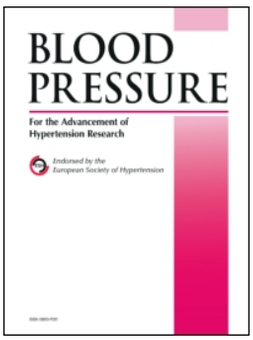

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Systemic vascular resistance predicts the development of hypertension: the cardiovascular risk in young Finns study

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ABSTRACT

Purpose: To study whether systemic hemodynamics, especially systemic vascular resistance, predicts the development of hypertension and improves the risk prediction of incident hypertension beyond common risk factors in the risk models in young adults.

Materials and methods: Typical risk factors for hypertension in the risk prediction models (systolic and diastolic blood pressure, parental history of hypertension, age, sex, body-mass index, smoking), laboratory values (high-density lipoprotein cholesterol, low-density lipoprotein cholesterol, triglycerides, glucose, insulin, C-reactive protein), heart rate (HR), stroke index (SI), and systemic vascular resistance index (SVRI) calculated by whole-body impedance cardiography were evaluated in 2007 and blood pressure in 2011 in 1293 Finnish adults (aged 30–45 years; females 56%; $n = 1058$ normotensive in 2007).

Results: Of hemodynamic variables, SVRI and HR evaluated in 2007 were independently associated with systolic blood pressure ($p < 0.001$ and $p = 0.047$, respectively) and SVRI with diastolic blood pressure measured in 2011 ($p = 0.014$), and SVRI and HR were independent predictors of incident hypertension ($p < 0.001$ and $p = 0.024$, respectively). SVRI was the most significant predictor of incident hypertension independently of other risk factors (odds ratio 2.73 per 1 standard deviation increase, 95% confidence interval 1.93–3.94, $p < 0.001$). The extended prediction model (including SVRI) improved the incident hypertension risk prediction beyond other risk factors, with an area under the receiver operating characteristic curve of 0.846 versus 0.817 ($p = 0.042$) and a continuous net reclassification improvement of 0.734 ($p < 0.001$).

Conclusions: These findings suggest that systemic vascular resistance index predicts the incidence of hypertension in young adults and that the evaluation of systemic hemodynamics could provide an additional tool for hypertension risk prediction.

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Introduction

Blood pressure is mainly determined by cardiac output and systemic vascular resistance. Typically, high systemic vascular resistance and sometimes high cardiac output cause primary hypertension [1–3], and increased systemic vascular resistance is known to elevate both systolic and diastolic pressure [4]. In spite of the central role of high systemic vascular resistance in the pathophysiology of hypertension, only a few studies have investigated the value of systemic hemodynamics in the prediction of hypertension. Systemic vascular resistance or cardiac output

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did not predict the future risk of hypertension in a 30-year follow-up study in a small sample of 73 young men [5]. When hemodynamic parameters were estimated using M-mode echocardiographic measurements, cardiac index and total peripheral resistance were not significant predictors of incident hypertension after adjustment for age and baseline blood pressure in the four-year follow-up of 1118 men and 1559 women [6].

Risk models to predict hypertension, such as the Framingham hypertension risk prediction model, usually include age, sex, body-mass index (BMI), systolic and diastolic blood pressure, cigarette smoking and parental history of hypertension [7,8]. Some risk models also include ethnicity or such laboratory values as glucose, C-reactive protein (CRP), lipoproteins or hypertriglyceridaemia, but not hemodynamic values, with the exception of blood pressure and sometimes heart rate (HR) [7]. To the best of our knowledge, the possible incremental value of the measurement of systemic hemodynamics for the prediction of hypertension is limited. Therefore, the objective of the present study was to evaluate whether systemic hemodynamics, especially systemic vascular resistance, predicts the development of hypertension in young adults and improves the risk prediction of incident hypertension beyond risk factors included in risk prediction models, such as age, sex, systolic and diastolic blood pressure, HR, parental history of hypertension, BMI, smoking, high-density lipoprotein (HDL) cholesterol, low-density lipoprotein (LDL) cholesterol, triglycerides, CRP, glucose and insulin.

Methods

Study population

The Cardiovascular Risk in Young Finns Study is a large, ongoing, multicenter, longitudinal, population-based study of cardiovascular risk factors in Finland. The first cross-sectional study was conducted in 1980 with 3596 participants aged 3–18 years. Several follow-up studies with extensive cardiovascular risk factor recordings have been performed since. In 2007, 1872 men and women underwent systemic hemodynamic measurements, and 1501 of them had blood pressure data available in 2011. After excluding subjects with incomplete risk factor data in 2007 or missing information regarding parental history of hypertension (collected in 2001), a total of 1293 men and women were included in the present analysis. A subpopulation of 1058 comprised those subjects who were normotensive in 2007. The association between systemic hemodynamic variables and risk factors for hypertension evaluated in 2007 and blood pressure measured in 2011 was studied in both populations. The association between systemic hemodynamics and risk factors for hypertension evaluated in 2007 and incident hypertension in 2011 was examined in the subpopulation of participants who were normotensive in 2007 ($n = 1058$). The study design and protocol have been described in detail previously [9]. The study was approved by local ethics committees, and informed consent was obtained from all participants.

Clinical measurements and questionnaires

Standard methods were used to determine blood pressure, fasting serum glucose, insulin, HDL cholesterol, LDL cholesterol, triglycerides and CRP [10–12]. Hypertension was defined as systolic blood pressure $\geq$ 140 mmHg or diastolic blood pressure $\geq$ 90 mmHg [13], self-reported use of antihypertensive medication, or a self-reported hypertension diagnosis. Parental history of hypertension and smoking habits were examined with a questionnaire. The subjects who had one or two parents with a history of hypertension were regarded as having a parental history of hypertension. The subjects who smoked daily were regarded as smokers. BMI (kg/m^2) was calculated by dividing the weight in kilograms by the square of the height in metres.

Systemic hemodynamics

Participants were instructed to avoid heavy exercise and alcohol on the previous evening and smoking, caffeine-containing products and heavy meals on the investigation day. A trained research nurse carried out the measurements in a quiet and temperature-controlled room. Participants lay in the supine position for at least 15 min before the measurement, during which period electrodes for whole-body impedance cardiography were placed on the body surface. A whole-body impedance cardiography (ICG_{WB}) device (CircMon B202, JR Medical Ltd, Tallinn, Estonia) was used to determine beat-to-beat HR, stroke index (SI; stroke volume/body surface area, ml/m^2), cardiac index (CI; cardiac output/body surface area, l/min/m^2) and systemic vascular resistance index (SVRI; systemic vascular resistance/body surface area, dyn·s/cm^5/m^2). Briefly, CircMon records the continuous changes in body electrical impedance during a cardiac cycle. The stroke volume and cardiac output values measured with CircMon are in agreement with

the values measured by the thermodilution method and 3-dimensional echocardiography [14–16]. The repeatability of cardiac output measurements by the impedance method has been reported to be even better than by the thermodilution method [14]. A more detailed description of the method has been previously reported [14,15].

Statistics

The data were analysed with R Statistics version 3.2.4 (R Development Core Team, Vienna, Austria). Of cardiac function-related hemodynamic variables, HR and SI performed substantially better than CI (=HR × SI) in the prediction of future blood pressure and hypertension and were therefore included in the models instead of CI. Linear regression was performed to study the association of hemodynamic variables (SI, SVRI) and hypertension risk factors included in the hypertension prediction models (systolic and diastolic blood pressure, HR, age, sex, parental history of hypertension, BMI, smoking, HDL cholesterol, LDL cholesterol, triglycerides, glucose, insulin and CRP) measured in 2007 with blood pressure measured in 2011. Logistic regression analysis was used to study the association of the above-mentioned systemic hemodynamic variables and hypertension risk factors measured in 2007 with hypertension in 2011. Because of skewed distributions, CRP, insulin, and triglycerides were log-transformed. All continuous predictor variables besides age were standardised to make the predictor variable effect sizes comparable to each other. Therefore, the regression coefficients (β) in the linear regression models and the odds ratio (OR) in the logistic regression model indicate the effect of a 1-standard-deviation (SD) change in a predictor variable on a given dependent variable. The effects of sex-by-age-by-BMI and SVRI-by-SI-by-HR interactions on hypertension in 2011 were tested using the stepwise Akaike information criterion. There were no statistically significant interactions between either group of above-mentioned variables and hypertension in 2011. Before the analyses, regression models were assessed for excess multicolinearity by stepwise Akaike's information criterion (AIC) and variance inflation factor (VIF) selection. All variables left in the model after stepwise AIC and having a VIF lower than 3 were included in the model simultaneously. After these steps, SI was excluded from models where dependent variable was systolic blood pressure or hypertension in year 2011 (140/90 mmHg cut-off), and HR was excluded from models where dependent variable was diastolic blood pressure or hypertension in year 2011 (130/80 and 120/80 mmHg cut-offs).

To study whether hemodynamic variables independently predicting incident hypertension improved the hypertension risk prediction, the area under the receiver operating characteristic curve (AUC) and continuous net reclassification improvement (NRI) [17, 18] were calculated. The first model included the above-mentioned hypertension risk factors, whereas the second model included hypertension risk factors, and SVRI. The potential additional value of SVRI was also assessed by the risk assessment plot [19]. All analyses were repeated with more stringent blood pressure cut-offs to define hypertension (systolic blood pressure $\geq$ 130 mmHg or diastolic blood pressure $\geq$ 80 mmHg; systolic blood pressure $\geq$ 120 mmHg or diastolic blood pressure $\geq$ 80 mmHg). A p-value of $<$ 0.05 was considered statistically significant.

Results

The baseline characteristics of the study populations are presented in Table 1. Some 44% of the whole study population and 42% of the normotensive subpopulation had a parental history of hypertension. 7.7% ($n = 81$) of normotensive subjects in 2007 had incident hypertension in 2011. Of hemodynamic variables, SVRI and HR evaluated in 2007 were independently associated with systolic blood pressure in both populations and SVRI with diastolic blood pressure measured in 2011 in whole population (Table 2). An increase of 1 SD in SVRI was associated with a 1.68–1.81 mmHg increase in systolic blood pressure in both populations (both $p < 0.001$) and a 0.77 mmHg increase in diastolic blood pressure measured in 2011 in whole population ($p = 0.014$) (Table 2). An increase of 1 SD in HR was associated with a 0.71–1.10 mmHg increase in systolic blood pressure ($p < 0.05$) (Table 2). Between 2007 and 2011, 53 participants in the whole population and 20 participants in the subpopulation initiated blood pressure-lowering medication. When initiation of blood pressure-lowering medication was included in the linear regression analysis as a dichotomous variable, in the whole population, initiation of medication was independently associated with systolic (5.34 mmHg decrease, $p < 0.001$) and diastolic blood pressure (3.14 mmHg decrease, $p = 0.013$) measured in 2011. Otherwise, the findings remained similar (data not shown). In the normotensive subpopulation, initiation of medication

Table 1. Baseline (2007) characteristics of study subjects.

Variable	Whole population ($n = 1293$)	Normotensive subpopulation ($n = 1058$)	Incident hypertension in 2011 ($n = 81$)
Female (% female)	56%	59%	40%
Age (y)	37.9 ± 5.0	37.4 ± 5.0	39.5 ± 4.4
Systolic blood pressure (mmHg)	120 ± 14	116 ± 11	124 ± 10
Diastolic blood pressure (mmHg)	75 ± 11	72 ± 9	79 ± 7
Heart rate (beats/min)	65.0 (58.0–71.0)	64.0 (58.0–70.0)	63.0 (58.0–70.0)
LDL cholesterol (mmol/L)	3.1 ± 0.8	3.0 ± 0.8	3.2 ± 0.7
HDL cholesterol (mmol/L)	1.3 ± 0.3	1.3 ± 0.3	1.2 ± 0.2
Triglycerides (mmol/L)	1.0 (0.8–1.6)	1.0 (0.8–1.5)	1.3 (0.9–2.0)
Body mass index (kg/m^2)	25.8 ± 4.6	25.3 ± 4.2	27.5 ± 4.9
C-reactive protein (mg/L)	0.8 (0.4–1.7)	0.8 (0.4–1.6)	1.1 (0.5–2.2)
Insulin (mU/L)	6.8 (4.2–10.3)	6.3 (4.0–9.8)	7.9 (5.5–16.2)
Glucose (mmol/L)	5.3 ± 0.7	5.2 ± 0.5	5.5 ± 0.6
Hypertension (% of subjects)	18%	0%	0%
Smoking (% of subjects)	17%	18%	26%
Family history of hypertension (% of subjects)	44%	42%	58%
SVRI (dyn·s/cm^5/m^2)	2591 (2297–2942)	2537 (2246–2870)	2972 (2484–3323)
SI (ml/m^2)	42.7 (39.0–46.7)	43.0 (39.3–46.7)	41.3 (37.3–44.7)
Cardiac Index (L/min/m^2)	2.78 (2.47–3.11)	2.77 (2.46–3.09)	2.54 (2.32–2.98)

Values are presented as mean ± standard deviation or geometric mean (25th–75th percentile) or percentage of subjects. SVRI: systemic vascular resistance index. SI: stroke index.

Table 2. Associations of risk factors measured in 2007 with blood pressure measured in 2011.

Variables measured in 2007	β ± SE	*p* value	Variables measured in 2007	β ± SE	*p* value
Systolic blood pressure measured in 2011					
Whole population ($n = 1293$)			Subpopulation ($n = 1058$)		
Systolic blood pressure	7.93 ± 0.46	<0.001	Systolic blood pressure	5.61 ± 0.41	<0.001
Sex	2.80 ± 0.71	<0.001	Sex	3.94 ± 0.75	<0.001
SVRI	1.68 ± 0.37	<0.001	SVRI	1.81 ± 0.38	<0.001
Parental history of hypertension	1.38 ± 0.58	0.017	Parental history of hypertension	1.62 ± 0.60	0.007
Diastolic blood pressure	−1.24 ± 0.45	0.006	BMI	1.11 ± 0.38	0.004
BMI	1.04 ± 0.38	0.007	Heart rate	1.10 ± 0.37	0.003
Insulin	0.77 ± 0.38	0.043	Diastolic blood pressure	−0.72 ± 0.40	0.074
Heart rate	0.71 ± 0.38	0.047	Insulin	0.69 ± 0.39	0.075
Age	0.34 ± 0.06	<0.001	Age	0.32 ± 006	<0.001
Diastolic blood pressure measured in 2011					
Whole population ($n = 1293$)			Subpopulation ($n = 1058$)		
Diastolic blood pressure	3.66 ± 0.35	<0.001	Sex	3.10 ± 0.62	<0.001
Sex	2.90 ± 0.58	<0.001	Diastolic blood pressure	2.69 ± 0.31	<0.001
Systolic blood pressure	1.19 ± 0.35	<0.001	Parental history of hypertension	1.27 ± 0.47	0.008
Parental history of hypertension	1.17 ± 0.45	0.009	BMI	1.11 ± 0.30	<0.001
BMI	0.90 ± 0.30	0.002	SVRI	0.56 ± 0.32	0.083
SVRI	0.77 ± 0.31	0.014	Triglycerides	0.52 ± 0.29	0.071
Triglycerides	0.64 ± 0.28	0.023	CRP	0.48 ± 0.26	0.068
Glucose	−0.46 ± 0.26	0.07	HDL cholesterol	0.46 ± 0.27	0.095
Age	0.22 ± 0.05	<0.001	Age	0.23 ± 0.05	<0.001

Multivariable models included sex, age, parental history of hypertension, HDL cholesterol, LDL cholesterol, triglycerides, glucose, insulin, body mass index (BMI), smoking, C-reactive protein, heart rate (HR), systolic and diastolic blood pressure and systemic vascular resistance index (SVRI) measured in 2007. Variables with a statistically significant or borderline significant ($p < 0.1$) association with blood pressure are reported. All continuous predictive variables, except age, were standardised before regression analysis. Regression coefficient β indicates the change in systolic or diastolic blood pressure measured in 2011 when a variable measured in 2007 changed by 1 standard deviation (SD). For sex (female/male) and smoking (nonsmoker/smoker), β indicates the change in systolic or diastolic blood pressure measured in 2011 when the category changed in 2007. SE: standard error. Subpopulation: subjects normotensive in 2007.

was independently associated with systolic blood pressure (4.67 mmHg decrease, $p < 0.039$), while he association between the initiation of antihypertensive medication and diastolic blood pressure was not statistically significant.

SVRI measured in 2007 was the most significant predictor of incident hypertension in 2011 in multivariable logistic regression analysis (OR 2.73 [95% CI, 1.93–3.94, $p < 0.001$]) (Table 3). When more stringent blood pressure cut-offs were used to define hypertension (systolic blood pressure ≥ 130 mmHg or diastolic blood pressure ≥ 80 mmHg), SVRI measured in 2007 was the second strongest predictor of incident hypertension in 2011 (OR 1.43 [95% CI, 1.07–1.93, $p = 0.018$]) (Table S1). Additionally, with the tightest blood pressure cut-offs (systolic blood pressure ≥

120 mmHg or diastolic blood pressure ≥ 80 mmHg), SVRI measured in 2007 was the strongest predictor of incident hypertension in 2011 (OR 1.69 [95% CI, 1.27–2.28, $p < 0.001$]) (Table S2). HR measured in 2007 was the fifth strongest independent predictor of incident hypertension in 2011 (OR 1.58, [95% CI, 1.17–2.14, $p = 0.003$]) (Table 3).

Two models were compared for their ability to classify participants into the normotensive and incident hypertensive categories in 2011 (Table 4). The first model included sex, age, parental history of hypertension, BMI, smoking, HDL cholesterol, LDL cholesterol, triglycerides, glucose, insulin, CRP, systolic and diastolic blood pressure and HR measured in 2007. The second model additionally included SVRI. The second model had a higher AUC (0.846) than the first model (0.817, $p = 0.042$). The continuous NRI for the second model was 0.734 ($p < 0.001$) (Table 4). The risk assessment plot supported the additional value of SVRI in the incident hypertension risk assessment (Figure 1).

When more stringent blood pressure cut-offs were used to define hypertension (systolic blood pressure ≥ 130 mmHg or diastolic blood pressure ≥ 80 mmHg) (Table S3), the continuous NRI for the second model was 0.374 ($p < 0.001$), and the AUC difference was 0.750 vs 0.764, respectively, ($p = 0.188$). With the tightest blood pressure cut-offs to define hypertension (systolic blood pressure ≥ 120 mmHg or diastolic blood pressure ≥ 80 mmHg) (Table S4), the continuous NRI for the second model was 0.237 ($p = 0.015$), and the AUC difference was 0.715 vs 0.726, respectively, ($p = 0.191$).

Table 3. Relationship between variables measured in 2007 and hypertension in 2011.

	Hypertension in 2011	
Variable measured in 2007	OR (95% CI)	*p* value
SVRI	2.73 (1.93–3.94)	<0.001
Smoking	2.16 (1.16–3.93)	0.013
Sex	1.91 (1.03–3.57)	0.003
Parental history of hypertension	1.66 (1.00–2.78)	0.057
Heart rate	1.58 (1.17–2.14)	0.024
Diastolic blood pressure	1.53 (1.06–2.25)	0.004
Systolic blood pressure	1.42 (0.99–2.04)	0.055
Age	1.09 (1.03–1.15)	0.004

OR: odds ratio per 1 SD increase in predictor variable, except for sex (female/male) and smoking (nonsmoker/smoker) per change in category. CI: confidence interval. The multivariable model included sex, age, parental history of hypertension, HDL cholesterol, LDL cholesterol, triglycerides, glucose, insulin, body mass index, smoking, C-reactive protein, heart rate (HR), systolic and diastolic blood pressure, and systemic vascular resistance index (SVRI) measured in 2007. Variables with a statistically significant or borderline-significant ($p < 0.1$) association with hypertension are reported. Analyses performed on 1058 subjects who were normotensive in 2007. Hypertension was defined as systolic blood pressure ≥ 140 mmHg or diastolic blood pressure ≥ 90 mmHg, self-reported use of antihypertensive medication, or self-reported hypertension diagnosis.

Discussion

The present study examining the development of hypertension among young adults showed that systemic hemodynamic variables, especially SVRI, independently predicted the development of hypertension. SVRI also improved the hypertension risk prediction beyond risk factors typically included in the risk models to predict hypertension.

Even though vascular resistance is a major determinant of blood pressure and elevated vascular resistance is a typical pathophysiological mechanism behind hypertension [1], only a few studies have evaluated the value of systemic hemodynamics in the prediction of hypertension. Vascular resistance did not predict the future risk of hypertension in a 30-year follow-up study in 73 young men [5]. When hemodynamic parameters were estimated using M-mode echocardiographic measurements, cardiac index or total peripheral resistance were not significant predictors of incident hypertension after adjustment for age and baseline blood pressure in a four-year follow-up of 1118 men and 1559 women [6]. The present study showed that SVRI was directly and independently associated with blood pressure progression and incident hypertension among young adults, thus extending the current knowledge regarding the value of systemic hemodynamics in the prediction of future hypertension.

Risk models to predict hypertension, such as the Framingham hypertension risk prediction model, typically include age, sex, BMI, systolic and diastolic blood pressure, cigarette smoking and parental history of hypertension [8,9]. Many risk models also include ethnicity or laboratory values, such as glucose, CRP,

Table 4. Comparison of models for the prediction of incident hypertension.

Model	AUC	95% CI	*p* value	NRI events	P value	NRI non-events	*p* value	NRI total	*p* value
Reference model	0.817	0.773–0.862	…	…	…	…	…	…	…
Reference model + SVRI	0.846	0.802–0.890	0.042	0.383	<0.001	0.351	<0.001	0.734	<0.001

SVRI: systemic vascular resistance index. AUC: area under the receiver operating characteristic curve. CI: confidence interval. NRI: continuous net reclassification improvement. Event: incident hypertension. Reference model: age, sex, parental history of hypertension, smoking, systolic and diastolic blood pressure, body mass index, LDL cholesterol, HDL cholesterol, triglycerides, glucose, insulin, heart rate and C-reactive protein measured in 2007. Hypertension was defined as systolic blood pressure ≥ 140 mmHg or diastolic blood pressure ≥ 90 mmHg, self-reported use of antihypertensive medication, or self-reported hypertension diagnosis.

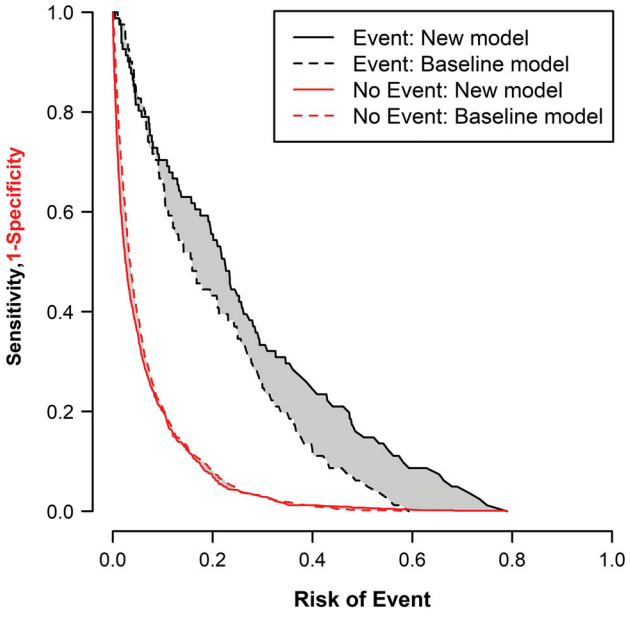

Figure 1. Additional value of systemic vascular resistance index (SVRI) compared to the baseline (reference) model for the prediction of incident hypertension. Risk assessment plot for baseline (reference) model (dashed lines) and the new model including SVRI (solid lines). Event curves (black lines) represent sensitivity versus calculated risk. No-event curves (red lines) represent 1-specificity versus calculated risk. Baseline (reference) model: age, sex, parental history of hypertension, smoking, systolic and diastolic blood pressure, body mass index, LDL cholesterol, HDL cholesterol, triglycerides, glucose, insulin, heart rate, and C-reactive protein. New model: baseline (reference) model + SVRI.

lipoprotein values or hypertriglyceridaemia, but not hemodynamic values, with the exception of blood pressure and in some models HR [8]. These risk models have displayed acceptable to good discrimination [8]. In the present study, the inclusion of SVRI in the prediction model improved the performance of the baseline model, including the above-mentioned typical parameters of hypertension risk prediction models. The reclassification of participants into the categories of normotensive and incident hypertensive subjects was also improved by adding SVRI into the model, with a continuous NRI as high as 0.734 in addition to traditional hypertension risk factors, which is a good improvement in reclassification [20].

Interestingly, the continuous NRI was higher for the highest blood pressure cut-offs that were used to define hypertension (systolic blood pressure $\geq$ 140 mmHg or diastolic blood pressure $\geq$ 90 mmHg) when compared to more stringent cut-offs (systolic blood pressure $\geq$ 130/120 mmHg or diastolic blood pressure $\geq$ 80 mmHg). Thus, SVRI appears to perform especially well when predicting the most clinically important patient group to be detected (i.e. those with the highest blood pressure in the follow-up). Nevertheless, significant continuous NRI was also observed for more stringent cut-offs, although the AUC difference between models was not significant. These findings highlight the importance of high peripheral resistance in the pathophysiology of incident hypertension. Therefore, our findings suggest that the evaluation of systemic hemodynamics could provide a valuable tool for future hypertension risk assessment in clinical practice.

HR was the fifth highest predictor of incident hypertension with highest blood pressure cut-off. This finding is in agreement with previous reports showing that higher HR predicts risk of developing hypertension [21,22]. Interestingly, HR was weaker predictor of incident hypertension than SVRI in the current study. Altogether, these findings provide further support for the incremental predictive value of SVRI when comparing hemodynamic variables. Of note, smoking was the second highest predictor of incident hypertension with the highest blood pressure cut-off, a finding which is supported with previous studies showing that smoking predicted incident hypertension and exercise blood pressure [23,24].

The number and the tonus of the arterioles are the main determinants of vascular resistance [25]. Vascular resistance is chiefly determined by the microcirculation, since they present the greatest resistance to blood flow [26,27]. Since smaller vessels contribute the largest increase to the resistance, possible pathophysiological mechanisms behind the predictive value of vascular resistance could especially be factors affecting the radius of the small resistance arteries. Potential mechanisms could include sympathetic regulation through direct innervation and secretion of vasoactive substances [28] or endothelial dysfunction [29,30]. Vascular resistance is also closely related to artery stiffness [31], and we and others have previously shown that arterial stiffness predicts the development of hypertension [32–35]. Nevertheless, while there are relationships between macro- and microcirculation, both steady state hemodynamics and pulsatile hemodynamics are complementary but conceptually different aspects of the circulation. Interestingly, an increased media-to-lumen ratio of small resistance arteries might play an important role in the increase of vascular resistance in hypertension [36]. Therefore, another potential mechanism behind the present findings could be hemodynamic changes caused by alterations in microvascular structure [36].

A limitation of the present study was the current hemodynamic measurement method. Systemic

hemodynamics was evaluated using non-invasive whole-body impedance cardiography. Invasive measurement of systemic hemodynamics is the gold standard, and non-invasive measurement findings need to be interpreted cautiously. For ethical reasons, invasive measurements are not justified in large epidemiological settings, and a well-validated non-invasive method is a relevant option in such research settings. The stroke volume and cardiac output values measured with the current methods are in agreement with the values measured by thermodilution and 3-dimensional echocardiography [14–16]. The repeatability of cardiac output measurements by the impedance method has been reported to be even better than by the thermodilution method [14]. Therefore, we consider the present methods to be suitable non-invasive methods for the evaluation of systemic hemodynamics in an epidemiological study setting with a low burden of diseases. Self-reported hypertension was one criterion of the incident hypertension in 2011, which can be considered as a limitation. However, incident hypertension diagnosis was based solely on this criterion only in three subjects in the current study. Another limitation was that our study population consisted of Caucasians, and therefore, the results may not be generalisable to other ethnicities.

Conclusions

Early identification of young individuals at risk for elevated blood pressure would have important public health implications for achieving more effective prevention. Our findings suggest that the evaluation of systemic hemodynamics, especially SVRI, predicts the development of hypertension and improves incident hypertension risk prediction among young adults. Evaluation of systemic hemodynamics could therefore provide a valuable additional tool in the search for individuals at high risk and in the implementation of preventive measures, such as lifestyle modifications and drug treatments.

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Disclosure statement

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