire inquiring about smoking habits, alcohol consumption and leisure time physical activity was completed.

Informed consent was obtained from all participants. The study protocol was approved by the ethics committee of the Medical Faculty, Göteborg University.

Study Population

Skara is a small city in a rural area in the southwest of Sweden with a total of 18 700 inhabitants. As only one health care centre and no hospital has been available in the community, practically all residents with HT have a registered medical record at the health care centre. All men and women with known HT but without diagnosis of type 1 diabetes, who were ≥40 years of age and who participated in the SKHYDIP study, were included in this study.

According to previous routines in the Skaraborg hypertension project, the study population was categorized in two age groups: age <70 years and age ≥70 years. Age distribution was also illustrated using 10-year increments from 40 through 79 years of age, while all patients ≥80 years were gathered in one category.

Methods

In accordance with contemporary guidelines for HT in Skaraborg county, controlled HT was defined as DBP ≤90 mmHg and SBP ≤160 mmHg. Uncontrolled HT was defined as DBP >90 mmHg or SBP >160 mmHg and was divided into two categories: (1) uncontrolled DBP defined as DBP >90 mmHg regardless of SBP level

and (2) isolated uncontrolled SBP defined as SBP >160 mmHg and DBP ≤90 mmHg.

Previous CVD was defined as a history of previous events of hospitalization for stroke or myocardial infarction or doctor's diagnosis of angina pectoris. Microalbuminuria was considered to be present, if Micral test showed that albumin concentration was at least 20 mg/l. Insulin resistance was calculated by the homeostasis model assessment (HOMA) using fasting glucose and fasting insulin levels (insulin resistance = fasting insulin (μU/ml) × fasting glucose (mmol/l) × 22.5^{-1}) [16].

In the questionnaire, the participants were asked when they at the latest, drank beer, wine or liquor. If alcohol consumption was admitted during the last 30 days, the participants were also asked specific questions about the quantity of consumed beer, wine and liquor and the number of days with consumption. The average daily alcohol consumption was calculated by the adjusted quantity-frequency method [17]. High consumers were defined as men consuming 20 g alcohol or more daily and women consuming 15 g or more [17]. Moderate alcohol consumption was defined as half of these amounts daily (10 g for men and 7.5 g for women). The four options on physical activity were: (1) mostly reading or watching television in leisure hours; (2) soft physical activity, like walking or bicycling, at least 4 h per week; (3) moderate physical exercise, like running, swimming, playing tennis or equivalent activity, at least 2 h per week; and (4) regular hard exercise. Sedentary lifestyle comprised the first two alternatives. Intensive blood pressure treatment was defined as treatment with three or more antihypertensive drugs.

Continuous variables were dichotomized into a low-risk and a high-risk category, using limits from WHO guidelines 1998 and 1999 [18,19] or, when more appropriate, the third quartile. An increased risk was assumed according to the WHO guidelines 1998 for: fasting blood glucose >5.5 mmol/l, HDL cholesterol <0.9 mmol/l in men and <1.0 mmol/l in women, fasting serum triglycerides ≥1.7 mmol/l, BMI >30 kg/m^2, WHR >0.9 in men and >0.85 in women, according to the WHO guidelines 1999 for: serum cholesterol >6.5 mmol/l, and according to the third quartile for insulin resistance >3.2 (HOMA index). The categorical variables, previous CVD, known diabetes, microalbuminuria, current smoking, moderate alcohol consumption and sedentary lifestyle were dichotomized as yes or no.

Statistical Analyses

Characteristics of subjects with uncontrolled DBP and subjects with isolated uncontrolled SBP were investigated using subjects with controlled HT as reference. SPSS Base System for Macintosh 10.0 was used for data analyses. Continuous variables were presented as age-adjusted means with 95% confidence intervals (CI). Differences in means between groups were examined by analysis of covariance. Proportions were age-standardized in 10-year intervals using the whole Skara population as standard, and proportions for CVD risk factors were presented with 95% CI. Associations between categorical data were analysed using logistic regression and were expressed as odds ratios (ORs) with 95% CI. All comparisons between groups were adjusted for differences in age and, when appropriate, for differences in gender. Insulin-treated diabetic subjects (25 patients) were excluded from the analyses of insulin resistance (HOMA). Log transformation was used to induce normality in the analyses of serum triglycerides and insulin resistance (HOMA). All tests were two-sided, and statistical significance was assumed at $p < 0.05$.

Results

Altogether, 894 patients (377 men and 517 women) were included in the study. The age-standardized prevalence of uncontrolled HT was 43%, of isolated uncontrolled SBP 18% and of uncontrolled DBP 25% (table 1). DBP ≤90 mmHg was achieved by 68% of male patients and by 82% of the female patients. Patients with isolated uncontrolled SBP were more often female (OR: 1.4, CI: 1.0–2.0, $p = 0.03$), whereas patients with uncontrolled DBP were more often male (OR: 2.1, CI: 1.5–2.8). Controlled HT was more common in ages below 70 years than in older patients (OR: 2.3, CI: 1.8–3.0). Isolated uncontrolled SBP was more common in ages ≥70 years than in younger patients (OR: 3.9, CI: 2.8–5.4). There were no differences in the intensity of the treatment between the different categories of blood pressure control. Compared with patients with controlled HT, the OR for patients treated with three or more antihypertensive drugs was 0.8 (CI: 0.6–1.2) for having isolated uncontrolled SBP, and correspondingly, the OR was 1.2 (CI: 0.8–1.7) for having uncontrolled DBP. Patients with known CVD did not have more intensive treatment than patients without known CVD. Compared with patients with known CVD, the OR for patients treated with three or more antihypertensive agents having unknown CVD were 0.9 (CI: 0.5–1.9).

The sex distributions of controlled HT, isolated uncontrolled SBP and uncontrolled DBP are shown in figure 1, which illustrates the increasing prevalence of isolated uncontrolled SBP with increasing age as well as the female preponderance of isolated uncontrolled SBP.

Evaluation of digit preference showed that 39% of all SBP measurements and 29% of all DBP measurements were ending in zero. When limits for controlled HT were

Table 1 Age-standardized prevalences of categories of blood pressure control by age and sex in patients aged 40 years and above

Categories of blood pressure control	Men [n (%)]*	Women [n (%)]†	All [n (%)]‡
All ages			
Controlled HT	186 (54)	278 (60)	464 (57)
Isolated uncontrolled SBP	81 (14)	154 (22)	235 (18)
Uncontrolled DBP	110 (32)	85 (18)	195 (25)
All	377 (100)	517 (100)	894 (100)
Below 70			
Controlled HT	119 (59)	174 (70)	293 (65)
Isolated uncontrolled SBP	23 (7)	46 (10)	69 (9)
Uncontrolled DBP	68 (34)	47 (20)	115 (27)
All	210 (100)	267 (100)	477 (100)
70 and above			
Controlled HT	67 (39)	104 (39)	171 (39)
Isolated uncontrolled SBP	58 (35)	108 (45)	166 (41)
Uncontrolled DBP	42 (26)	38 (16)	80 (20)
All	167 (100)	250 (100)	417 (100)

Data are numbers (n) and percentages. Prevalences were age-standardized using Skara population as standard. HT, hypertension; SBP, systolic blood pressure; DBP, diastolic blood pressure. Controlled HT = DBP $\leq$90 mmHg and SBP $\leq$160 mmHg. Isolated uncontrolled SBP = SBP >160 mmHg and DBP $\leq$ 90 mmHg. Uncontrolled DBP = DBP >90 mmHg regardless of SBP level.

*n = 377.

†n = 517.

‡n = 894.

set at <160/90 mmHg instead of $\leq$160/90 mmHg, the age-standardized prevalance of controlled HT decreased from 57 to 42% ($p < 0.001$).

Gender-specific age-adjusted means and 95% CI on continuous CVD risk factors are summarized in table 2. Men and women with isolated uncontrolled SBP were older than both men and women with controlled HT and men and women with uncontrolled DBP.

Age-standardized proportions of categorical CVD risk factors are summarized in table 3. Compared with controlled HT, significant differences of previous CVD (lower), known diabetes (higher), current smoking

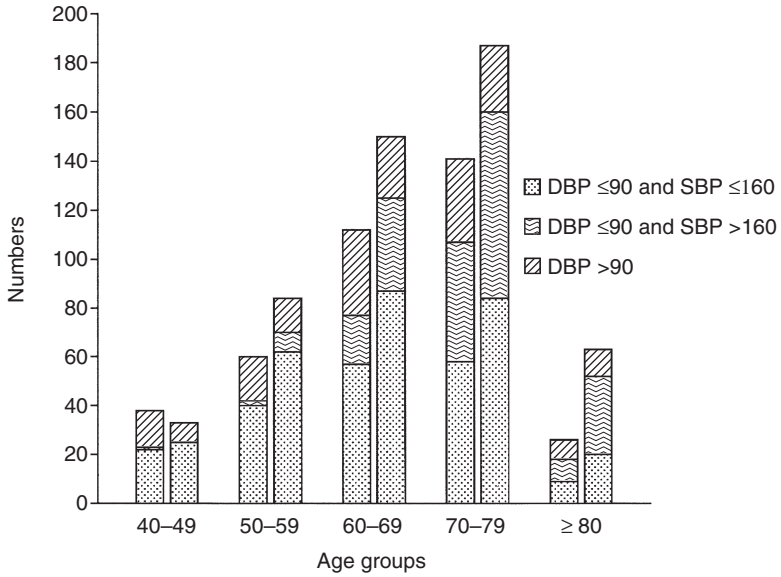

Fig. 1 Numbers of men and women with controlled hypertension, isolated uncontrolled systolic blood pressure (SBP) and uncontrolled diastolic blood pressure (DBP). Left bars, men; right bars, women.

Table 2 Cardiovascular disease risk factor levels in different categories of blood pressure control in men and women

	Controlled HT [m (CI)]*	Isolated uncontrolled SBP [m (CI)]†	Uncontrolled DBP [m (CI)]‡
Men			
Age (years)	64 (63–66)	73 (70–75)	65 (63–67)
Systolic blood pressure (mmHg)	144 (143–146)	173 (170–176)	167 (165–169)
Diastolic blood pressure (mmHg)	84 (83–84)	85 (83–86)	96 (95–97)
Fasting blood glucose (mmol/l)	5.9 (5.7–6.2)	6.4 (6.0–6.8)	6.4 (6.1–6.7)
Insulin resistance (HOMA index)	1.9 (1.7–2.1)	1.8 (1.5–2.2)	2.1 (1.8–2.4)
Total cholesterol (mmol/l)	5.8 (5.6–6.0)	5.9 (5.6–6.1)	5.9 (5.7–6.1)
HDL cholesterol (mmol/l)	1.0 (0.9–1.0)	1.0 (1.0–1.1)	1.0 (1.0–1.0)
Fasting triglycerides (mmol/l)	1.5 (1.4–1.6)	1.5 (1.3–1.7)	1.6 (1.5–1.8)
Body mass index (kg/m^2)	27.6 (27.0–28.1)	27.8 (26.9–28.7)	28.5 (27.7–29.2)
Waist/hip ratio	0.95 (0.95–0.96)	0.96 (0.95–0.98)	0.96 (0.95–0.97)
Women			
Age (years)	65 (64–66)	73 (72–75)	67 (65–69)
Systolic blood pressure (mmHg)	146 (145–148)	172 (170–174)	171 (168–173)
Diastolic blood pressure (mmHg)	80 (79–81)	83 (81–84)	96 (94–97)
Fasting blood glucose (mmol/l)	5.8 (5.6–6.0)	5.8 (5.6–6.1)	6.2 (5.9–6.6)
Insulin resistance (HOMA index)	1.9 (1.7–2.1)	1.8 (1.6–2.1)	2.2 (1.9–2.6)
Total cholesterol (mmol/l)	6.3 (6.1–6.5)	6.3 (6.1–6.5)	6.5 (6.2–6.7)
HDL cholesterol (mmol/l)	1.1 (1.1–1.2)	1.2 (1.1–1.2)	1.1 (1.1–1.2)
Fasting triglycerides (mmol/l)	1.4 (1.3–1.5)	1.4 (1.3–1.6)	1.5 (1.4–1.7)
Body mass index (kg/m^2)	28.1 (27.5–28.7)	28.1 (27.3–29.0)	29.8 (28.8–30.9)
Waist/hip ratio	0.84 (0.84–0.85)	0.84 (0.83–0.85)	0.88 (0.86–0.89)

Data are means (m) and 95% confidence intervals (CI) adjusted for differences in age by analysis of covariance. Geometric means were used in analyses of serum insulin resistance and triglycerides. Insulin-treated patients (11 men and 14 women) were excluded from the analyses of insulin resistance. DBP, diastolic blood pressure; HDL, high-density lipoprotein; HOMA, homeostasis model assessment (insulin resistance = fasting insulin (μU/ml) × fasting glucose (mmol/l) × 22.5^{-1}); HT, hypertension; n, number of patients; SBP, systolic blood pressure. Controlled HT = DBP ≤90 mmHg and SBP ≤160 mmHg. Isolated uncontrolled SBP = SBP >160 mmHg and DBP ≤90 mmHg. Uncontrolled DBP = DBP >90 mmHg regardless of SBP level.

*n = 186 (men); n = 278 (women).

†n = 81 (men); n = 154 (women).

‡n = 110 (men); n = 85 (women).

(lower) and moderate alcohol consumption (lower) were found in the isolated uncontrolled SBP category in men, and of known diabetes (higher) in the uncontrolled DBP category in women.

Alcohol consumption during the last 30 days was admitted by 349 patients (39%, 207 men and 142 women). The average weekly consumption in these 349 patients was 41 g of alcohol. No drinking during the latest year was declared by 308 patients (35%, 81 men and 227 women). High alcohol consumption was found in 20 patients (6%, 18 men and 2 women) and moderate consumption in 56 patients (6%, 48 men and 8 women). High alcohol consumption was not associated with uncontrolled blood pressure.

Both men and women with previously known CVD less often had isolated uncontrolled SBP than patients with controlled HT (table 4). Men with known diabetes more often had uncontrolled DBP, and men with known CVD less often had uncontrolled DBP. Men with fasting blood glucose >5.5 mmol/l and men with a sedentary lifestyle more often had isolated uncontrolled SBP. In women, fasting blood glucose >5.5 mmol/l, insulin resistance >3.2 (HOMA index), fasting triglycerides ≥1.7 mmol/l, BMI >30 kg/m^2, WHR >0.85 cm/cm, known diabetes and microalbuminuria were associated with uncontrolled DBP.

Previously known CVD was in 14% based on diagnosis of stroke without known coronary heart disease, whereas 86% of patients with CVD had either angina pectoris or previously known myocardial infarction, with or without previous stroke.

Discussion

Accounting for both uncontrolled DBP and isolated uncontrolled SBP, the prevalence of uncontrolled HT was high. Uncontrolled DBP was in both sexes related to type 2 diabetes, and in women, furthermore, related to several other

Table 3 Age-standardized prevalences of dichotomized cardiovascular disease risk factors and lifestyles in men and women

	Controlled HT [n (%) (95% CI)]*	Isolated uncontrolled SBP [n (%) (95% CI)]†	Uncontrolled DBP [n (%) (95% CI)]‡
Men			
Previous CVD	48 (20) (14.4–25.8)	16 (8) (4.1–11.6)	18(11) (5.9–15.9)
Known diabetes	36 (17) (11.5–22.1)	27 (47) (41.7–52.3)	39 (27) (19.3–35.2)
Microalbuminuria	45 (23) (15.7–29.2)	26 (26) (8.7–44.0)	29 (21) (14.2–28.2)
Current smoking	32 (20) (12.6–26.9)	7 (2) (0.0–4.4)	15 (16) (7.6–23.7)
Moderate alcohol consumption	28 (20) (12.8–27.4)	4 (2) (0.0–4.4)	16 (22) (13.2–30.9)
Sedentary lifestyle	35 (25) (11.7–32.8)	16 (33) (28.6–37.1)	19 (19) (10.2–28.0)
Women			
Previous CVD	62 (18) (13.9–21.9)	30 (15) (7.5–21.8)	13 (14) (5.5–21.8)
Known diabetes	39 (14) (8.9–19.0)	33 (14) (7.8–19.8)	30 (33) (23.0–43.4)
Microalbuminuria	29 (14) (7.8–19.2)	30 (14) (7.6–20.7)	21 (28) (15.4–39.8)
Current smoking	33 (16) (10.5–21.9)	9 (6) (0.9–11.7)	11 (17) (7.0–27.6)
Moderate alcohol consumption	3 (2) (0.0–4.7)	2 (1) (0.0–2.5)	3 (4) (0.0–8.7)
Sedentary lifestyle	16 (8) (3.3–12.0)	6 (4) (0.0–9.2)	3 (4) (0.0–8.0)

Data are numbers (n) and percentages with 95% confidence intervals (CI). Prevalences were age-standardized using the Skara population as standard. CVD, cardiovascular disease; DBP, diastolic blood pressure; HT, hypertension; SBP, systolic blood pressure. Controlled HT = DBP ≤90 mmHg and SBP ≤160 mmHg. Isolated uncontrolled SBP = SBP >160 mmHg and DBP ≤90 mmHg. Uncontrolled DBP = DBP >90 mmHg, regardless of SBP level. Microalbuminuria = at least 20 mg/l in first morning urine. Current smoking = daily smoking. Moderate alcohol consumption = on average at least 10 g alcohol daily for men and at least 7.5 g alcohol daily for women. Sedentary lifestyle = less than 2 h of moderate exercise per week, like running, swimming, playing tennis or equivalent activity. Missing cases: Microalbuminuria (48 men and 74 women), current smoking (11 men and 24 women), moderate alcohol consumption (22 men and 55 women) and sedentary lifestyle (8 men and 21 women).

*n = 186 (men); n = 278 (women).

†n = 81 (men); n = 154 (women).

‡n = 110 (men); n = 85 (women).

CVD risk factors of the metabolic syndrome. Isolated uncontrolled SBP was in both sexes related to older age.

At the time this study was conducted, national guidelines for HT only recommended the level of DBP and not SBP, to be used as basis for definition and as target goal for treatment [10]. Considering national guidelines and local target goals, the treatment results thus become more acceptable and also better than in several similar contemporary studies. In a Swedish cross-sectional study (1993), from 128 health care centres, only 52% of the males and 61% of the females had DBP ≤90 mmHg [20], and in 1997, a Norwegian study of 2468 hypertensive patients, 59% of the males and 62% of the females had DBP ≤90 mmHg [21] compared with 68% of the males and 82% of the women in the present study.

In 1990, a study revealed that the rule of halves was still valid in Scotland [6]. A 1998 British study of elderly people showed a somewhat better control than expected from the rule of halves [22]. In this study, 54% of hypertensive-treated patients had blood pressure ≤160/90 mmHg. However, changing the target goal to <160/90 mmHg reduced the percentage of controlled HT to 37%, as a marked digit preference was found, with 86% of all systolic pressures and 77% of all diastolic pressures ending in zero. The relatively better treatment results and the lesser digit preference of the present study might be credited to the highly structured care in Skara using local guidelines and specially trained nurses [13].

Poor patient compliance together with physician's neglect of high blood pressure levels might be important reasons for uncontrolled HT. The present study is limited in not having evaluated these problems. Other reasons for uncontrolled HT, which are not analysed in this study, are increased mental stress, obstructive sleep apnea, different salt sensitivity, chronic pain and the use of anti-inflammatory drugs.

A consistent finding in women was the association between risk factors of the metabolic syndrome including type 2 diabetes and uncontrolled DBP. A strong association between metabolic syndrome risk factors and uncontrolled DBP in women is consistent with earlier results in this project [13]. A plausible explanation of this phenomenon is that male patients with several risk factors died earlier than women, as male gender is a strongly additive risk factor and as this study was cross-sectional. Another explanation might be that women in this study population, more often than men, were treated with older types of antihypertensive drugs suggested to

Table 4 Associations between high cardiovascular disease risk factor levels and categories of blood pressure control

	Controlled HT (OR)*	Isolated uncontrolled SBP [(OR) (95% CI)]†	Uncontrolled DBP [(OR) (95% CI)]‡
Men			
Fasting glucose >5.5 (mmol/l)	1.0	1.9 (1.03–3.54)	1.2 (0.95–1.56)
Insulin resistance >3.2 (HOMA)	1.0	1.2 (0.62–2.39)	1.1 (0.84–1.49)
Serum cholesterol >6.5 (mmol/l)	1.0	1.2 (0.63–2.38)	1.2 (0.89–1.54)
HDL cholesterol <0.9/1.0 (mmol/l)	1.0	0.7 (0.39–1.28)	0.9 (0.69–1.15)
Fasting triglycerides ≥1.7 (mmol/l)	1.0	1.5 (0.81–2.62)	1.1 (0.88–1.44)
BMI >30 (kg/m^2)	1.0	1.5 (0.77–3.07)	1.2 (0.93–1.61)
WHR >0.90/0.85	1.0	1.0 (0.51–2.04)	1.0 (0.74–1.35)
Previous CVD	1.0	0.4 (0.22–0.90)	0.5 (0.29–0.98)
Known diabetes	1.0	1.5 (0.80–2.86)	2.3 (1.34–4.09)
Microalbuminuria	1.0	1.3 (0.67–2.36)	1.2 (0.66–2.05)
Current smoking	1.0	0.6 (0.25–1.59)	0.9 (0.63–1.24)
Moderate alcohol consumption	1.0	0.6 (0.17–1.77)	1.1 (0.53–2.12)
Sedentary lifestyle	1.0	2.3 (1.07–5.09)	1.0 (0.71–1.33)
Women			
Fasting glucose >5.5 (mmol/l)	1.0	1.1 (0.71–1.72)	1.4 (1.08–1.79)
Insulin resistance >3.2 (HOMA)	1.0	1.0 (0.56–1.66)	1.4 (1.07–1.89)
Serum cholesterol >6.5 (mmol/l)	1.0	1.1 (0.72–1.70)	1.0 (0.77–1.28)
HDL cholesterol <0.9/1.0 (mmol/l)	1.0	0.8 (0.50–1.30)	1.2 (0.91–1.53)
Fasting triglycerides ≥1.7 (mmol/l)	1.0	1.3 (0.82–2.02)	1.4 (1.10–1.84)
BMI >30 (kg/m^2)	1.0	1.2 (0.71–1.88)	1.5 (1.14–1.91)
WHR >0.90/0.85	1.0	0.9 (0.49–1.50)	1.7 (1.27–2.22)
Previous CVD	1.0	0.5 (0.32–0.93)	0.5 (0.27–1.05)
Known diabetes	1.0	1.4 (0.80–2.39)	3.3 (1.85–5.72)
Microalbuminuria	1.0	1.4 (0.67–2.59)	3.2 (1.68–6.22)
Current smoking	1.0	1.0 (0.40–2.24)	1.1 (0.76–1.64)
Moderate alcohol consumption	1.0	1.2 (0.16–8.99)	3.7 (0.72–18.78)
Sedentary lifestyle	1.0	1.2 (0.41–3.58)	0.8 (0.42–1.50)

Associations between high levels of cardiovascular disease (CVD) risk factors and categories of uncontrolled blood pressure were analysed by logistic regression with age as covariable and expressed as odds ratios (OR) and 95% confidence intervals (CI), using patients with controlled hypertension (HT) as reference. Geometric means were used in analyses of insulin resistance and triglycerides. BMI, body mass index; DBP, diastolic blood pressure; HDL, high-density lipoprotein; HOMA, homeostasis model assessment (insulin resistance = fasting insulin (μU/ml) × fasting glucose (mmol/l) × 22.5^{-1}); n, numbers of patients; SBP, systolic blood pressure; WHR, waist/hip ratio. Controlled HT = DBP ≤90 mmHg and SBP ≤160 mmHg. Isolated uncontrolled SBP = SBP >160 mmHg and DBP ≤90 mmHg. Uncontrolled DBP = DBP >90 mmHg regardless of SBP level.

*n = 186 (men); n = 278 (women).

†n = 81 (men); n = 154 (women).

‡n = 110 (men); n = 85 (women).

have more metabolic side effects [23]. The preponderance of male prevalence of uncontrolled DBP might be explained by hormonal factors, as the level of androgen hormones has been shown to be related to higher blood pressures both in animal and human studies [24,25].

Insulin resistance is one probable mechanism for uncontrolled DBP and might explain the reduced efficacy of some antihypertensive drugs, which do not improve but rather reduce insulin sensitivity [26]. Several mechanisms have been discussed to explain the association between insulin resistance and HT [27]. As hyperinsulinaemia has been shown to be associated with proliferation of smooth muscle cells [28], a likely mechanism may be that insulin has a trophic effect on smooth muscle cells in the walls of the resistance vessels and thereby promotes HT. In the present study, specific mechanisms cannot be evaluated. However, it is important to identify the patients with uncontrolled DBP, as they are likely to have several other cardiovascular risk factors and, therefore, constitute a category at high risk.

Patients with isolated uncontrolled SBP were older and more often female. Women with isolated uncontrolled SBP did not have significant metabolic disorders. Data from the Framingham heart study suggest that high SBP in elderly people is caused by increasing stiffness of large arteries [29], which could either be due to less

elastin and more collagen fibers in the arterial wall, proliferation of smooth muscle cells or to increased atherosclerosis [30]. The preponderance of female patients amongst those with isolated uncontrolled SBP is consistent with other studies, showing that age-related stiffness of large arteries is more pronounced in women than in men [31].

Differences in lifestyle were found to be associated with isolated uncontrolled SBP, only in men. All of the demonstrated differences, less smoking, less alcohol consumption and less physical activity may be explained by the older age of this patient category.

A history of known CVD was consistently associated with controlled HT. As the definition of CVD was mainly based on coronary heart disease, a plausible explanation of these observations might be that ischemic heart disease induces myocardial dysfunction causing lower blood pressure [32]. High blood pressure is a well known risk factor for development of coronary heart disease [1], but once developed, it seems that coronary artery disease is associated with lower blood pressure, as demonstrated in the present study. Low blood pressure in patients with CVD was not explained by a more intensive treatment.

Based on these observations, different forms of uncontrolled HT can be clinically identified with a different pattern in the two genders. In men, the metabolic profiles of isolated uncontrolled SBP and of uncontrolled DBP are similar. In women, uncontrolled DBP is related to components of the metabolic syndrome. These patients have multiple risk factors and are thus a group at high risk. As the risk factors act with synergistic effect [9], all metabolic and clinical disturbances in these patients should be identified and evaluated. Treatment of these patients should also focus on means to reduce insulin resistance. Isolated uncontrolled SBP in women is related to high age and not to metabolic disturbances. Treatment of these patients should emphasize on reduction of SBP. More research should focus on the management of uncontrolled HT and on the means to reduce insulin resistance in these patients.

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