socioeconomic status have a greater waist circumference (7). A recent Whitehall II study, with an average 14-year-follow-up, showed an association between chronic work stress and the metabolic syndrome, more exposure to a state of low support with job strain being associated with a greater risk of the metabolic syndrome even after adjustment for employment grade and health behavior (8).

Many epidemiologic investigations have used waist circumference or waist-to-hip ratio as an anthropometric measurement index of abdominal obesity, which is closely related to the metabolic syndrome. Rosmond et al (9) and Rosmond & Björntorp (10) reported that inferior work conditions, such as less satisfaction with work management, less influence on work situations, and a lack of attempts to alter work situations, were associated with an increased waist-to-hip ratio.

In our previous cross-sectional investigation on Japanese employees, we found no statistically significant correlation between job demand–control and body mass index (BMI) or waist-to-hip ratio (11). However, we believe that a follow-up study would better clarify the influence of job demand–control on anthropometric measures, waist circumference, or waist-to-hip ratio, since, for example, considerable time must elapse before any changes in anthropometric measurements become apparent after exposure to certain work conditions. In addition, in the past decade, many companies in industrial countries have been trying to dynamically outrun others in the global economy race by introducing various managerial innovations, such as just-in-time production and total quality management (12). As a result, we can expect a rapid change in the work stress perceived by employees.

Therefore, in this study, we compared the results of two psychosocial work characteristics of the same persons in investigations conducted at an interval of 6 years and examined how changes in job demand–control affected the workers' anthropometric measurements.

Study population and methods

In our study, nonmanual and manual employees working for an aluminum-products factory in a rural area of Japan were asked to reply to the Japanese version of the job content questionnaire (13), about the status of job demand–control–support as individual psychosocial work characteristics. The survey was conducted twice, first from April 1996 through March 1997 and then from April 2002 through March 2003. On both occasions, only the persons who had provided their written consent to participate were included in the investigation. The selected workers were aged 30 to 53 years at the time of the first examination so that they were under 60 years of age, namely, the retirement age of the factory, at the time of the second examination. The participation rate of the first examination was 91.4% of the registered workers, or 2821 men and 1701 women, excluding pregnant women, as of 1 May 1996. Altogether 121 men and 39 women out of this population missed the opportunities or refused to consent to having their waist circumference measured. Before the second examination, 186 men and 184 women had resigned and 185 men had been transferred, and consequently they were excluded from the follow-up. Furthermore, 72 men and 97 women who did not reply to the second job content questionnaire or failed to undergo the second waist circumference measurement were also excluded.

Altogether, we included 2200 men and 1371 women as eligible participants whose data from the questionnaire and anthropometric measurements at both examinations were available and who had given complete replies to the questions concerning the confounding factors, such as sedentary job, shift work, and other health behavior, at the first examination. Managers and professionals accounted for 14% of all the men, whereas only 2% of the women were managers or professionals.

Job strain was calculated as a value of job demand divided by job control. The median value of each psychosocial work characteristic of the participants from the age of 30 to 53 years did not change between the two surveys. The median values of the job demand scores, the job control scores, and the scores for worksite support were 66, 32 and 23 for the men and 60, 32, and 22 for the women, respectively. But the median values of the job strain scores slightly changed, from 0.485 for the men and 0.533 for the women in the first examination to 0.500 for the men and 0.536 for the women, respectively, in the second examination. The scores for job control, job demand, worksite support, and job strain in each examination were dichotomized at the median value for the men and women separately and then categorized into three groups as follows: group I: low score in both the first and second examinations, group II: low score in the first examination and high score in the second (or high in the first and low in the second), and group III: high in both the first and second examinations (figure 1).

Anthropometric measurements

Anthropometric measurements were conducted within a month before or after the questionnaire survey on both occasions, the weight, height, and waist circumference of the participants being measured with them wearing light clothes. The BMI (kg/m^2) of the participants was calculated by dividing their weight by their height squared. The waist circumference (centimeters) was

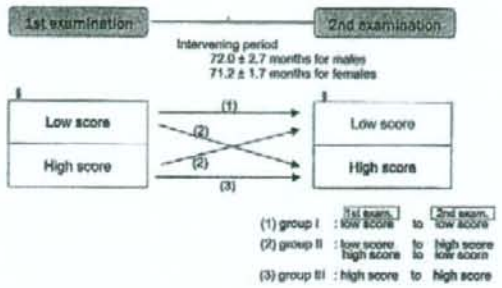

Figure 1. Categorization according to the change in psychosocial work characteristics. [§ = The scores for job control, job demands, worksite support, and job strain (demand and control) in each examination were dichotomized at the median value for 2200 men and 1371 women after those with no job content questionnaire or anthropometric measurement data on either occation were excluded or who resigned or transferred after the 1st examination.]

measured at the umbilicus level by experienced nurses. Underwear worn to correct body shape was removed.

Sedentary job and shift work as other work characteristics

Sedentary job was categorized into three groups according to the average number of sedentary hours per workday in the previous year ("<1 hour", "≥1 and ≤4 hours", and "≥5 hours"). The three-shift workers who worked nights were categorized as a shift work group, as opposed to a nonshift work group. No female worker in the factory was engaged in three-shift work.

Other health behavior

Queries were made about several lifestyle factors. The workers were classified as "non- or ex-smokers" and "current smokers". Alcohol consumption was measured in terms of grams of ethanol consumed per week and was categorized into five groups for the men (ie, no drinking, 1–175 g/week, 176–350 g/week, 351–525 g/week, and ≥526 g/week). As only five women ingested more than 350 grams of alcohol per week, alcohol consumption was re-categorized into three groups as follows: nondrinker, 1–175 g/week, and ≥175 g/week. Exercise for the men was classified as "almost no exercise", "light exercise", "brisk and sweating exercise once or twice a week" and "brisk and sweating exercise more than three times a week". The degree of education for the men was determined by the total years of education and was classified as "<11 years", "11–12 years", "13–14 years", and "≥15 years" of education. Since relatively few women participated in brisk and sweating exercise more than three times a week or had more than 15 years of education, exercise and education were re-categorized into three groups for the women ("almost no exercise", "light exercise", and "brisk and sweating exercise" and "<11 years", "11–12 years", and "≥13 years", respectively). Marital status was divided into "married" and "previously or never married".

This study was approved by the Ethics Committee of the Kanazawa Medical University.

Statistical analyses

The data were analyzed separately for the men and women using an SAS program package (SAS Inc, Cary, NC, USA). Changes in BMI and waist circumference were expressed as (second examination value – first examination value) / first examination value. The BMI and waist circumference in the first examination, the change in BMI, and the change in waist circumference were compared among different groups using a general linear model. The data for sedentary job, shift work, smoking habits, alcohol consumption, exercise, education, and marital status (inquired about in the first examination) were adopted as potential confounding factors.

Logistic regression analyses were used to calculate the odds ratios of the change in BMI and the change in waist circumference above the 75th percentile according to changing job strain; they were 0.0458 and 0.0600 for the men and 0.0456 and 0.1080 for the women, respectively.

Results

The mean period from the first to the second examination of the job content questionnaire was 72.0 (SD 2.7) months for the men and 71.2 (SD 1.7) months for the women.

Table 1 shows the differences in the mean values for age, BMI, waist circumference, and psychosocial work characteristics in the first examination between the workers with complete data from the two surveys and those for whom only data from the first examination were available. For the men, those who participated in both examinations were younger and had lower job control than those who participated only in the first examination. For the women, the latter group was younger and had

Table 1. Mean levels and standard deviations (SD) of the body mass index (BMI), waist circumference, and psychosocial work characteristics at the first examination for those who participated in both the baseline and the follow-up examinations and those who participated only at the baseline.

	Men							Women						
	N	Participation at baseline and in follow-up		N	Participation at baseline only		P-value	N	Participation at baseline and in follow-up		N	Participation at baseline only		P-value
		Mean	SD		Mean	SD			Mean	SD		Mean	SD	
Age	2200	41.8	6.4	778	42.7	6.8	<0.01	1371	41.7	6.3	378	43.9	7.7	<0.01
BMI (kg/m²)		23.2	2.8	778	23.3	2.8	0.42		22.4	3.2	378	22.6	3.4	0.24
Waist (cm)		79.6	7.7	657	80.2	7.4	0.09		71.7	8.7	328	73.3	9.9	<0.01
Job control		65.2	10.0	751	66.3	10.4	0.02		58.6	10.0	348	58.1	10.4	0.35
Job demand		32.0	4.8	761	32.0	4.7	0.82		31.6	5.0	357	31.7	5.0	0.81
Worksite support		21.8	3.2	748	21.8	3.1	0.78		21.3	3.3	370	21.2	3.8	0.74
Job strain		0.504	0.118	740	0.495	0.119	0.06		0.557	0.141	329	0.567	0.174	0.33

Table 2. Body mass index (BMI) and waist circumference in the first examination according to the change in the psychosocial work characteristics. (group I = low score in both the first and second examinations, group II = low score in first examination and high score in second examination or high score in first examination but low score in second examination, group III = high score in both the first and second examinations)

	Men					Women				
	N	BMI (kg/m²)		Waist (cm)		N	BMI (kg/m²)		Waist (cm)	
		Unadjusted	Adjusted[a]	Unadjusted	Adjusted[b]		Unadjusted	Adjusted[a]	Unadjusted	Adjusted[b]
Job control										
Group I	883	23.0	23.5	79.1	80.6	569	22.4	23.2	71.7	72.0
Group II	635	23.1	23.6	79.1	80.4	442	22.4	23.1	71.5	71.8
Group III	702	23.5	23.8	80.8	81.5	360	22.4	23.3	72.2	72.4
P-value		<0.01	0.17	<0.01	0.05		0.98	0.86	0.50	0.62
Job demand										
Group I	591	23.3	23.8	80.3	81.8	371	22.3	23.1	72.1	72.6
Group II	731	23.0	23.5	78.8	80.2	509	22.4	23.2	71.1	71.6
Group III	878	23.3	23.8	79.9	81.1	491	22.5	23.2	72.1	72.5
P-value		0.03	0.04	<0.01	<0.01		0.66	0.89	0.12	0.17
Worksite support										
Group I	615	23.3	23.8	79.5	81.0	496	22.5	23.3	71.9	72.0
Group II	802	23.2	23.6	79.6	80.9	510	22.5	23.2	71.7	71.8
Group III	783	23.2	23.6	79.7	80.9	365	22.1	22.9	71.6	71.7
P-value		0.60	0.39	0.91	0.90		0.14	0.20	0.86	0.86
Job strain										
Group I	619	23.4	23.8	80.5	81.5	358	22.3	23.1	72.3	72.6
Group II	801	23.1	23.6	79.4	80.6	554	22.6	23.3	71.7	72.0
Group III	780	23.1	23.7	79.2	80.7	459	22.4	23.1	71.4	71.8
P-value		0.22	0.46	<0.01	0.07		0.36	0.58	0.35	0.46

[a] Adjusted for age, sedentary job, shift work (only men), smoking, alcohol, exercise, education, and marital status in model 1.
[b] Adjusted for the factors listed for model 1 and also BMI in the first examination.

slenderer waists. The mean scores for job control, job demand, and worksite support among the workers who participated in both examinations were 65.2 (SD 10.0), 32.0 (SD 4.8), and 21.8 (SD 3.2), respectively, for the men and 58.6 (SD 10.0), 31.6 (SD 5.0), and 21.3 (SD 3.3), respectively, for the women. These scores did not differ very much from the scores of other large population studies of Japanese (14) and Belgians (15).

Regarding the association between psychosocial work characteristics and lifestyle at the first examination, there were no differences in smoking habits or alcohol consumption between the low and high psychosocial

Table 3. Change in body mass index (BMI) and waist circumference according to changes in job control, job demand, and worksite support. (group I = low score in both the first and second examinations, group II = low score in first examination and high score in second examination or high score in first examination but low score in second examination, group III = high score in both the first and second examinations)

	Men		Women	
	Change in BMI [a]	Change in waist circumference [b]	Change in BMI [a]	Change in waist circumference [b]
Job control				
Group I	0.009	0.018	0.021	0.061
Group II	0.013	0.022	0.020	0.057
Group III	0.011	0.016	0.017	0.050
P-value	0.36	0.16	0.56	0.32
Job demand				
Group I	0.009	0.016	0.019	0.049
Group II	0.010	0.017	0.018	0.057
Group III	0.012	0.021	0.019	0.055
P-value	0.39	0.18	0.92	0.50
Worksite support				
Group I	0.012	0.018	0.017	0.056
Group II	0.012	0.019	0.021	0.061
Group III	0.009	0.017	0.019	0.049
P-value	0.48	0.84	0.65	0.21

[a] Adjusted for age, sedentary job, shift work (only men), smoking, alcohol, exercise, education, and marital status in model 1.
[b] Adjusted for the factors listed for model 1 and also for BMI in the first examination.

work characteristic groups of either gender. More men in the high job-strain group had standing work, shift work, no regular exercise, and shorter education and were not married in comparison with the men in the low job-strain group. The women in the high job-strain group had more standing work, less regular exercise, and shorter education than those in the low job-strain group. The men in the low worksite-support group had more standing work and shorter education than those in the high worksite-support group. No difference between the low and the high worksite-support groups was found for the women (data not shown).

Table 2 on page 291 shows the mean BMI levels and waist circumference values according to the subgroups of job control, job demand, worksite support, and job strain in the first examination. For the men, both the BMI and waist circumference were larger in group III than in group I for job control and similarly larger in group I and III than in group II for job demand. As regards job strain, group I had the largest waist circumference among the three groups. For the women, there were no statistically significant differences in BMI or waist circumference among the subgroups of any of the psychosocial work characteristics. After adjustment for potential confounding factors, these differences did not change much for either gender.

The associations of the change in BMI and the change in waist circumference (after adjustment for the confounding factors) with job control, job demand, worksite support, and job strain are shown in table 3 and table 4. No significant difference was found in the change in BMI among the three different groups of the psychosocial work characteristics for either gender. The change in waist circumference was significantly higher in group III for job strain than in groups I and II among the men, and also a marginally significant similarity was found for the women. There was no significant interaction between job strain and the other work conditions (ie, sedentary work and shift work) with respect to the values of the change in BMI or the change in waist circumference. In the analyses of the relationship between job strain and the change in BMI and the change in waist circumference, BMI was categorized into slender, moderate, and overweight groups. Hereupon the moderate group denoted the mean value plus or minus one standard deviation of the BMI in the first examination. The ranges of the slender, moderate, and overweight groups were <20.38 kg/m², 20.38–26.02 kg/m², and ≥26.03 kg/m² for the men and <19.18 kg/m², 19.18–25.66 kg/m², and ≥25.67 kg/m² for the women, respectively. For the men, the proportions of people in the overweight group at the first examination who gained weight or had an increase in their waist circumference during the period between the two examinations were 53.1% (BMI) and 59.3% (waist). The rates were lower than those in the slender and moderate groups at the first examination. The change in BMI in the overweight group at the first examination was also smaller than that in the slender or moderate group for both genders.

On the other hand, the change in waist circumference increased in all of the BMI categories of slender, moderate, and overweight at the first examination. The change in waist circumference among the men was larger in group III than that in group I or group II. The change in waist circumference in group III was similarly larger than that in group I or group II for both the moderate and overweight women in the first examination.

For those who lost weight during the interval between the first and second examinations, no significant difference in the change in BMI or the change in waist circumference was found among the three job-strain groups (data not shown).

Table 5 shows the odds ratios of the change in BMI and the change in waist circumference above the 75th percentile according to the changes in job strain. Regarding the change in waist circumference for both genders, group III showed a significantly higher rate of change than group I. The odds ratios were 1.13 [95% confidence interval (95% CI) 0.87–1.46] in group II and 1.39 (95% CI 1.07–1.79) in group III for the men and 1.27 (95%

Table 4. Change in body mass index (BMI) and waist circumference in relation to job strain according to the BMI category in the first examination. (job-strain group I = low score in both the first and second examinations, job-strain group II = low score in first examination and high score in second examination or high score in first examination but low score in second examination, job-strain group III = high score in both the first and second examinations)

BMI in the first examination	Change in BMI					Change in waist circumference				
	Persons with weight gain (%)	Job-strain group I	Job-strain group II	Job-strain group III	P-value	Persons with waist increase (%)	Job-strain group I	Job-strain group II	Job-strain group III	P-value
Slender[a]										
Men (<20.38 kg/m²) (N=345)[b]	65.2[c]	0.011	0.016	0.020	-	65.5[c]	0.023	0.009	0.015	-
Women (<19.18 kg/m²) (N=170)[b]	62.9[c]	0.012	0.019	0.022	-	60.6[c]	0.040	0.064	0.059	-
Moderate[a]										
Men (20.38–26.02 kg/m²) (N=1523)[b]	62.4[c]	0.012	0.016	0.015	-	66.6[c]	0.031	0.033	0.032	-
Women (19.18–25.66 kg/m²) (N=1003)[b]	63.5[c]	0.016	0.023	0.025	-	66.1[c]	0.021	0.030	0.042	-
Overweight[a]										
Men (≥26.03 kg/m²) (N=332)[b]	53.1[c]	−0.008	−0.009	0.008	-	59.3[c]	−0.005	0.002	0.007	-
Women (≥25.67 kg/m²) (N=198)[b]	60.6[c]	0.013	0.012	0.022	-	65.7[c]	0.073	0.074	0.084	-
Total										
Men	-	0.008[d]	0.010	0.013	0.26	-	0.013[d]	0.019	0.022	0.03
Women	-	0.018[d]	0.019	0.020	0.89	-	0.046[d]	0.055	0.065	0.04

[a] BMI category: slender = <(mean−SD), moderate = (mean−SD) - (mean+SD), overweight = ≥(mean+SD).
[b] Number of persons in each BMI category.
[c] Percentage of persons in each BMI category with weight gain or waist increase during the period.
[d] Adjusted for age, sedentary job, shift work (only men), smoking, alcohol, exercise, education, and marital status in model 1.
[e] Adjusted for the factors listed for model 1 and also BMI in the first examination.

Table 5. Odds ratios (OR) and their 95% confidence intervals (95% CI) for the change in body mass index (BMI) and waist circumference above the 75th percentile according to job-strain change. (group I = low score in both the first and second examinations, group II = low score in first examination and high score in second examination or high score in first examination but low score in second examination, group III = high score in both the first and second examinations)

Job strain	Change in BMI[a]				Change in waist circumference[a]			
	Men		Women		Men		Women	
	OR	95% CI	OR	95% CI	OR	95% CI	OR	95% CI
Group I	1	-	1	-	1	-	1	-
Group II	1.05	0.82–1.35	1.05	0.77–1.44	1.13	0.87–1.46	1.27	0.90–1.78
Group III	1.23	0.95–1.59	0.92	0.66–1.29	1.39	1.07–1.79	1.78	1.26–2.52

[a] Adjusted for age, sedentary job, shift work (only men), smoking, alcohol, exercise, education, and marital status in model 1.
[b] Adjusted for the factors listed for model 1 and also for BMI in the first examination.

CI 0.90–1.78) in group II and 1.78 (95% CI 1.26–2.52) in group III for the women.

Discussion

This 6-year follow-up study showed that the change in waist circumference in job-strain group III increased more than that in job-strain group I, even though no statistically significant association was noted between the psychosocial work characteristics and the change in BMI. Moreover, the prevalence rate of the change in waist circumference above the 75th percentile among both the men and women increased progressively in order from group I to group II to group III of job strain after adjustment for age, BMI, sedentary job, shift work, smoking, alcohol, exercise, education, and marital status. The results of this study showed that high job strain may contribute to abdominal obesity.

Although two previous cross-sectional investigations referred to the association between job strain and abdominal obesity among men (16, 17), one review noted that the association was not clear (18). Recently,

Brunner et al (19) showed that job strain partly caused abdominal obesity, because a dose–response relationship between work stress and obesity was found in their 19-year follow-up study. With an increased number of cases classified as iso-strain (ie, the lowest tertile of worksite support combined with job strain, evaluated on four occasions during the follow-up), the incidences of a high BMI of ≥30 kg/m² for both genders and a large waist circumference of >102 cm among the men and >88 cm among the women increased.

Rosmond & Björntorp (20) and Rosmond (21) have suggested that, as one of the pathophysiological mechanisms underlying the association between job strain and waist circumference, psychosocial disadvantage pressure affects the activity of the hypothalamic–pituitary–adrenal axis and, as a result, increases the cortisol level. This increase in the cortisol level then causes abdominal fat to accumulate and therefore leads to an increased waist circumference.

The measurement of saliva cortisol has frequently been used to examine the neuroendocrine excretion status in field studies. Those who perceived high chronic work overload (22) and high social stress (23) showed increased cortisol levels on awakening in the morning. The mean cortisol level of workdays was higher in a low job-control group than in a high job-control group among the men, and, among the women with a low socioeconomic status, the mean cortisol level of the workdays was higher in a high job-demand group than in a low job-demand group (24). In addition, for men, a positive association was found between the waist-to-hip ratio and the cortisol response to waking (25), and, for women, the urinary cortisol level per 24 hours was increased (26).

It is well known that there is an inverse correlation between socioeconomic status and BMI among people in developed countries (27). Although people with a low socioeconomic status are expected to be under high work stress (ie, low job control), the influence of job demand–control on BMI is obscure. Job strain has not been found to be associated either with BMI in various large cross-sectional population studies among Japanese–Americans, working women, and Canadian white-collar workers (28–30), nor with weight gain in a 5-year prospective study on civil servants (31). High job demand or low job control was not associated with weight gain in the past year (32). On the other hand, according to the data collected from the 32 worksites in a cross-sectional study, the women in the high-strain group had a higher BMI than those in the other groups, but this trend was not found for the men (33). A study in France found a relationship between high job demand and overweight among women, but not among men (34). Kivimäki et al (31) pointed out the bidirectional effect of work stress on BMI as one reason for the inconsistent correlation between work stress and BMI, because work stress could not only lead to hyperphagia but also to hypophagia. The population of our study may have included some workers who lost weight due to work stress. However, no significant difference in the change in BMI or the change in waist circumference existed among the three job-strain groups for those who lost weight during the intervening period. It is possible that some of the workers who lost weight due to severe anorexia caused by work-stress-induced depression were not able to participate in the examinations because they were not working on the occasions and consequently were excluded from the participants.

Notably, in spite of focusing on the same target population, a 19-year follow-up study found work stress to be related to weight gain, while another 5-year follow-up study found no such relationship (19, 31). The former study noted the accumulated effect of work stress, and the observation lasted for a longer period in comparison with that of the latter study. In addition, another study pointed out that the evaluation of job strain at a single point in time possibly underestimated the association between job strain and CHD (35). Thus our previous cross-sectional study may similarly have underestimated the association between job strain and the waist-to-hip ratio.

No changes in the mean scores of job demand, job control, or worksite support were found between the first and second examinations in our study. Prior research showed stability for scores of the job content questionnaire on two occasions, before and after an average interval of 6.6 years among 2490 Europeans who remained in the same job (15). In addition, the scores of the work characteristics for the same persons did not change appreciably over a 5-year interval in Japan (36). However, the Japanese study also found that the scores were less stable when there was a position change even within the same company. Likewise, about-one-third of the participants of our study showed some changes in the scores of the job content questionnaire during the 6-year period, shifting from the high group to the low group of psychosocial work characteristics and vice versa.

We categorized the persons with improved psychosocial work characteristics and those who showed deterioration in this respect together as group II, because they were likely to have experienced greater changes in other work conditions, such as workplace, shift work, and sedentary job than group I and group III did. In addition, it is difficult to know exactly when the particular change in psychosocial work characteristics started, as the effect of a change in an anthropometric measurement does not manifest itself immediately but, rather, takes time.

Adopting many factors as potential covariates may weaken the relationship between job strain and the change in BMI or the change in waist circumference.

For instance, many people in the high-strain group had less regular exercise in association with an increased BMI and waist circumference.

Incidentally, the job-strain scores of the women in this study were higher than those of the men. Furthermore, the women rarely changed their occupations and tended to remain in a relatively low employment job. These facts may have affected the results of this follow-up study, making the relationship clearer between job strain and the change in waist circumference.

Some investigations have also shown that work stress, when evaluated in a job demand–control model, was associated with glucose metabolism, blood coagulation, and fibrinolytic function as risk factors of cardiovascular disease in Japan, as well as in other developed countries (37). Obesity (BMI ≥30 kg/m^2) is certainly less common in Japan than in western Europe and the United States (38). However, the proportions of overweight (BMI ≥25 kg/m^2) Japanese men are 32.7% for those 40–49 years of age and 30.8% for those 50–59 years of age. The corresponding proportions for Japanese women are 17.9% and 24.1%, respectively. In addition, one in every two men and one in every five women are said to have suspected or potential metabolic syndrome (39). Therefore, the national government has begun to make a concerted effort to tackle the metabolic syndrome by making the measurement of waist circumference mandatory when people aged 40–74 years are screened in medical checkups (40).

There were several potential limitations in this study. First, we evaluated and classified psychosocial work characteristics for the same people using the job content questionnaire twice at an interval of 6 years, but we have no data on the fluctuation of the psychosocial work characteristics during this period. Similarly, although we used the scores of several confounding factors at the first examination, we did not record their subsequent changes. In addition, as about 25% of the men and about 20% of the women of all of the participants either retired, were transferred, did not fill out the questionnaire completely, or refused to participate in this examination, they were excluded from the follow-up survey. This exclusion may have conceivably affected the results, although a large population of both genders was available for continued follow-up. Second, the waist circumference was lower for group III in the first examination. This initial low score may possibly have contributed to the increase in waist circumference in the second examination. However, especially for the women, the difference in the change in waist circumference among the three job-strain groups was larger than the difference affected by the initial potential bias. Third, we did not make a dietary survey with respect to weight gain. However, a large-scale survey of 25 000 Japanese by Kawakami et al (41) did not reveal any evident connection between job strain and total energy intake, even after adjustment for age, educational background, and occupation. Fourth, since the participants of our study were all from a single company, whether our results can be generalized or not will have to be determined in further studies.

In conclusion, we examined psychosocial work characteristic twice for 2200 men and 1371 women with an interval of 6 years between the examinations. We admit that there was a bidirectional influence of work stress on BMI and waist circumference, and yet the results of our study showed that high job strain increased the change in waist circumference even when several potential confounding factors were taken into consideration. This result supports the finding of Brunner et al (19), who reported that chronic work stress may contribute to abdominal obesity. Hence it is important that we take measures to reduce the chronic work stress of workers in terms of preventing atherosclerotic and other diseases triggered by the metabolic syndrome.

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OBSERVATIONS

BMI May Be Better Than Waist Circumference for Defining Metabolic Syndrome in Japanese Women

We previously addressed sex differences in the associations between anthropometric indexes of obesity and blood pressure and showed that blood pressure was more strongly related to BMI than to waist circumference in Japanese women (1). As hypertension is a major component of metabolic syndrome in Japanese patients, a similar sex difference may exist in the association between anthropometric indexes and the metabolic components of metabolic syndrome. We investigated the possible sex differences of these associations.

Study subjects consisted of 2,935 men and 1,622 women between 35 and 59 years of age; 13% of the women were postmenopausal. Detailed information regarding this study population has been provided elsewhere (1). Metabolic abnormalities were determined using the Japanese criteria of metabolic syndrome (2). In a multiple linear regression analysis (supplemental Table 1A, available in an online appendix at http://dx.doi.org/10.2337/dc07-0309), both BMI and waist circumference were related independently to serum triglyceride and HDL cholesterol level. The relationship of anthropometric indexes to fasting plasma glucose (FPG) level was weaker than that to blood pressure (1) and to serum lipid levels. In multiple logistic regression analyses (supplemental Table 1B), waist circumference was more strongly associated with dyslipidemia (defined as having high triglycerides or low HDL cholesterol) and high FPG in men, whereas BMI was more strongly associated with dyslipidemia in women. Although high FPG was more strongly associated with waist circumference in women, the association was weaker than the relationship between BMI and hypertension (1) or dyslipidemia. The presence of two or more of three metabolic abnormalities (hypertension, dyslipidemia, and high FPG) was observed in 22.6% of men and 9.1% of women. The risk ratio of having accumulations of two or more metabolic abnormalities was higher for waist circumference than for BMI in men, whereas it was higher for BMI in women. When BMI and waist circumference were included simultaneously in a model, waist circumference showed a stronger association than BMI with the accumulation of metabolic abnormalities in men, and only BMI showed an independent association in women. The results were similar using the International Diabetes Federation definition (3) to determine the metabolic abnormalities.

In lean Asian women, for whom subcutaneous fat has a stronger influence on waist circumference(4), BMI may be a more appropriate index for total and abdominal fat. Thus, we should pay more attention to BMI in defining metabolic syndrome in Asian women.

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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
（日循予防誌　44：1－9，2009）

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

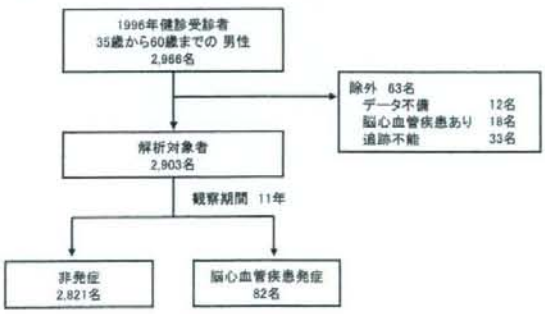

図1 研究デザイン

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[9, 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。

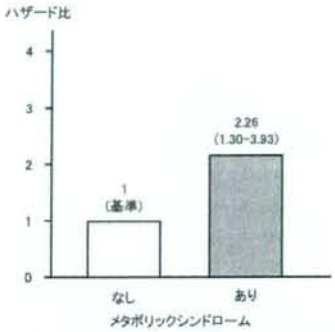

図2 メタボリックシンドロームの有無による脳心血管疾患発症の多変量調整ハザード比

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*		
	なし	あり	P†
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乗検定にて行った。

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

	腹部肥満なし*			腹部肥満あり*		
代謝異常合併数	0	1	2,3	0	1	2,3
N	1,052	764	288	202	345	252
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	69.0／21.8／5.2／4.0
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[7-10]。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

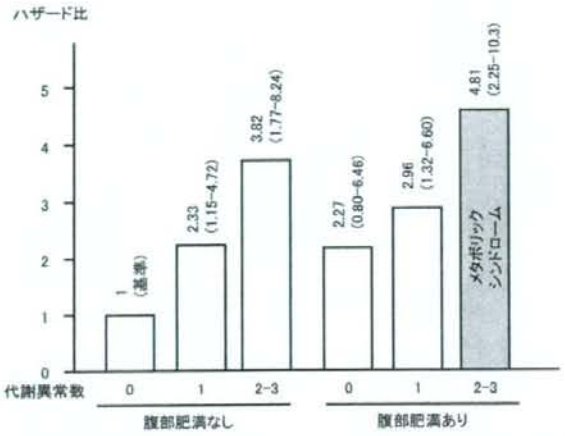

図3　ベースラインの腹部肥満の有無および代謝異常合併数と脳心血管疾患発症の多変量調整ハザード比
年齢、喫煙、飲酒、運動習慣で調整。腹部肥満、代謝異常は日本内科学会のメタボリックシンドローム診断基準で判定した。

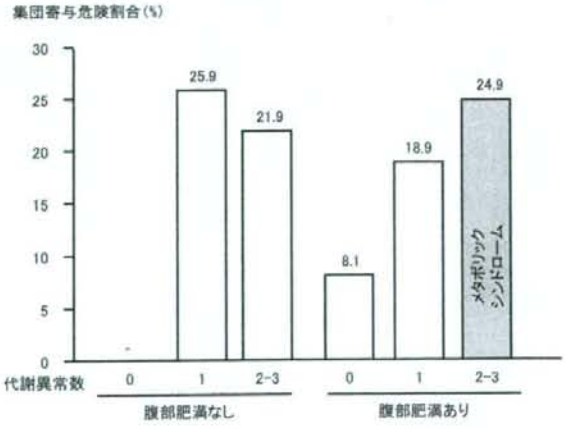

図4　ベースラインの腹部肥満の有無および代謝異常合併数ごとの脳心血管疾患発症に対する集団寄与危険割合
腹部肥満、代謝異常は日本内科学会のメタボリックシンドローム診断基準で判定した。

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[12]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[1]。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[2)~4)]、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[3),4)]。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[7]。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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愛媛県南西部地区コホート研究

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研究要旨：愛媛県南西部地域における循環器疾患発症登録と同地域における約 4.5 千人の 10 年間に及ぶコホート研究から、最近の脳卒中発症率の動向と脳卒中発症に及ぼす肥満関連要因について検討した。平成 11～19 年までの 9 年間をそれぞれ 3 年間毎の 3 期に分け、各期の年齢調整済み脳卒中発症率を男女別に算出したところ、男女とも脳卒中発症率は減少傾向であった。また、ウエスト周囲径と BMI に関して脳卒中発症にかかる性年齢調整済ハザード比は有意ではなかった。当域において脳卒中発症にかかる肥満の影響は現時点では小さいことが示唆された。

A. 研究目的

わが国の循環器疾患対策の中で依然として脳卒中対策はもっとも重要な課題である。脳卒中死亡率は（脳血管障害）は減少してきたとはいえ、高齢化に伴いその患者数は増加の一途をたどっている。また、要介護の原因の一位は脳卒中であることから、生活習慣病予防に加えて介護予防、ひいては医療費適正化の面から最優先されるべき課題といえる。しかしながら、脳卒中の一次予防対策の評価を検討するためには、死亡率ではなく発症率による評価が適切であると考えられるが、本邦ではその整備が遅れ健康指標としての活用は十分ではない。また、メタボリックシンドローム対策に備え、その有効性についての評価は、長期にわたるコホート研究が必要と考えられる。

本研究は、地域の循環器疾患発症登録とその中でのコホート研究の成果を合わせ、循環器疾患対策の評価について検討を行う。

B. 研究方法

本研究は、愛媛県南西部に位置する O 市（人口 50,774 人,平成 19 年）を対象集団として実施する、当地域においては、平成 11 年（1999 年）から地域の基幹病院を対象に、心筋梗塞と脳卒中の発症登録を実施してきた。今年度、さらに平成 17 年 1 月から 19 年末までの循環器疾患発症登録調査を実施し、これまでのデータと併せ、脳卒中発症率の推移を検討した。発症登録は、厚生労働省研究班循環器発症登録基準に準じ各病院へ出張採録を行った。脳卒中発症基準は、「急激に神経症状が出現し、症状が 24 時間以上持続もしくは 24 時間以内に死亡したもの」とし、臨床症状として、①意識障害、②四肢麻痺、③感覚麻痺、④言語障害、⑤皮質症状（視力障害、失認・失行）、検査所見として①心電図、②剖検、③画像診断、等を把握した。

また、1996～1998 年に設定したコホート（5161 人）を 2007 年末まで追跡し、腹囲・BMI の脳卒中罹患に及ぼすハザード比を算出した。

本研究計画は愛媛大学における医の倫理委員会による承認を受け、コホート研究に関しては書面による同意を得て実施している。

C. 研究結果

1. 地域脳卒中発症登録の結果

平成 11 年～平成 13 年を第 1 期、平成 14 年～平成 16 年を第 2 期、平成 17 年～平成 19 年を第 3 期とし、第 1 期を基準集団として、第 2 期、第 3 期の全脳卒中の年齢調整発症率を求めた。また第 3 期については CT 分類別の脳卒中病型を求めた。

脳卒中の発症件数は第 1 期で 155 件、第 2 期で 133 件、第 3 期で 189 件であった。病型別にみると、第 1 期では脳出血が 23 件（14.8%）、脳梗塞が 125 件（80.6%）、くも膜下出血が 7 件（4.5%）であった。第 2 期では脳出血が 23 件（17.3%）、脳梗塞が 92 件（69.2%）、くも膜下出血が 18 件（13.5%）であった。第 3 期では脳出血が 29 件（15.3%）、脳梗塞が 152 件（80.4%）、くも膜下出血が 8 件（4.2%）であった。

年齢調整別脳卒中発症率（40 歳以上）を見ると、男性では第 1 期 3.16、第 2 期 2.24、第 3 期 2.43 であった。女性では第 1 期 1.74、第 2 期 1.64、第 3 期 1.20 となった（図 1）。また、CT 分類による脳卒中の病型分類では、穿通枝系脳梗塞が 52.8%と過半数を占め、出血を含めると 73.1%となった（図 2）。

2. コホート研究の結果

同城における脳卒中既往歴のない 40 歳以上の 4536 人を 2007 年末まで追跡した。その間、新規の脳卒中発症者 145 人を把握した。平均追跡期間は 10.1 年であった。この間の粗発症率は、1000 人年当たり男性 4.73、女性 2.34 であった。

ベースラインのウエスト周囲径別に脳卒中発症に対するハザード比を求めた。ウエスト周囲径 75cm 未満の群に比べて、85-89.9cm の群の脳卒中発症ハザード比が 1.49 (0.93-2.39)とやや高くなったが、90cm 以上の群では上昇を認めなかった。同様に、BMI についても検討行ったが、このウエスト周囲径の傾向とほぼ同様であった。

本コホートにおいて、ウエスト周囲径や BMI レベルに代表される肥満関連の指標と脳卒中発症との明らかな関連は認めなかった。

D. 考察

90 年代後半からの当地域の年齢調整済み脳卒中発症率は男女とも減少傾向にあった。発症率は一次予防の効果を見る上で、重要な指標となる。このような脳卒中発症率の推移は他の地域に準じた結果であった。同地域において脳卒中発症率の低下は、血圧のコントロールが改善したこと、医療体制が整ったことと、脳卒中予防に関する健康教育や保健指導の成果が考えられた。また、CT 分類では、穿通枝系脳梗塞と出血が全体の 4 分の 3 となったことから、いわゆる農村型の脳卒中が依然として多数を占めていることが特徴といえる。

一方、コホート研究の結果からは肥満関連要因は脳卒中の発症に大きな影響を与えているとは言い難い。この地域の脳卒中の病型などを考え合わせると、血圧要因の強さを伺わせた。脳梗塞に絞った解析、もしくは、比較的若い世代においての解析を今後はしていくことも重要であり、そのためには長期の追跡が必要となる。

今後も脳卒中発症の状況を検討し、脳卒中予防対策に活かせる検討を行っていく必要がある。