

The Metabolic Syndrome Predicts Incident Stroke A 14-Year Follow-Up Study in Elderly People in Finland

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Background and Purpose—Limited information is available on the role of the metabolic syndrome (MetS) to predict stroke. We investigated the relationship of the MetS and its single components, defined by 6 different criteria, with stroke in a prospective population-based study.

Methods—The MetS was defined according to the World Health Organization, the European Group for the Study of Insulin Resistance, the National Cholesterol Education Program (NCEP), the American College of Endocrinology, the International Diabetes Federation, and the American Heart Association (updated NCEP) criteria. We investigated the relationship of the MetS with stroke using Cox regression analyses in 991 Finnish subjects without diabetes, aged 65 to 74 years at baseline, and followed-up for 14 years.

Results—The MetS defined by the World Health Organization, European Group for the Study of Insulin Resistance, NCEP, International Diabetes Federation, and updated NCEP criteria was significantly associated with incident stroke (fatal and nonfatal) when adjusted for confounding variables (HR, 1.52 to 1.72). After exclusion of subjects with myocardial infarction, these 5 definitions still predicted stroke (HR, 1.49 to 1.80). Of the single components of the MetS, the following predicted stroke in multivariable models when subjects with myocardial infarction were excluded: impaired glucose tolerance (2-hour glucose in an oral glucose tolerance test, 7.8 to 11.0 mmol/L) by the World Health Organization and American College of Endocrinology criteria (HR, 1.66); insulin resistance (HR, 1.60) by the European Group for the Study of Insulin Resistance criteria; and central obesity (HR, 1.52) by the NCEP criteria.

Conclusions—The MetS defined by the 6 criteria except for the American College of Endocrinology definition predicts stroke in elderly subjects. However, impaired glucose tolerance alone is as strong a predictor of stroke as is the MetS defined by the World Health Organization, NCEP and updated NCEP criteria. (*Stroke*. 2008;39:1078-1083.)

Key Words: component ■ definition ■ incidence ■ metabolic syndrome ■ stroke

During the past few years, 6 different criteria for the metabolic syndrome (MetS) have been published, including the World Health Organization (WHO) in 1999,¹ the European Group for the Study of Insulin Resistance (EGIR) in 1999,² the National Cholesterol Education Program (NCEP) Expert Panel in 2001,³ the American College of Endocrinology (ACE) in 2003,⁴ the International Diabetes Federation (IDF) in 2005,⁵ and the American Heart Association and the National Heart, Lung, and Blood Institute (updated the NCEP criteria) in 2005.⁶ One of main purpose of the definitions for the MetS is to provide a useful tool to identify individuals at a high risk for cardiovascular disease. Several prospective studies have shown that the MetS defined by these criteria is associated with the risk of coronary heart disease (CHD), and cardiovascular disease morbidity and mortality.⁷⁻¹⁸ However, there is less information available on the role of the MetS to predict stroke.¹⁹⁻²³ Furthermore, it is unclear whether the MetS predicts stroke beyond and above

its individual components. Recently, we showed that the MetS predicts cardiovascular disease mortality.¹⁸ Risk factors for stroke and CHD differ, and they might be different also in fatal and nonfatal cases. The aim of the present study was to investigate whether the MetS and its single components, defined by the aforementioned 6 criteria, predict fatal and nonfatal stroke in an elderly cohort of Finnish subjects during a 14-year follow-up.

Subjects and Methods

Baseline Study

The formation²⁴ and representativeness²⁵ of the study population have been described in detail previously. Briefly, the study was conducted in Kuopio, east Finland, between 1986 and 1988. Altogether, 1910 subjects born between 1912 and 1921 were randomly selected from the population register including all inhabitants of Kuopio. This random sample covered 35% of all residents in the age group of 65 to 74 years. The overall participation rate was 71%. According to the WHO criteria for definite and possible stroke,²⁶

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Table 1. Definitions of the MetS According to the WHO, EGIR, NCEP, ACE, IDF and Updated NCEP Criteria

	WHO	EGIR	NCEP	ACE	IDF	Updated NCEP
Required	Fasting insulin in top 25%; fasting glucose ≥ 6.1 mmol/L; 2-hour glucose ≥ 7.8 mmol/L	Fasting insulin in top 25%	—	High risk of being insulin-resistant*	For Europeans: waist ≥ 94 cm in men or ≥ 80 cm in women	—
No. of abnormalities	and ≥ 2 of:	and ≥ 2 of:	≥ 3 of:	and ≥ 2 of:	and ≥ 2 of:	≥ 3 of:
Fasting glucose		≥ 6.1 mmol/L	≥ 6.1 mmol/L	≥ 6.1 mmol/L	≥ 6.1 mmol/L	≥ 5.6 mmol/L
2-hour glucose				or 7.8–11.0 mmol/L		
HDL cholesterol	< 0.9 mmol/L in men or < 1.0 mmol/L in women or	< 1.0 mmol/L	< 1.03 mmol/L in men or < 1.29 mmol/L in women	< 1.03 mmol/L (men) or < 1.29 mmol/L (women)	< 1.03 mmol/L (men) or < 1.29 mmol/L (women)	< 1.03 mmol/L (men) or < 1.29 mmol/L (women)
Triglycerides	≥ 1.7 mmol/L	> 2.0 mmol/L	≥ 1.7 mmol/L	≥ 1.7 mmol/L	≥ 1.7 mmol/L	≥ 1.7 mmol/L
Obesity	Waist/hip ratio > 0.90 in men or > 0.85 in women; BMI ≥ 30 kg/m ²	Waist ≥ 94 cm in men or ≥ 80 cm in women	Waist ≥ 102 cm in men or ≥ 88 cm in women			Waist ≥ 102 cm in men or ≥ 88 cm in women
Hypertension	$\geq 140/90$ mm Hg or using antihypertensive medication	$\geq 140/90$ mm Hg or using antihypertensive medication	$\geq 130/85$ mm Hg or using antihypertensive medication	$\geq 130/85$ mm Hg or using antihypertensive medication	$\geq 130/85$ mm Hg or using antihypertensive medication	$\geq 130/85$ mm Hg or using antihypertensive medication
Microalbuminuria	Urinary albumin/urinary creatinine ratio ≥ 3.39 mg/mmol (30 mg/g)					

*At least 1 of the following: diagnosis of cardiovascular disease, hypertension, polycystic ovary syndrome, nonalcoholic fatty liver disease, or acanthosis nigricans; family history of type 2 diabetes, hypertension, or cardiovascular disease; history of gestational diabetes or glucose intolerance; non-white ethnicity; sedentary lifestyle; BMI > 25 kg/m² or waist > 102 cm for men or > 88 cm for women; and age older than 40 years.

subjects with previous stroke were identified and excluded from the analyses for incident stroke. The WHO criteria¹ for impaired glucose tolerance (IGT) and diabetes mellitus were used in the classification of subjects without previously known diabetes based on fasting plasma glucose and 2-hour postglucose load values at baseline. According to the criteria, 136 had known diabetes and 133 had newly diagnosed diabetes at baseline, and these subjects were excluded from the study. Thus, a total of 991 nondiabetic subjects, aged 65 to 74 years at baseline, were included in the present study.

Previous verified definite and possible myocardial infarction (MI) before the baseline study were defined according to the WHO MONICA project criteria²⁷ as modified by the FINMONICA AMI Register Study Group.²⁸

Weight, height, waist and hip circumference, and blood pressure were measured. Waist-to-hip ratio was defined as waist circumference to hip circumference. Body mass index was calculated as the weight in kilograms divided by the square of the height in meters. Smoking status was defined as present smoking. With respect to alcohol consumption, subjects were classified as alcohol users or nonusers. Physical activity during leisure time was classified as physically inactive (little and occasional activity) and physically active (regular exercise at least once per week and at least 30 minutes per time).

Blood samples were taken in the morning after a 12-hour overnight fast. All subjects underwent an oral glucose tolerance test (75 g glucose). Plasma glucose and insulin, serum lipids and lipoproteins, and urinary albumin were determined as previously described.^{24,29} Ratio of urinary albumin (mg/L) to urinary creatinine (mmol/L) was used as a measure of albumin excretion.

The study complies with the Declaration of Helsinki and was approved by the Ethics Committee of Kuopio University Hospital. All study subjects gave informed consent.

Diagnosis of Incident Stroke

Medical records of all study subjects who participated in the baseline study between 1986 and 1988 were reviewed by 2 of the authors (S.R., J.K.). Copies of death certificates of all those who had died of fatal stroke during the 14-year follow-up were obtained from medical records or from the files of the Central Statistical Office in Finland and reviewed (S.R., J.K.). Deaths were recorded until the end of June 2001. The 9th revision of the International Classification of Disease codes 430 to 438 were classified as stroke. Among 28 subjects who died of stroke, 8 had hemorrhagic stroke (codes 430 to 431), 19 had ischemic stroke (codes 433 to 434), and 1 had other and ill-defined cerebrovascular disease (code 437).

Nonfatal stroke events during the follow-up were obtained from medical records of the Kuopio University Hospital. In Kuopio town area, all stroke patients are treated at the Kuopio University Hospital. Medical records of 122 study subjects with a nonfatal stroke were reviewed by 2 of the authors (S.K., J.K.) until the end of June 2001.

WHO criteria for stroke were used in the ascertainment of a new stroke as well as a previous stroke: a clinical syndrome consisting of a neurological deficit observed by a neurologist and persisting > 24 hours (nonfatal stroke), without other diseases explaining the symptoms. Thromboembolic and hemorrhagic strokes, but not subarachnoid hemorrhagic stroke, were included in the diagnosis of stroke.

CT or MRI was performed in most patients but was not required for the diagnosis of stroke. CT or MRI was performed in 77% of

nonfatal strokes. Autopsy was performed in 29% of fatal stroke cases. If a subject had multiple nonfatal strokes during the follow-up, the first stroke was considered as the end point.

Definitions of the MetS

The present study was based on the WHO, EGIR, NCEP, ACE, IDF, and updated NCEP definitions. Each component of the 6 definitions was defined according to the original criteria. Criteria for the 6 definitions of the MetS are shown in Table 1.

Statistical Analyses

All statistics were performed with the SPSS 14.0 statistical programs. Because of the skewed distribution of fasting insulin, triglycerides concentration, and ratio of urinary albumin to urinary creatinine, these variables were log-transformed for statistical analyses. Differences in baseline characteristics between subject with and without incident stroke were tested by χ^2 test and adjusted for age and gender by ANOVA. The baseline variables not included in the definitions of MetS, and showing a statistically significant association with incident stroke, were added into the multivariable Cox regression models as covariates. The multivariable Cox regression analyses were applied to investigate the association of the MetS defined by the 6 criteria with incident stroke in adjusted models (model 1, adjusted for age and gender; model 2, adjusted for age, gender, and excluding subjects with MI; model 3, adjusted for age, gender, and all continuous variables that were the components of each corresponding MetS definition; model 4, adjusted for age, gender, and all components (using cut-off points) of each corresponding MetS). In addition, age- and sex-adjusted Cox model including only all individual components of each corresponding definition of the MetS were analyzed in nondiabetic subjects without MI (model 5). The c-statistic was used to compare each subject's predicted relative risk derived from the multivariate Cox regression model with the actual outcome. A c-statistic of 1.0 indicates perfect prediction, whereas 0.5 indicates no predictive value. A product term of gender \times MetS defined by 6 different criteria was added into the model to investigate interaction. The null hypothesis of no interaction was tested using the change in -2 log likelihood between Cox models with and without the product term. The effect of the single components of the MetS on incident stroke was tested by the multivariable Cox regression models adjusted for other risk factors. $P<0.05$ (2-sided) was the limit of statistical significance. Exact probability values and CI are given in Tables.

Results

The median follow-up for incident stroke was 13.8 years (the 25th and the 75th quartiles were 13.4 and 14.5 years, respectively). Of 150 subjects with stroke events during the follow-up, 13 had a history of MI. More male subjects experienced stroke during the follow-up (men vs women, 19% vs 13%; Table 2). Compared with subjects without incident stroke, subjects with incident stroke had higher levels of 2-hour postload glucose and lower levels of high-density lipoprotein cholesterol. There was a trend that more subjects with incident stroke had antihypertensive medication at baseline compared with those without stroke (30.7 vs 23.3%), but the difference between the groups was not statistically significant ($P=0.058$).

Table 3 shows HRs of the MetS defined by the 6 different criteria to predict stroke during the 14-year follow-up among nondiabetic subjects. When adjusted for age and gender (model 1), the MetS by the WHO, EGIR, NCEP, IDF, and updated NCEP criteria was associated with a 1.52- to 1.75-fold risk for incident stroke. After excluding subjects with MI (model 2), the MetS defined by the WHO, EGIR, NCEP, IDF, and updated NCEP criteria was associated with a statistically

Table 2. Baseline Characteristics of Subjects by Incident Stroke During the 14-Year Follow-Up in Nondiabetic Subjects

	Incident Stroke (n=150)	Nonstroke (n=841)	P
Male/Female	67/83	293/548	0.023
Age, yr	69.3 \pm 2.9	68.9 \pm 2.9	0.061
Previous MI	15 (10.0)	81 (9.6)	0.889
Current smokers	15 (10.0)	87 (10.3)	0.898
Alcohol user	49 (32.7)	250 (29.7)	0.473
Physically inactive at leisure time	37 (24.7)	200 (23.8)	0.815
Use of antihypertensive medication	46 (30.7)	196 (23.3)	0.058
Body mass index, kg/m ²	27.1 \pm 3.9	27.0 \pm 3.9	0.786
Waist circumference, cm	92.0 \pm 11.7	90.2 \pm 10.5	0.065
Systolic blood pressure, mm Hg	156 \pm 25	157 \pm 23	0.922
Urinary albumin to urinary creatinine ratio, mg/mmol	2.9 \pm 5.7	3.3 \pm 14.6	0.433
Total cholesterol, mmol/L	6.48 \pm 1.30	6.57 \pm 1.23	0.397
Triglycerides, mmol/L	1.73 \pm 0.76	1.67 \pm 0.76	0.389
HDL cholesterol, mmol/L	1.25 \pm 0.33	1.31 \pm 0.33	0.024
Fasting insulin, pmol/L	93 \pm 45	87 \pm 41	0.094
Fasting plasma glucose, mmol/L	5.7 \pm 0.5	5.6 \pm 0.5	0.070
2-hour postload glucose, mmol/L	6.8 \pm 1.7	6.5 \pm 1.6	0.033

Data are means \pm SD or N of participants (percentages).

significant 1.49- to 1.80-fold risk for stroke. However, the MetS defined by the ACE criteria did not predict stroke in model 1 and model 2. Model 2 (the ACE criteria) had the lowest c-statistic (0.590) compared with those of other criteria. Interaction terms between the gender and the MetS based on the 6 definitions were not significant for stroke ($P>0.25$). We also added smoking, alcohol consumption, physical activity, and total cholesterol as covariates into the models, but only minor changes in HRs were observed. In addition, to investigate whether the MetS predicts stroke above and beyond its individual components, individual components of the corresponding MetS definitions were entered into multivariable models as continuous variables (model 3) or using cut-off points as defined by the corresponding MetS definitions (model 4). Model 5, analyzed in age- and sex-adjusted Cox regression model in nondiabetic subjects without MI, included only individual components of each corresponding definition of the MetS. The IDF definition was associated with a statistically significant 1.73- to 2.12-fold risk for stroke in model 3 and model 4, and the EGIR definition was significantly associated with a 1.90-fold risk for stroke in model 3. The MetS by the other criteria did not predict stroke in model 3 or model 4. Model 4 including the IDF criteria had the highest c-statistic (0.626) among all definitions of the MetS. The c-statistic of model 4 and model 5, which showed significant association between IGT and incident stroke, gave higher values compared to those of model 2 (0.614 vs 0.590, respectively).

Table 3. Hazard Ratios of the MetS to Predict Incident Stroke (n=150) According to Different Criteria for the MetS in 991 Nondiabetic Subjects During the 14-Year Follow-Up

Models	HR (95% CI)					
	WHO Definition	EGIR Definition	NCEP Definition	ACE Definition	IDF Definition	Updated NCEP Definition
MetS, n (%)†	416 (42.0)	215 (21.7)	417 (42.1)	653 (65.9)	552 (55.7)	503 (50.8)
1	1.56 (1.13–2.14)¶	1.75 (1.23–2.47)¶	1.62 (1.17–2.24)¶	1.20 (0.85–1.69)	1.64 (1.17–2.31)¶	1.52 (1.10–2.11)*
2	1.57 (1.12–2.19)¶	1.80 (1.25–2.59)¶	1.60 (1.14–2.25)¶	1.24 (0.86–1.78)	1.77 (1.24–2.54)¶	1.49 (1.06–2.10)*
c-statistic	0.607	0.602	0.610	0.590	0.619	0.605
3	1.31 (0.71–2.40)	1.90 (1.10–3.27)*	1.58 (0.95–2.61)	0.95 (0.59–1.53)	1.73 (1.06–2.80)*	1.32 (0.81–2.16)
4	1.10 (0.62–1.96)	4.69 (0.62–35.23)	1.53 (0.80–2.93)	0.81 (0.46–1.42)‡	2.12 (1.09–4.11)*	1.19 (0.64–2.20)
c-statistic	0.624	0.616	0.610	0.614	0.626	0.609
5 (significant hazard ratio of single components)	1.56 (1.05–2.30)§
c-statistic	0.609	0.608	0.601	0.614	0.601	0.605

†Number/percentage of subjects with the MetS by each definition. Model 1, adjusted for age and gender; model 2, subjects with previous MI (n=79) were excluded from model 1 (incident stroke: n=137); model 3, all continuous variables for components of each corresponding definition are entered into model 2; model 4, all components of each corresponding definition are entered into model 2. Model 5: only all components of each corresponding definition were included.

‡Hazard ratio of IGT for incident stroke was 1.63 (95% CI, 1.07–2.46), $P=0.022$.

§Hazard ratio of IGT for incident stroke, $P=0.028$.

* $P<0.05$.

¶ $P<0.01$.

Table 4 shows HRs for the single components of the MetS definitions for risk of stroke in multivariable Cox regression models. Of the single components of the MetS, the following predicted stroke in nondiabetic subjects after adjustment for age and gender (model 1): IGT defined by 2-hour glucose level 7.8 to 11.0 mmol/L in an oral glucose tolerance test (HR, 1.63) according to the WHO and ACE criteria; insulin resistance (upper quartile of fasting insulin; HR, 1.56); central obesity (waist ≥ 102 cm for men and ≥ 88 cm for women; HR, 1.43) according to the NCEP criteria; elevated triglycerides (triglycerides >2.0 mmol/L; HR, 1.51) according to the EGIR criteria; low high-density lipoprotein cholesterol (high-density lipoprotein cholesterol <0.9 mmol/L in men or <1.0 mmol/L in women; HR, 1.49) according to the WHO criteria, and microalbuminuria (ratio of urinary albumin to urinary creatinine ≥ 3.39 mg/mmol; HR 1.45) according to the WHO criteria. After exclusion of subjects with MI (model 2), the following single components of the MetS still predicted stroke: IGT (HR: 1.66); insulin resistance (upper quartile of fasting insulin; HR, 1.60); and central obesity (waist ≥ 102 cm for men and ≥ 88 cm for women; HR, 1.52); and further adjustment for other risk factors did not essentially change the results.

Discussion

In the present study, the MetS defined by all present criteria except for the ACE definition, predicted stroke in elderly Finnish subjects. Even after the adjustment for individual components of the MetS, the MetS by the EGIR and IDF definitions was predictive of stroke. The IDF definition was the best predictor of stroke among all definitions. One of the single components of the MetS, IGT, predicted stroke comparably with the MetS defined by the WHO, NCEP, and updated NCEP definitions.

Several prospective studies have evaluated the value of the NCEP and WHO definitions to predict stroke,^{19–23} but most of these studies have used modified definitions other than those originally proposed.^{19–21} Moreover, these studies have varied with respect to characteristics of the baseline population, number of deaths, and statistical analyses. The Cardiovascular Disease Risk Factor Two-Township Study²² reported that the NCEP criteria predicted ischemic stroke (HR, 4.30) in 3453 subjects without excluding initial diabetes and CHD. In that study, the diagnoses of diabetes and CHD were based on the self-report instead of an oral glucose tolerance test and clinical records. The Framingham Offspring Study²³ also found that the MetS defined by the NCEP criteria was associated with stroke, but the subjects with CHD at baseline were not excluded from the study. The diagnosis of diabetes was not based on an oral glucose tolerance test, but instead on fasting plasma glucose or receiving treatment of diabetes. Our study has several advantages. First, this is a prospective population-based study investigating the relationship between stroke and the MetS using all 6 present criteria including all components of each definition. Second, because diabetes is a powerful predictor of stroke independently of the MetS,²³ an oral glucose tolerance test was used to exclude all diabetic subjects from our study. Third, considering that the MetS is associated with CHD,¹⁸ we also investigated the MetS as a predictor of stroke in subjects without MI at baseline. Fourth, our study was performed in a population of elderly subjects, in whom most events of stroke occur. Finally, because it is unclear whether the MetS predicts stroke above and beyond its individual components, our study investigated this issue using c-statistic.

Among the single components of the 6 definitions for the MetS, insulin resistance (upper quartile of fasting insulin) by the EGIR and central obesity by the NCEP criteria were

Table 4. Hazard Ratios for the Individual Components of the MetS to Predict Incident Stroke in Nondiabetic Subjects During the 14-Year Follow-Up

	HR (95% CI)	
	Model 1	Model 2
Fasting plasma glucose ≥ 6.1 mmol/L	1.30 (0.91–1.86)	1.33 (0.92–1.92)
Fasting plasma glucose ≥ 5.6 mmol/L	1.29 (0.93–1.79)	1.27 (0.91–1.80)
2-hour postload glucose 7.8–11.0 mmol/L	1.63 (1.14–2.33) [†]	1.66 (1.14–2.41) [†]
Upper quartile of fasting insulin	1.56 (1.10–2.20)*	1.60 (1.11–2.29)*
Blood pressure $\geq 130/85$ mm Hg or use of medication	0.89 (0.53–1.49)	0.87 (0.50–1.51)
Blood pressure $\geq 140/90$ mm Hg or use of medication	0.94 (0.63–1.40)	0.89 (0.59–1.34)
Waist circumference ≥ 94 cm (women: ≥ 80 cm)	1.32 (0.91–1.92)	1.48 (0.99–2.22)
Waist circumference ≥ 102 cm (women: ≥ 88 cm)	1.43 (1.02–2.01)*	1.52 (1.06–2.17)*
Waist-to-hip ratio >0.90 (women: >0.85)	1.05 (0.70–1.55)	1.13 (0.74–1.72)
BMI ≥ 30 kg/m ²	1.16 (0.78–1.73)	1.19 (0.79–1.78)
Triglycerides ≥ 1.7 mmol/L	1.34 (0.97–1.86)	1.27 (0.90–1.78)
Triglycerides >2.0 mmol/L	1.51 (1.07–2.12)*	1.43 (1.00–2.06)
HDL cholesterol <1.0 mmol/L	1.39 (0.95–2.03)	1.27 (0.84–1.92)
HDL cholesterol <0.9 mmol/L (women: <1.0 mmol/L)	1.49 (1.00–2.22)*	1.43 (0.93–2.20)
HDL cholesterol <1.03 mmol/L (women: <1.29 mmol/L)	1.23 (0.89–1.71)	1.25 (0.89–1.76)
Urinary albumin-to-urinary creatinine ratio ≥ 3.39 mg/mmol	1.45 (1.00–2.11)*	1.45 (0.98–2.15)

* $P<0.05$.[†] $P<0.01$.

Model 1, adjusted for age and gender; model 2, subjects with previous MI (n=79) were excluded from model 1 (incident stroke, n=137).

associated with incident stroke. Accordingly, the EGIR and IDF definitions, which included insulin resistance or central obesity as obligatory components in their definitions, were predictive of stroke events. The other definitions, such as the WHO, NCEP, and updated NCEP, which included obesity as a single component despite different definitions for obesity, also predicted stroke. In contrast, the ACE definition excluded obesity from its definition and did not predict stroke. In our study, if obesity, especially central obesity, was included in the definition of the MetS, then the MetS predicted stroke, supporting the conclusions reported in the previous studies.^{30,31} We also found that IGT predicted stroke with a HR that was comparable with those of the WHO, NCEP, and updated NCEP criteria. This finding is consistent with a previous study showing that IGT predicted fatal stroke in elderly subjects.³² Our results based on c-statistic and Cox analyses suggest that IGT predicted stroke events above and beyond the ACE definition. Furthermore, the MetS defined by other 5 criteria was a stronger predictor of stroke events than its individual components.

Although hypertension is a classic risk factor for stroke,³³ our data did not show any association between elevated blood pressure and stroke. Two reasons could explain this finding. First, our study was a population-based study in elderly subjects who have higher blood pressure levels than younger persons. Second, even though mean blood pressure levels have decreased markedly during the past 30 years, the prevalence of hypertension in Finland is still among the highest in the world.^{34,35} In our study, 81.1% had hypertension according to blood pressure $\geq 140/90$ mm Hg. Thus, the high prevalence of hypertension in the entire study cohort makes it difficult to demonstrate the effect of blood pressure on the risk of stroke. However, if hypertension was defined only by treatment of antihypertensive medication, hypertension tended to be associated with stroke.

Because of quite a small number of stroke events, analyses could not be performed in subgroups according to the category of stroke. This is a limitation of our study. In addition, the absence of middle-aged individuals in the cohort may lead to bias of the incidence of stroke. However, a recent Finnish study in middle-aged men reported similar results to ours based on the NCEP and modified WHO criteria.²¹ Because of several definitions of the MetS, multiple testing also increases the likelihood of false-positive probability values.

In conclusion, the MetS defined by all 6 criteria except for the ACE definition predicts incident stroke in elderly subjects. However, IGT alone is as strong a predictor of stroke as the MetS according to the WHO, NCEP, and updated NCEP criteria. Therefore, our results may indicate that the MetS defined by the 6 present criteria except for the ACE definition predicts stroke events, possibly even above and beyond its individual components.

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Disclosures

None.

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