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Risk of Smoking and Metabolic Syndrome for Incidence of Cardiovascular Disease

—— Comparison of Relative Contribution in Urban Japanese Population: The Suita Study ——

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Background: Risk factor clustering, the so-called metabolic syndrome (MetS), is an important risk factor for cardiovascular disease (CVD). Smoking is also an important CVD risk factor with still a high prevalence. However, few previous studies have compared the risk for CVD or the population-attributable fraction (PAF) of smoking, MetS, and both.

Methods and Results: The present study was an 11.9-year cohort study of 1,822 men and 2,089 women, aged 40–74 years, selected randomly from an urban general population in Japan. MetS was defined according to the National Cholesterol Education Program on Adult Treatment Panel III (NCEP-ATPIII) guideline modified by the Asian criteria for waist circumference. The prevalence of smoking was 49.5% in men and 11.1% in women, and that of MetS was 19.8% and 23.5%, respectively. In men, the multivariate-adjusted hazard ratio for CVD incidence, compared with non-smoking participants without MetS, was 2.07 (1.26–3.40) in those who smoked, 2.09 (1.08–4.04) in those with MetS, and 3.56 (1.89–6.72) in those with both. In men the PAF for CVD incidence was 21.8% because of smoking, 7.5% because of MetS, and 11.9% because of both.

Conclusions: Although countermeasures for MetS are important, smoking should continue to be considered an important public health problem and antismoking campaigns should be promoted, especially for men, to prevent CVD. (*Circ J* 2009; **73:** 2258–2263)

Key Words: Cohort; Hazard ratio; Metabolic syndrome; Smoking

Risk factor clustering, the so-called metabolic syndrome (MetS), is an important risk factor for cardiovascular disease (CVD), and previous studies have shown the risk of MetS for CVD in the Japanese population.[1–4] In addition, health guidance for people aged 40–74 years who fulfill the Japanese MetS criteria[5] began in April 2008 and countermeasures for MetS has become a national project.[6]

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However, cigarette smoking is a widely accepted risk factor for CVD,[7–9] and the prevalence of smoking is still high in Japan compared with Western developed countries.[10] Accordingly, in Japan, countermeasures for MetS are being applied with a still high prevalence of smoking, which might be different from the situation in Western developed countries with a lower prevalence of smoking.[10] To improve this situation, it is important to examine and show the combined risk of MetS and smoking, and compare the impact of each risk factor and both for CVD from the viewpoint of the impact not only on the individual but also on the population using indicators such as population-attributable fraction (PAF). In addition, such an assessment could be useful for motivating individuals with MetS, smoking, or both because both MetS and smoking are targets of lifestyle modification. However, few studies have compared the risk of smoking, MetS, and both for CVD.

Our a priori hypothesis was that the coexistence of smoking and MetS worsens the CVD risk, and that the PAF of smoking in Japanese men is larger than that of MetS because of their high prevalence of smoking. To examine this hypothesis, we performed a 11.9 year (mean length) cohort study in an urban general Japanese population to compare the effects of smoking, MetS and both on CVD risk.

Methods

Population

The Suita study,[2,11–14] a cohort study of CVD, was established in 1989 in Suita City, Osaka. In that study, 6,485 participants who were randomly selected from the municipal population registry participated in a baseline survey at the National Cardiovascular Center (NCVC) between

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Table 1. Baseline Characteristics of the Participants According to the Combination of Smoking and MetS

	MetS (−)		MetS (+)	
	Non-smoker	Smoker	Non-smoker	Smoker
Men				
n	732	730	189	171
Age (years)	58.9±9.9	56.1±9.4	59.3±8.4	57.4±9.1
Waist (m)	0.82±0.07	0.81±0.07	0.89±0.07	0.89±0.07
BMI (kg/m^2)	22.7±2.7	22.1±2.5	24.9±2.5	24.8±2.5
Total cholesterol (mmol/L)	5.26±0.88	5.08±0.85	5.49±0.88	5.44±0.98
Non-HDL-cholesterol (mmol/L)	3.90±0.88	3.79±0.88	4.41±0.85	4.41±0.98
High blood pressure (%)	48.6	39.3	86.8	84.8
High triglycerides (%)	19.3	22.5	83.1	80.7
Low HDL-cholesterol (%)	13.5	19.6	63.0	69.6
High blood glucose (%)	9.6	10.0	47.1	42.1
Abdominal obesity (%)	13.9	7.5	56.1	59.1
Medication				
For hypertension (%)	32.7	33.7	36.8	39.3
For hypercholesterolemia (%)	1.0	0.5	4.8	4.1
For hypertriglyceridemia (%)	0.5	0.4	2.1	1.2
For diabetes (%)	14.9	12.9	26.9	14.3
Smoking				
Never (%)	37.8	0.0	32.3	0.0
Ex (%)	62.2	0.0	67.7	0.0
Current (%)	0.0	100.0	0.0	100.0
Alcohol drinking				
Never (%)	20.9	19.6	20.6	22.8
Ex (%)	4.2	2.5	5.8	3.5
Current (%)	74.9	77.9	73.5	73.7
Women				
n	1,424	174	433	58
Age (years)	55.3±9.4	52.6±9.1	60.3±8.7	59.3±8.6
Waist (m)	0.77±0.09	0.75±0.09	0.88±0.09	0.87±0.09
BMI (kg/m^2)	21.8±2.8	21.4±3.0	24.8±3.3	24.7±3.2
Total cholesterol (mmol/L)	5.57±0.90	5.39±0.98	5.93±1.00	5.83±0.98
Non-HDL-cholesterol (mmol/L)	4.02±0.90	3.97±1.03	4.75±1.01	4.77±0.95
High blood pressure (%)	35.1	20.1	85.2	70.7
High triglycerides (%)	6.6	6.3	58.0	81.0
Low HDL-cholesterol (%)	18.3	34.5	82.0	87.9
High blood glucose (%)	4.3	1.7	30.5	24.1
Abdominal obesity (%)	30.1	27.6	86.6	79.3
Medication				
For hypertension (%)	33.7	17.4	43.6	44.4
For hypercholesterolemia (%)	1.6	0.0	6.5	3.4
For hypertriglyceridemia (%)	0.1	0.0	1.4	1.7
For diabetes (%)	16.7	0.0	17.5	30.0
Smoking				
Never (%)	97.1	0.0	94.2	0.0
Ex (%)	2.9	0.0	5.8	0.0
Current (%)	0.0	100.0	0.0	100.0
Alcohol drinking				
Never (%)	67.4	50.6	75.5	65.5
Ex (%)	1.0	5.7	1.6	0.0
Current (%)	31.6	43.7	22.9	34.5

Data are value±indicate standard deviation.
MetS=presence of 3 or more of the following: (1) abdominal obesity defined as a waist circumference ≥90 cm in men and ≥80 cm in women; (2) high blood pressure defined as average systolic/diastolic blood pressures of ≥130/85 mmHg and/or current medication for hypertension; (3) high triglycerides defined as serum level ≥1.68 mmol/L; (4) low HDL-cholesterol defined as serum level <1.03 mmol/L in men and <1.29 mmol/L in women; (5) high blood glucose defined as fasting blood glucose ≥6.10 mmol/L and/or current use of insulin or oral medication for diabetes.
MetS, metabolic syndrome; BMI, body mass index; HDL, high-density lipoprotein.

September 1989 and February 1994. Of the 4,285 participants who were aged 40–74 years at baseline, a total of 374 were excluded for the following reasons: past history of CVD (ischemic heart disease and stroke: n=127), non-fasting visit (n=155), and missing information at the time of the baseline survey or lost to follow-up (n=92). The data for the remaining 3,911 participants (1,822 men and 2,089 women) were then analyzed. Informed consent was given by all participants. The present cohort study was approved by the Institutional Review Board of the NCVC.

Baseline Examination

Well-trained nurses obtained information on smoking (never, ex-, or current smoker), alcohol drinking (never, ex-, or current drinker), and the medical history of each participant. If the participant answered yes to "current smoker", information was obtained for how many cigarettes per day were smoked.

Table 2. HRs and 95% CIs of Smoking for Incidence of CVD (Stroke+MI), Stroke, Ischemic Stroke, and MI

	Never-smoker	Ex-smoker	Current-smoker	
			≤20 cigarettes/day	>20 cigarettes/day
Men (n)	338	583	524	373
Person-years	4,147	6,837	5,965	4,343
CVD (stroke+MI)				
Cases (n)	11	29	40	16
Incidence (/1,000 person-years)	2.65	4.24	6.71	3.68
Multivariate-adjusted HR (95%CI)	1.00	1.34 (0.67–2.69)	2.65 (1.35–5.21)	2.31 (1.06–5.05)
Stroke				
Cases (n)	8	18	30	12
Incidence (/1,000 person-years)	1.93	2.63	5.03	2.76
Multivariate-adjusted HR (95%CI)	1.00	1.07 (0.46–2.48)	2.47 (1.12–5.45)	2.48 (1.00–6.20)
Ischemic stroke				
Cases (n)	4	16	24	8
Incidence (/1,000 person-years)	0.96	2.34	4.02	1.84
Multivariate-adjusted HR (95%CI)	1.00	1.94 (0.64–5.86)	4.06 (1.40–11.83)	3.37 (1.00–11.41)
MI				
Cases (n)	3	11	10	4
Incidence (/1,000 person-years)	0.72	1.61	1.68	0.92
Multivariate-adjusted HR (95%CI)	1.00	2.21 (0.61–8.00)	2.74 (0.80–10.90)	1.89 (0.41–8.70)
Women (n)	1,790	67	209	23
Person-years	21,881	727	2,363	240
CVD (stroke+MI)				
Cases (n)	45	0	10	1
Incidence (/1,000 person-years)	0.21	–	4.23	4.17
Multivariate-adjusted HR (95%CI)	1.00	–	2.70 (1.34–5.45)	2.80 (0.36–21.55)
Stroke				
Cases (n)	37	0	5	1
Incidence (/1,000 person-years)	1.69	–	2.12	4.17
Multivariate-adjusted HR (95%CI)	1.00	–	1.60 (0.62–4.16)	2.70 (0.34–21.68)
Ischemic stroke				
Cases (n)	19	0	4	1
Incidence (/1,000 person-years)	0.87	–	1.69	4.17
Multivariate-adjusted HR (95%CI)	1.00	–	3.00 (1.00–8.97)	7.15 (0.84–60.64)
MI				
Cases (n)	8	0	5	0
Incidence (/1,000 person-years)	0.37	–	2.12	–
Multivariate-adjusted HR (95%CI)	1.00	–	8.35 (2.64–26.48)	–

Multivariate-adjusted HR (95%CI): age, BMI, systolic blood pressure, blood glucose, non-HDL-cholesterol, glomerular filtration rate, and alcohol drinking were adjusted.
HRs, hazard ratios; CIs, confidence intervals; CVD, cardiovascular disease; MI, myocardial infarction. Other abbreviations see in Table 1.

Well-trained physicians measured blood pressure (BP) 3 times in the right arm using a standard mercury sphygmomanometer while the participant was seated after a 5-min rest. The average of the 2nd and 3rd measurements was used in the analyses. Height in stockings and weight in light clothing were measured. Trained public health nurses or technicians measured waist circumference at the umbilical level while the participant was standing.

Blood samples were collected at the NCVC after the participants had fasted for at least 12 h. The samples were centrifuged immediately, and a routine blood examination, which included serum total cholesterol (TC), high-density lipoprotein cholesterol (HDLC), triglycerides and glucose levels, was then carried out. Non-HDLC was calculated by subtracting the HDL from the TC. Serum creatinine (Cre) was measured by the non-compensated kinetic Jaffe method. The glomerular filtration rate (GFR: $ml \cdot min^{-1} \cdot 1.73 m^{-2}$) was calculated using the MDRD equation modified by the Japanese coefficient (0.881): $186 \times (\text{Cre (mg/dl)})^{-1.154} \times (\text{age (years)})^{-0.203} \times 0.881 \times (0.742 \text{ if female})$.[15,16]

Definition of MetS

In the present study, MetS was defined using the criteria recommended in the National Cholesterol Education Program on Adult Treatment Panel III guideline with a modification (modified NCEP-ATP III criteria).[17,18] Specifically, abdominal obesity was defined as a waist circumference ≥90 cm in men and ≥80 cm in women according to the International Obesity Task Force central obesity criteria for Asia.[17] High BP was defined as average systolic/diastolic BPs ≥130/85 mmHg and/or current medication for hypertension. High triglyceride was defined as a serum level ≥1.68 mmol/L. Low HDLC was defined as a serum level <1.03 mmol/L in men and <1.29 mmol/L in women. High blood glucose was defined as fasting blood glucose (FBG) ≥6.10 mmol/L and/or current use of insulin or oral medication for diabetes. MetS was defined as the presence of 3 or more of these components.

Follow-up and Endpoints

The method of follow-up has been described elsewhere.[2,11–14] Briefly, the participants were followed until December 31, 2005. The first step in the survey involved checking the health status of all participants by repeat visits to NCVC every 2 years and yearly questionnaires conducted by mail or telephone interview. The in-hospital medical records of the participants who were suspected of having had a myocardial infarction (MI) or stroke were reviewed

Table 3. Risk of Smoking and MetS for CVD (Stroke+MI)

	MetS (−)		MetS (+)	
	Non-smoker	Smoker	Non-smoker	Smoker
Men				
n	732	730	189	171
Person-years	8,721	8,506	2,263	1,835
CVD (stroke+MI) cases (n)	26	41	14	16
CVD incidence (/1,000 person-years)	2.98	4.82	6.19	8.72
Multivariate-adjusted HR (95%CI)†	Reference	2.03(1.24–3.33)	2.11(1.10–4.04)	3.39(1.81–6.33)
Multivariate-adjusted HR (95%CI)‡	Reference	2.07(1.26–3.40)	2.09(1.08–4.04)	3.56(1.89–6.72)
PAF		21.8	7.5	11.9
Women				
n	1,424	174	433	58
Person-years	17,684	2,027	4,925	577
CVD (stroke+MI) cases (n)	23	6	22	5
CVD incidence (/1,000 person-years)	1.30	2.96	4.47	8.67
Multivariate-adjusted HR (95%CI)†	Reference	2.64(1.07–6.51)	2.58(1.42–4.69)	5.40(2.04–14.25)
Multivariate-adjusted HR (95%CI)‡	Reference	2.67(1.07–6.65)	2.33(1.25–4.34)	4.84(1.81–12.97)
PAF		6.7	22.4	7.1

Multivariate-adjusted HR (95%CI): †adjusted for age.
Multivariate-adjusted HR (95%CI): ‡adjusted for age, alcohol drinking (never-, ex-, current-), glomerular filtration rate and non-HDL-cholesterol.
PAF, population attributable fraction. Other abbreviations see in Tables 1,2.

by registered hospital physicians or research physicians who were unaware of the baseline information.

The criteria for definite and probable MI were defined according to the criteria of the Monitoring Trends and Determinants of Cardiovascular Disease (MONICA) project,[19] which requires evidence from an ECG, cardiac enzymes, and/or autopsy. Stroke was defined according to the National Survey of Stroke criteria,[20] which require rapid onset of a constellation of neurological deficits lasting at least 24h or until death. Strokes were classified as ischemic stroke (thrombotic or embolic), intracerebral hemorrhage, subarachnoid hemorrhage, or undetermined type. A definite stroke was defined by autopsy or diagnostic imaging, such as computed tomography or magnetic resonance imaging. In the present study, cases of definite MI or stroke were used in the analysis.

Statistical Analysis

To compare baseline risk characteristics among the 4 groups classified by the combination of MetS and smoking status, analysis of variance was used for continuous variables, and the chi-squared test was used for dichotomous variables. In this analysis, ex-smoker and never-smoker were classified as non-smokers.

Sex-specific analyses were performed. First, the Cox proportional hazards model was used to estimate the hazard ratios (HR) of smoking status for the incidence of CVD (stroke+MI) and its subtypes. Smoking status was classified as never-, ex-, or current smoker (≤20 cigarettes/day and >20 cigarettes/day). In this analysis, age, body mass index (BMI), systolic BP, FBG, non-HDLC,[11] GFR, and alcohol drinking (never-, ex-, and current drinker) were included as confounding factors.

Second, the source population was divided into 4 groups according to the combination of smoking and the presence of MetS. In this analysis, ex-smoker and never-smoker were also classified as non-smokers. The 2 models were used for estimating the HRs of the combinations for CVD incidence. To adjust for the confounding factors, only age was included in model 1, and alcohol drinking (never, ex-, and current drinker), GFR and non-HDLC were also included in model 2. To express the impact of smoking on CVD incidence in the participants, the PAF (%) was estimated as $Pe \times (HR-1)/HR$, in which Pe is the proportion of incident cases in each category.[21]

All statistical analyses were performed using SPSS statistical software, version 15.0 J (SPSS, Tokyo, Japan). $P<0.05$ (2-tailed) was considered statistically significant.

Results

Baseline Characteristics

Among the participants, 901 of the 1,822 men and 232 of 2,089 women were current smokers (smoking rate: men, 49.5%; women, 11.1%). Similarly, 360 men and 491 women had MetS (prevalence: men, 19.8%; women, 23.5%). **Table 1** summarizes the baseline characteristics of the participants classified into 4 groups according to the combination of current smoking and MetS by sex. All variables, except for alcohol drinking in men, were significantly different among the 4 groups.

Risk of Smoking for CVD Incidence

In the present study, the mean follow-up period was 11.9 years, and 42 definite cases of MI and 111 of definite stroke occurred.

Table 2 shows the multivariate-adjusted HRs and 95% confidence intervals (CI) of smoking status for the incidence of CVD and its subtypes. In men, the HR of current smokers who were smoking ≤20 cigarettes/day compared with never smokers was 2.65 (95%CI 1.35–5.21) for CVD, 2.47 (95%CI 1.12–5.45) for stroke, 4.06 (95%CI 1.40–11.83) for ischemic stroke, and 2.74 (95%CI 0.80–10.90) for MI. Similarly in women, the HR was 2.70 (95%CI 1.34–5.45) for CVD, 1.60 (95%CI 0.62–4.16) for stroke, 3.00 (95%CI 1.00–8.97) for ischemic stroke, and 8.35 (95%CI 2.64–26.48) for MI. Among the participants who were smoking >20 cigarettes/day, the HRs for CVD incidence were similar to those who were smoking ≤20 cigarettes/day, although in both men and women most of them did not reach to statistical significance because of the small sample size.

Among the ex-smokers, the HR was 1.34 (95%CI 0.67–

2.69) for CVD incidence, 1.07 (95%CI 0.46–2.48) for stroke, 1.94 (95%CI 0.64–5.86) for ischemic stroke, and 2.21 (95%CI 0.61–8.00) for MI in men. In women, there was no case of CVD among ex-smokers.

Risk of Smoking and MetS for CVD Incidence

Table 3 shows the multivariate-adjusted HRs of the combination of smoking and MetS for CVD incidence.

In men, the multivariate-adjusted HRs were 2.07 (95%CI 1.26–3.40) for participants with smoking without MetS, 2.09 (95%CI 1.08–4.04) for those with MetS without smoking, and 3.56 (95%CI 1.89–6.72) for those with both, compared with those both smoking and MetS. In women, the multivariate-adjusted HRs were 2.67 (95%CI 1.07–6.65) for participants with smoking without MetS, 2.33 (95%CI 1.25–4.34) for those with MetS without smoking, and 4.84 (95%CI 1.81–12.97) for those with both, compared with those without both smoking and MetS. When we excluded the ex-smokers among women in this analysis, the HRs were almost similar to the results shown in **Table 3**. And these results were not substantially affected when TC instead of non-HDLC was included as a confounding factor in the Cox proportional hazard models.

In men the PAF for CVD incidence was 21.8% because of smoking, 7.5% because of MetS, and 11.9% because of both. In women, the respective PAFs were 6.7%, 22.4%, and 7.1%.

Discussion

To our knowledge, this is the first report of a comparison of the CVD risk of smoking, MetS, and both. The magnitude of the HR of smoking or MetS was almost equal. As expected, the risk for the participants with both was the highest. The PAF for CVD incidence among men with smoking alone was much higher than that among those with MetS alone. In women, the PAF among those with MetS was higher than that among those with smoking.

Furthermore, this is also the first report to show the risk of smoking for CVD in an urban area of Japan. In the present study, the prevalence of smoking was 49.5% in men and 11.1% in women. Compared with the data from the National Health and Nutrition Survey conducted in 1989 (men aged 40–69 years in 1989, 50.4–59.5%; women aged 40–69 years in 1988, 6.8–10.6%)[22] and several large collaborative cohort studies in Japan,[8,9,23,24] the prevalence of smoking in the present study was lower in men and higher in women, but is most consistent with the current Japanese prevalence of smoking (men: 39.9%; women: 10.0%). The present study might reflect the prevalence of smoking in urban Japanese communities around the 1990s. In addition, the high smoking prevalence in women and low prevalence in men in the present study is consistent with that in most of the Asia-Pacific region.

Our study showed that smoking is a prominent risk factor for CVD in an urban Japanese cohort, as shown in previous studies in Japanese rural populations.[9,23,24] Similarly, as previously reported,[1,25–27] MetS was a risk factor for CVD in our cohort.[2] The association between MetS and CVD has been reported in several Japanese cohort studies; however, the number of participants was fewer than in the present study,[1] or non-fasting blood samples and BMI were used instead of waist circumference for the analysis.[25] These points are another important strength of our study.

MetS has been reported as associated with high percent plaque volume and abnormal plaque quality in coronary arteries,[28] and chronic subclinical inflammation.[29] As for smoking, Howard et al reported that smoking is associated with progression of an index of atherosclerosis expressed as the intima–medial thickness of the carotid artery.[30] Antoniades et al also stated that smoking induces both functional and structural abnormalities in the vascular wall, by mechanisms involving endothelial dysfunction and impairment of vascular smooth muscle cells in the human arterial tree.[31] They also stated that smoking must be approached within the context of the overall lifestyle: smoking coexists with a pro-atherogenic metabolic profile.[31] The reason for the elevated CVD risk among the present participants with both MetS and smoking is unclear, but the concurrent effect on plaque formation by MetS and smoking, and the additional abnormality in function of vascular smooth muscle cells because of smoking, might be associated with the highest CVD risk among the participants with both risk factors in the present study. Individuals with both smoking and MetS are inevitably in the highest risk group for CVD and should be targeted for intervention.

We compared the HRs of these important CVD risk factors, and the HRs of smoking or MetS for CVD incidence were almost consistent. Accordingly, we calculated the PAF, which shows the impact on CVD incidence. As the result, the PAF of smoking was higher than that of MetS in men, and that of MetS was higher than that of smoking in women, a result that may reflect the higher smoking rate in men. Our study results offer a simple key to solving the problem of "which risk factor should we intervene on first for the population to improve their health outcome". Recently, the smoking rate has been decreasing in Japanese men; however, compared with the United States for example,[10] it remains still high. As well as countermeasures against MetS, we need to continue considering smoking as an important public health problem and promoting antismoking campaigns in Japan.

In Western developed countries such as the United States, evaluating the risk of MetS under a high prevalence of smoking is difficult because the prevalence of smoking is much lower[10] than in Japan. Although the data of the present study are limited to 1 city in Japan, it might offer evidence of the risk of MetS under a high prevalence of smoking.

There has been controversy about defining the optimal diagnostic criteria for MetS. We have already compared the predictive value between the Japanese criteria and the modified NCEP-ATPIII criteria.[2] The results suggested that the modified NCEP-ATPIII criteria are suitable for predicting CVD in the Japanese community setting, as well as in the Hisayama study.[1] Accordingly, in the present study MetS was defined using the modified NCEP-ATPIII criteria[17,18] Some investigators consider that MetS is an adipose tissue disease different from obesity. If it is an adipose tissue disease, it would be characterized by inflammation detected through high-sensitivity C-reactive protein (hs-CRP) and insulin resistance, reflecting histological changes in adipose tissue.[32] Thus, inflammation-related factors such as hs-CRP might be a candidate for 1 of the components of MetS.[33] Furthermore, according to the Japanese MetS criteria, the prevalence of MetS tends to be very low in women because obesity is a required component and the definition of obesity is waist circumference ≥90cm. In addition, because some previous studies showed that the prevalence of non-obese individuals with several metabolic risk factors is high

and their CVD risk is also high, the simple exclusion of non-obese participants from the diagnosis of MetS may overlook their potential risk for CVD.[25–27] We might misclassify participants with a high risk for CVD if we adopt the Japanese MetS criteria.

Study Limitations

First, we could not assess the risk of smoking on the incidence of hemorrhagic stroke because of the small number of cases. Second, the measurement of single MetS components and the questionnaire for smoking in the baseline survey may have underestimated the relationship between these risk factors and CVD because of a regression dilution bias.

In conclusion, smoking is still an important risk factor for CVD in urban areas of Japan, and the combination of smoking and MetS worsens the risk for CVD. Lifestyle modification for not only MetS but also smoking continues to be important in populations with a high PAF for CVD because of a high prevalence of smoking.

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Disclosure

None.

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原　著

中年期日本人男性における腹部肥満の有無別に見た代謝異常集積と脳心血管疾患発症との関連

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要　約　働き盛りの日本人男性における腹部肥満の有無別に見た代謝異常集積と脳心血管疾患発症との関連を検討し、腹部肥満の脳心血管疾患発症に与える寄与の大きさを検討した。北陸の某製造業事業所において、35歳から60歳（平均45.5歳）の男性2,903名を11年間追跡し、新規脳心血管疾患（CVD）発症を観察した。11年間で82名のCVD新規発症（脳卒中41、心筋梗塞29、突然死6、狭心症にて冠動脈インターベンション施行6）を観察した。日本内科学会の基準を用いてメタボリックシンドロームを診断したところ、252名（8.7%）がメタボリックシンドロームと判定された。CVD発症率（対1,000人年）は、メタボリックシンドロームなし群で2.49、メタボリックシンドローム群で6.55であり、メタボリックシンドローム群における年齢、喫煙、飲酒、運動習慣で調整したCVD発症ハザード比（95%信頼区間）は2.26(1.30-3.93)と有意に上昇していた。腹部肥満なし・代謝異常なし群と比較し、腹部肥満なし・代謝異常集積群、および腹部肥満あり・代謝異常集積群のCVD発症ハザード比は、それぞれ3.82 (1.77-8.24)、4.81 (2.25-10.3)と、ともに有意に上昇していた。メタボリックシンドローム群のCVDの集団寄与危険割合は24.9%に対し、非肥満者におけるCVDの集団寄与危険割合の合計は47.8%に達した。代謝異常集積者では、腹部肥満の有無にかかわらずCVD発症リスクは高く、非肥満者でも同様のリスク管理が必要と考えられる。

キーワード：コホート研究，脳心血管疾患，肥満，メタボリックシンドローム
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I. 緒　　言

メタボリックシンドロームは、心筋梗塞や脳卒中などの脳心血管疾患の高リスク群として、疾病予防の点で重要な概念である。平成17年に日本内科学会によるメタボリックシンドロームの判定基準が発表され[1]、また、わが国では平成20年度からメタボリックシンドロームの概念を導入した特定健診・特定保健指導が開始され、メタボリックシンドロームの概念は国民に広く認識されてきている。

メタボリックシンドロームは、肥満、特に腹部肥満を背景に代謝異常や動脈硬化性疾患を集積しやすい状態である。日本人では肥満の有病率が少なく、はたしてどれ程メタボリックシンドロームが日本人の動脈硬化症に影響を与えているか疑問視されてきたが、近年、わが国においてもメタボリックシンドロームは脳心血管疾患のリスクを増加させることが報告されてきている[2-7]。

平成18年の国民健康栄養調査の結果、40-74歳のメタボリックシンドローム該当者数は約960万人、予備軍も含めると1940万人にものぼり、特にこの年代の男性では2人に1人がメタボリックシンドロームまたはその予備群と考えられている[8]、メタボリックシンドローム対策の重要な目

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的の一つとして、このような中年男性を脳心血管疾患から守ることが挙げられるが、働き盛りの中年期の男性におけるメタボリックシンドロームと脳心血管疾患発症との関連を検討した日本人の報告はまだ少ない。

そこで今回、大規模な職域コホートにおける11年間の追跡研究から、働き盛りの日本人男性における腹部肥満の有無別に見た代謝異常集積と脳心血管疾患発症との関連を検討した。また、腹部肥満の脳心血管疾患発症に与える寄与の大きさを検討した。

II. 方　　法

対象者の概要

北陸の某製造業事業所に勤務する男性従業員を対象とした。1996年、35歳から60歳の男性従業員3,423人のうち、2,966人が定期集団健診を受診した（受診率86.6%）。定期健診の結果でウエスト周囲径や空腹時採血のデータに不備がある者12人、すでに脳心血管疾患を有する者18人を除いた2,936人を11年間追跡し、新規脳心血管疾患発症を確認した。このうち、ベースライン調査以降追跡不可能であった33名を除外した2,903人を最終的な解析の対象とした（図1）。

ベースライン調査

ベースライン調査は、1996年の定期健診時に行った。身長、体重を測定しBody Mass Index(BMI)を求めた。ウエスト周囲径は立位で肋骨の最下位と腸骨稜との中間点で測定した。5分間座位で安静を保った後、水銀血圧計を用いて看護師が収縮期・拡張期血圧を1回測定した。空腹時採血にて空腹時血糖値、中性脂肪、HDLコレステロール値を測定した。問診票を用いて、脳心血管疾患の既往、高血圧、高脂血症、糖尿病の治療の有無、喫煙習慣、飲酒習慣、余暇の運動習慣を確認した（表1）。

代謝異常・メタボリックシンドロームの判定

日本内科学会によるメタボリックシンドロームの診断基準[1]をもとに腹部肥満、および各代謝異常を判定した（腹部肥満、ウエスト周囲径男性85cm以上；血圧高値、収縮期血圧130 mmHg以上または拡張期血圧85 mmHg以上；脂質代謝異常、中性脂肪150 mg/dl以上またはHDLコレステロール40mg/dl未満；空腹時血糖高値、空腹時血糖110 mg/dl以上）。各代謝異常に対して内服加療中のものは、代謝異常あり、と判定した。

また、日本内科学会の腹部肥満の判定基準であるウエスト周囲径85cm以上のかわりに、アジア人の基準である90cm以上[9,10]を用いて腹部肥満を判定した場合について、同様の検討を行った。

脳心血管疾患の発症確認

在職中のものは、毎年の健診にて生存確認を行った。イベント発症は産業医活動の中で確認し、発症者には本人から医療機関調査の同意書を取得した。退職者に対しては、退職者健康調査にて生存確認を行った。退職者健康調査は、1990年以降の退職者に対し、年1回、健康状態や脳心血管イベント発症についての郵送による質問票調査を行った。退職者健康調査においてイベントの発症を申告した者から医療機関調査の同意書を取得した。退職後の死亡に関しては、退職者組織から死亡の情報を得て、死亡に関する調査を行った。

在職中、および退職後のイベント発症者に対し

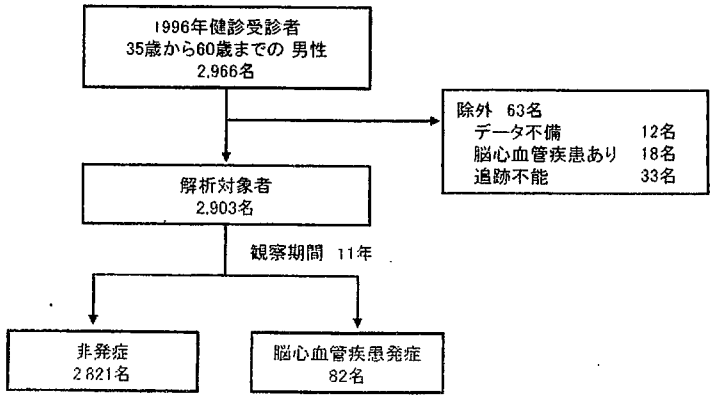

図1 研究デザイン

て医療機関での診療録調査を行った。診療録から脳卒中（脳梗塞、脳出血、クモ膜下出血）、急性心筋梗塞、発症後1時間以内および24時間以内の突然死、狭心症に対するインターベンションを判定し、これらの疾患の発症を脳心血管疾患の発症と定義した。

統計および解析手法

メタボリックシンドローム合併の有無による2群のベースライン要因の比較はt検定を用いた。メタボリックシンドロームの有無、または腹部肥満の有無と代謝異常合併数（0、1、2-3）で6群に分類した各群において循環器疾患発症の発症率を求めた。Cox比例ハザードモデルを用いて、年齢、喫煙、飲酒、運動習慣で調整した多変量調整ハザード比（HR）を算出した。また、腹部肥満の有無と代謝異常合併数で分類した6群において、各群の集団寄与危険割合を算出した。解析はSPSS for Windows 日本語版 (Ver 12.0J) を用いた。

表1　対象者の背景（n=2,903）

年齢（歳）	45.5 ± 6.5
身長（cm）	167.6 ± 6.1
体重（kg）	65.6 ± 9.0
Body Mass Index (kg/m²)	23.3 ± 2.8
ウエスト周囲径（cm）	80.1 ± 7.7
収縮期血圧（mmHg）	122.6 ± 14.5
拡張期血圧（mmHg）	77.1 ± 10.6
総コレステロール（mg/dl）	204.9 ± 33.5
中性脂肪（mg/dl）	123.9 ± 83.3
HDLコレステロール（mg/dl）	55.1 ± 15.2
空腹時血糖（mg/dl）	93.8 ± 17.5
ヘモグロビンA1c（%）	5.1 ± 0.6
喫煙（%）	
非喫煙／禁煙／喫煙	29.7／11.3／59.0
飲酒（%）	
無／少量／多量	23.0／30.0／47.0
運動習慣（%）	
無／軽度／中等度／高度	66.1／19.9／9.8／4.2
代謝異常有病率（%）*	
腹部肥満	27.5
血圧高値	37.7
脂質代謝異常	30.9
血糖高値	9.0
メタボリックシンドローム	8.7
薬物治療者（%）	
高血圧／脂質異常／糖尿病	5.6／1.3／0.9

平均値±標準偏差、または%。
*代謝異常およびメタボリックシンドロームは日本内科学会のメタボリックシンドロームの診断基準を用いて判定

III. 結　　果

1996年のベースライン調査における対象者の背景を表1に示す。平均年齢45.5歳、平均BMI 23.3 kg/m²、平均ウエスト周囲径 80.1cm であった。また、日本内科学会によるメタボリックシンドロームの診断基準で判定された代謝異常の有病率は、腹部肥満27.5%、血圧高値37.7%、脂質代謝異常30.9%、血糖高値9.0%であり、252名（8.7%）がメタボリックシンドロームと診断された。

11年間の追跡期間中に82名の新規脳心血管疾患の発症を観察した。内訳は、脳卒中41名（脳梗塞25名、脳出血12名、クモ膜下出血4名）、急性心筋梗塞29名、突然死6名、狭心症による冠動脈インターベンション施行6名であった。また、63名の死亡（うち14名が脳心血管死）を確認した。

メタボリックシンドロームの有無で、新規脳心血管疾患発症を比較した（表2）。脳心血管疾患発症率（対1,000人年）は、メタボリックシンドロームなし群で2.49、メタボリックシンドローム群で6.55であった。メタボリックシンドローム群の脳心血管疾患発症の多変量調整ハザード比は2.26(95%信頼区間、1.30-3.93)と、有意に上昇していた（図2）。

次に、腹部肥満の有無、および代謝異常合併数と脳心血管疾患の発症を検討した（表3）。脳心血管疾患発症率（対1,000人年）は、腹部肥満なし・代謝異常なし群で1.12、腹部肥満なし・代謝異常合併数2-3の代謝異常集積群で5.37、腹部肥満あり・代謝異常なし群で2.52、腹部肥満あり・代謝異常集積群で6.55であった。腹部肥満なし・代謝異常なし群を基準とした脳心血管疾患発症の多変量調整ハザード比は、肥満なし・代謝異常集積群で3.82 (1.77-8.24)、肥満あり・代謝異常集積群で4.81 (2.25-10.3)であり、腹部肥満の有無にかかわらず、代謝異常合併数の増加に伴い脳心血管疾患発症ハザード比は有意に上昇していた（図3）。各群での集団寄与危険割合は、腹部肥満なし・代謝異常1つ合併群で25.9%と最も大きく、次いで、腹部肥満あり・代謝異常集積群（メタボリックシンドローム群）で24.9%、腹部肥満なし・代謝異常集積群で21.9%であった（図4）。すなわち、非肥満者における脳心血管疾患発症の集団寄与危険割合の合計47.8%は、肥満者の集団寄与危険割合

の合計51.9%とほぼ同等であった。

ウエスト周囲径85cmの代わりにアジア人の基準90cm[20, 10]を用いて腹部肥満を判定し同様の検討を行った。メタボリックシンドロームの有病率は4.1%で、ウエスト周囲径85cmを用いた時の有病率8.7%の約半分であった。脳心血管疾患発症率（対1,000人年）は、非メタボリックシンドローム群で2.63、メタボリックシンドローム群で7.88であり、メタボリックシンドローム群における脳心血管疾患発症の多変量調整ハザード比は2.60(1.29-5.21)と有意に上昇していた。腹部肥満の有無、および代謝異常合併数別にみた脳心血管疾患発症ハザード比は、肥満なし・代謝異常なし群と比較し、肥満なし・代謝異常集積群で3.23(1.68-6.21)、肥満あり・代謝異常集積群で4.85(2.13-11.1)と、ともに有意に上昇していた。また、非肥満者における脳心血管疾患発症の集団寄与危険割合の合計は49.6%であり、肥満者の集団寄与危険割合の合計21.4%の約2倍であった。

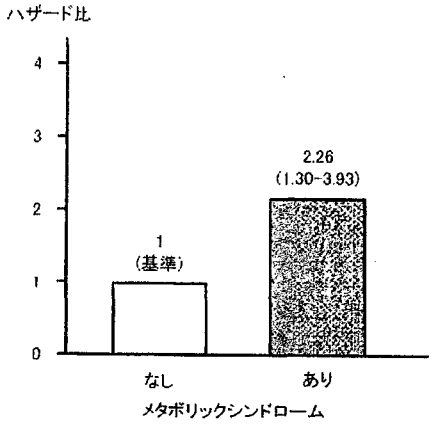

図2　メタボリックシンドロームの有無による脳心血管疾患発症の多変量調整ハザード比

年齢、喫煙、飲酒、運動習慣で調整。メタボリックシンドロームは日本内科学会の診断基準で判定した。

IV. 考　　察

働き盛りの中年男性を対象とした11年間の追跡研究において、日本内科学会の基準で判定したメタボリックシンドロームを有する者の脳心血管疾患発症ハザード比は、2.26であった。また、腹部肥満の有無にかかわらず代謝異常集積に伴い脳心血管疾患発症のハザード比は上昇した。さらに、脳心血管疾患発症の集団寄与危険割合は、メタボリックシンドローム群で24.9%、メタボリックシ

表2　メタボリックシンドロームの有無でみた対象者の背景と11年間の脳心血管疾患発症

	メタボリックシンドローム*		P†
	なし	あり	
N	2,651	252	
年齢(歳)	45.3 ± 6.5	47.6 ± 6.9	<0.001
Body Mass Index (kg/m²)	23.0 ± 2.6	26.5 ± 2.3	<0.001
ウエスト周囲径(cm)	79.2 ± 7.2	90.2 ± 4.7	<0.001
収縮期血圧(mmHg)	121.3 ± 13.9	135.5 ± 13.6	<0.001
拡張期血圧(mmHg)	76.2 ± 10.2	86.3 ± 10.3	<0.001
総コレステロール(mg/dl)	203.6 ± 33.0	218.2 ± 35.5	<0.001
中性脂肪(mg/dl)	115.9 ± 77.5	208.5 ± 94.1	<0.001
HDLコレステロール(mg/dl)	56.0 ± 15.2	45.2 ± 11.4	<0.001
空腹時血糖(mg/dl)	92.7 ± 16.4	105.8 ± 23.6	<0.001
喫煙(%)			
非喫煙・禁煙・喫煙	29.4・11.4・59.2	32.9・10.3・56.7	0.136
飲酒(%)			
無・少量・多量	22.9・30.2・46.9	25.0・27.4・47.6	0.578
運動習慣(%)			
無・軽度・中等度・高度	65.8・19.7・10.2・4.3	69.0・21.8・5.2・4.0	0.137
脳心血管疾患発症数	66	16	
観察人年	26,507	2,442	
発症率(対1,000人年)	2.49	6.55	

平均値±標準偏差、または%
*メタボリックシンドロームは日本内科学会の診断基準を用いて判定
†平均値の比較はt検定、割合の比較はカイ2乗検定を行った

表3　腹部肥満の合併、および代謝異常合併数別にみた対象者の背景と11年間の脳心血管疾患発症

代謝異常合併数	腹部肥満なし*			腹部肥満あり*		
	0	1	2,3	0	1	2,3
N	1,052	764	288	202	345	252
平均年齢(歳)	44.3 ± 6.3	46.0 ± 6.6	47.3 ± 6.4	44.9 ± 6.2	45.6 ± 6.4	47.6 ± 6.9
Body Mass Index (kg/m²)	21.8 ± 2.0	22.4 ± 2.1	22.7 ± 2.2	25.8 ± 2.0	26.2 ± 2.2	26.5 ± 2.3
ウエスト周囲径(cm)	75.4 ± 5.4	77.5 ± 4.9	78.2 ± 4.8	88.7 ± 3.7	89.5 ± 4.3	90.2 ± 4.7
収縮期血圧(mmHg)	113.4 ± 8.6	126.7 ± 14.0	135.9 ± 13.8	115.3 ± 7.8	125.1 ± 12.9	135.5 ± 13.6
拡張期血圧(mmHg)	70.9 ± 7.2	79.8 ± 10.4	84.3 ± 10.6	72.9 ± 7.0	79.5 ± 9.8	86.3 ± 10.3
総コレステロール(mg/dl)	199.0 ± 30.5	204.2 ± 33.8	210.3 ± 40.4	203.7 ± 28.3	211.2 ± 32.3	218.2 ± 35.5
中性脂肪(mg/dl)	82.7 ± 28.2	119.1 ± 64.5	202.0 ± 133.8	95.6 ± 28.1	150.1 ± 90.8	208.5 ± 94.1
HDLコレステロール(mg/dl)	59.9 ± 14.1	56.7 ± 16.9	49.6 ± 13.8	53.0 ± 9.7	49.9 ± 14.4	45.2 ± 11.4
空腹時血糖(mg/dl)	88.5 ± 7.8	93.4 ± 16.8	108.1 ± 31.6	90.1 ± 7.9	92.5 ± 11.0	105.8 ± 23.6
喫煙(%)						
非喫煙 / 禁煙 / 喫煙	29.8 / 10.3 / 59.9	29.7 / 11.5 / 58.8	27.1 / 9.7 / 63.2	29.2 / 15.3 / 55.5	29.3 / 13.6 / 57.1	32.9 / 10.3 / 56.7
飲酒(%)						
無 / 少量 / 多量	25.0 / 30.5 / 44.5	21.2 / 31.8 / 47.0	19.1 / 25.0 / 55.9	19.8 / 31.2 / 49.0	24.9 / 29.6 / 45.5	25.0 / 27.4 / 47.6
運動習慣(%)						
無 / 軽度 / 中等度 / 高度	66.7 / 17.1 / 11.4 / 4.8	63.4 / 22.3 / 9.7 / 4.6	68.8 / 19.1 / 8.3 / 3.8	66.8 / 21.3 / 8.4 / 3.5	65.5 / 21.4 / 10.4 / 2.6	69.0 / 21.8 / 5.2 / 1.0
脳心血管疾患発症数	12	22	15	5	12	16
観察人年	10,750	7,624	2,791	1,982	3,359	2,441
発症率(対1,000人年)	1.12	2.89	5.37	2.52	3.57	6.55

平均値 ± 標準偏差、または%
*腹部肥満、代謝異常(↑血圧高値、脂質異常、血糖高値)は日本内科学会のメタボリックシンドロームの診断基準を用いて判定。

ンドロームも加えた肥満群で51.9%に対して、肥満のない代謝異常者の合計は47.8%に達し、集団全体の脳心血管疾患の予防対策としては、肥満・メタボリックシンドロームのみならず非肥満者への対策の重要性が示された。

これまでの日本人を対象とした疫学研究において、メタボリックシンドロームを有するものでは、非メタボリックシンドロームの対象と比較し、脳心血管疾患発症のハザード比は1.5-2.5倍と有意に上昇することが示されている[2-10]。これらの研究では、メタボリックシンドロームの判定にNational Cholesterol Education Program - Adult Treatment Panel III (NCEP-ATPIII)の基準[11]を用いたものが多く、日本内科学会の提唱するメタボリックシンドロームの基準を用いた本研究の結果とは直接比較はできないものの、本研究でもメタボリックシンドロームを有するものでは約2倍に脳心血管疾患発症リスクが上昇しており、これまでの報

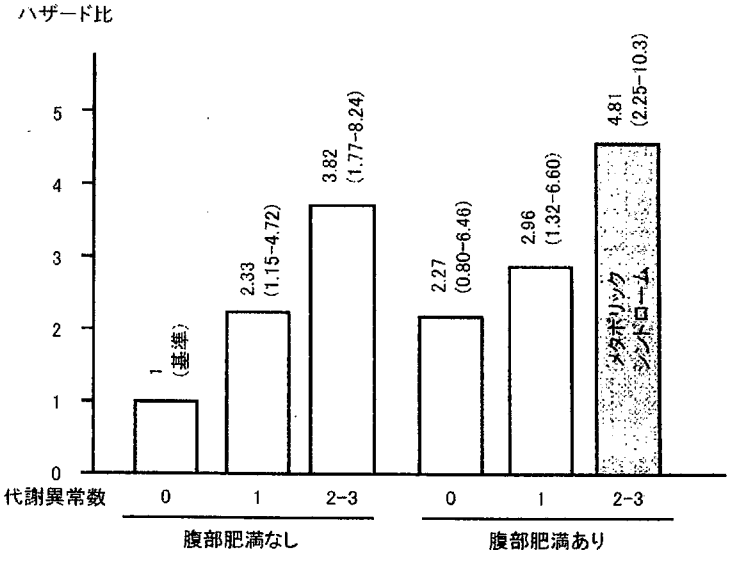

図3 ベースラインの腹部肥満の有無および代謝異常合併数と脳心血管疾患発症の多変量調整ハザード比
年齢、喫煙、飲酒、運動習慣で調整。腹部肥満、代謝異常は日本内科学会のメタボリックシンドローム診断基準で判定した。

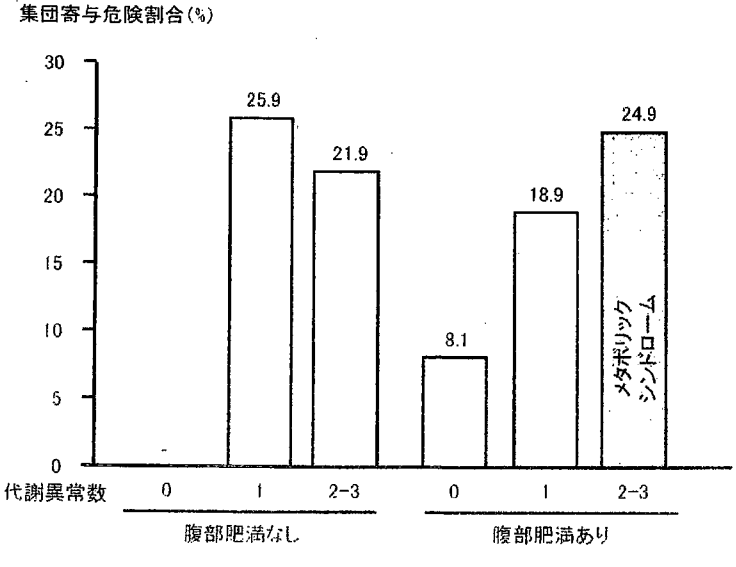

図4 ベースラインの腹部肥満の有無および代謝異常合併数ごとの脳心血管疾患発症に対する集団寄与危険割合
腹部肥満、代謝異常は日本内科学会のメタボリックシンドローム診断基準で判定した.

告と同等な結果であった。

メタボリックシンドロームの診断基準は、これまで数多く提唱されてきた。メタボリックシンドロームにおける腹部肥満の捉え方として、NCEPの基準をもとにAmerican Heart Associationなどが提唱する腹部肥満を他の代謝異常と同等の一つのコンポーネントとして判定する基準[5]と、International Diabetes Federation (IDF)の提唱する腹部肥満をメタボリックシンドロームの必須項目とする基準[9,10]と、大きく分けて2通りの基準がある。日本内科学会のメタボリックシンドロームの基準は、IDFの基準と同様に、判定に腹部肥満を必須とし、またウエスト周囲径のカットオフ値を内臓脂肪面積100cm²に相当する男性85cm、女性90cmとする点が特徴的である[11]。肥満の有病率が大きい欧米では、腹部肥満を必須とするIDFの基準は、これまでのNCEPの基準と比較し、将来の脳心血管疾患を予知するのに同等に有用であることが報告されている[13-15]。しかし、肥満の有病率の少ない日本人において、判定に腹部肥満を必須とする日本人の基準がどれほど脳心血管リスクの評価に有用であるかは、まだ十分明らかになっていない。

これまでの日本基準で判定したメタボリックシンドロームと心血管病発症の関連を検討した久山町研究の報告では[21-24]、メタボリックシンドロームの心血管病発症の相対危険は男性で1.4、女性で2.0と女性でのみ有意に上昇していた。また、腹部肥満の判定にアジア人のウエスト周囲径の基準（男性90cm、女性80cm）を用いることで、メタボリックシンドロームは男女とも有意な心血管病リスク上昇を予知することを報告している。今回の我々の検討では、日本内科学会の基準で判定したメタボリックシンドロームでも中年男性においては、有意な脳心血管疾患のリスクとなることが示され、わが国の基準の妥当性が示された。

久山町研究では、非肥満者と比較し、肥満者ではメタボリックシンドロームの構成要素の合併数が2つ以上で有意な心血管病の相対危険が上昇することを報告した[23,24]。この結果は、肥満で代謝異常を集積する者では有意に心血管疾患の発症リスクが増大する、という基本的なメタボリックシンドロームの概念を支持するものである。今回の我々の検討では、肥満者のみならず非肥満者においても、代謝異常合併数の増加に伴い脳心血管疾患発症ハザード比は有意に上昇した。さらには、非肥満代謝異常なしを基準とした脳心血管疾患発症ハザード比は、非肥満代謝異常集積者、肥満代謝異常集積者ともに有意に上昇していた。同様な結果は、地域集団におけるメタボリックシンドロームと脳卒中発症との関連を検討した斎藤らの報告や[16]、BMI 25 kg/m²以上で判定した肥満の有無および代謝異常合併数と心血管死との関連を検討したNIPPON DATAの報告からも確認されている[17]。今回、脳心血管疾患発症における集団寄与危険割合は、肥満がなく代謝異常を1つ有するもので最も高値であり、非肥満者の代謝異常合併者の集団寄与危険割合の合計は47.8%に達し、メタボリックシンドローム群よりも高値であった。この結果は、脳卒中発症の集団寄与危険割合が内臓肥満のない代謝異常合併者で高値であった、とする斎藤らの報告と同様の結果であった[16]。さらに今回、日本内科学会などが提唱するウエスト周囲径85cmの基準のかわりに、アジア人の基準90cmを用いて腹部肥満を判定したところ、脳心血管疾患発症における非肥満者の集団寄与危険割合の合計は、肥満者の約2倍に達した。肥満のない代謝異常合併者では、脳心血管疾患発症のリスクが有意に増大しているだけでなく、集団全体の脳心血管疾患の発症に大きく影響していることを考慮し、今後はメタボリックシンドローム対策のみならず、肥満のない代謝異常集積者に対する脳心血管疾患の予防対策が必要であろう。

本研究の長所として、地域ではコホート設定が困難な中年期の働き盛りの男性を対象としている点、比較的大規模な対象者を長期間に追跡している点、また、職域コホートでは追跡が困難とされる退職者のイベント発症を把握している点などが挙げられる。しかしながら、本研究の制限として、職域を対象としたコホート研究のため代謝異常や脳心血管疾患の発症が少ない比較的健康な対象者である可能性がある点（Healthy worker's effect）、ウエスト周囲径の測定が特定健診で行われている臍周囲レベルではなく、検査当時の標準的方法である肋骨の最下位と腸骨稜との中間点で測定している点、メタボリックシンドローム脳卒中と虚血性心疾患とを区別せずに脳心血管疾患全体としての分析をしている点、女性では検討を行っていない点などが挙げられる。また、イベントの追跡方法として、退職者に対しては年1回の

追跡調査をおこなっているものの、回答率は毎回約90%であり、一部の対象者では退職時に追跡が打ち切りになっている点、などが挙げられる。しかし、これらのことを踏まえても、我が国の基準で判定したメタボリックシンドロームが有意に脳心血管疾患の発症を上昇させることが示された点は、今後、特に働き盛りの中年男性のメタボリックシンドローム対策を考える上で貴重な結果と考えた。

メタボリックシンドロームは、肥満を背景に代謝異常が集積することで脳心血管疾患の高リスク群となる点、また、肥満の介入によりこれらの代謝異常や、さらには脳心血管疾患発症リスクが軽減する可能性があることから、その対策の重要性が認識されている。しかしながら、メタボリックシンドロームにおける腹部肥満の重要性のみがあまりにも注目されたため、非肥満者への対策が軽視される風潮がある。今後は、肥満者に対する減量対策はもちろんのこと、非肥満者においても高血圧、糖尿病、脂質異常症、喫煙などの脳心血管疾患の各危険因子、およびその集積をより重視した予防対策が必要であろう。

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ABSTRACT

Relationship between abdominal obesity, accumulation of metabolic abnormalities and risk of cardiovascular disease: An 11-year follow-up of middle-aged Japanese men

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This study investigated the relationship between metabolic syndrome and the incidence of cardiovascular disease (CVD) in middle-aged Japanese men. The study participants were 2,903 male employees (35-60 years old) of a metal-products factory in Japan. At the baseline examination, 252 participants (8.7%) were diagnosed as having metabolic syndrome (MetS). The incidence of CVD was surveyed in annual medical examinations or with questionnaires by mailing during an 11-year follow-up, and was confirmed by medical records. During the follow up, 82 CVD events occurred. In the participants with MetS, the risk of CVD events was significantly higher than those without MetS even after adjusting for the following confounding factors: age, smoking habits, alcohol intake, and regular exercise (hazard ratio, 2.26; 95% CI, 1.27 to 3.93). Compare to the healthy non-obese participants, the hazard ratio (95% CI) of the incidence of CVD was 3.82 (1.77-8.24) for non-obese participants with metabolic abnormalities and 4.81 (2.25-10.3) for obese participants with metabolic abnormalities. Our findings suggest that MetS is a significant risk factor for the development of CVD in middle-aged Japanese men. However, not only the participants with MetS, but also non-obese participants with metabolic abnormalities should be considered as high risk for CVD.

Key Words : *cohort study, cardiovascular disease, obesity, metabolic syndrome*

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