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【 ORIGINAL ARTICLE 】

Impact of Metabolic Syndrome on the Mortality Rate among Participants in a Specific Health Check and Guidance Program in Japan

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Abstract:

Objective In Japan, the Specific Health Check and Guidance (Tokutei-Kenshin) program was started in 2008 to decrease the social burden related to metabolic syndrome (MetS). However, so far this program has not been found to have any impact on the mortality rate.

Methods The subjects consisted of individuals who participated in the Tokutei-Kenshin in seven districts between 2008 and 2015. Using a National database of death certificates, we identified those who might have died and then further confirmed such deaths with the collaboration of the regional National Health Insurance agency and public health nurses. The diagnosis of MetS was made according to the Japanese criteria. The causes of death were classified by ICD-10. Mortality risk was evaluated after adjusting for age, sex, smoking, alcohol intake and past medical history such as stroke, heart disease and kidney disease.

Results Among the total of 664,926 subjects, we identified 8,051 fatal cases by the end of 2015. The crude death rate was 1.6% for those with MetS, 1.3% for those with preliminary metabolic syndrome, and 1.1% those without MetS. In MetS, the adjusted hazard ratio (95% confidence interval) was 1.08 (1.02-1.15) for all-cause and 1.39 (1.22-1.58) for cardiovascular disease mortality when the reference was for those without MetS.

Conclusion The death rate was found to be significantly higher among the participants with MetS.

Key words: metabolic syndrome, cardiovascular disease (CVD), all-cause mortality rate, obesity, social burden

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Introdcution

Obesity and metabolic syndrome (MetS) are considered to be a pre-disease state as they are often associated with conventional risk factors of cardiovascular disease (CVD) such as diabetes mellitus (DM), hypertension, and dyslipidemia (1-3). Since 2008, Specific Health Check and Guidance (Tokutei-Kenshin) has been advocated to decrease this health burden in Japan, particularly regarding lifestyle-related dis-

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ease (1). In this nationwide screening program, the early detection and early modification of lifestyle for those identified to have MetS was the primary goal. We have been conducting many epidemiological studies mainly related to chronic kidney disease (CKD) (4-8) and also the all-cause mortality risk (9-13) by using baseline variables. However, the impact of the baseline MetS on mortality has not yet been examined.

The risk of death due to CVD will increase with obesity (3), but the deaths related to malnutrition, infection, and malignancies are higher among those with less obese people. The relationship between MetS and survival is therefore U-shaped (14). Currently, the leading cause of death is related to cancer in Japan with an increasingly elderly population (15). MetS is also related to cancer deaths (2).

In the present study, we examined the mortality risk by the presence of MetS among the participants of Tokutei-Kenshin both got all-caused and deaths due to CVD and cancer. For this purpose, we extended the follow-up period and added one large cohort from a previous report (15). Furthermore, we confirmed the presence of MetS by using consecutive follow-up screening.

Materials and Methods

Screened subjects

The Specific Health Check and Guidance program, which is called Tokutei-Kenshin in Japanese, was started on 2008 in Japan for adult population ranging from 40 to 74 years of age. The details of this cohort have been published previously (2, 15). In the present study as a second cohort, we included the new participants up to 2014, and extended the follow-up to 2015. Databases included in this study were from Fukushima, Ibaraki, Toyonaka, Fukuoka, Miyazaki, Okinawa, and Niigata and ethical approval was obtained from the respective institute review board. Part of the data were sent to a data center called the NPO Japan Clinical Research Support Unit to be verified. Eligible participants visited a pre-assigned clinic or hospital and responded to a questionnaire regarding a past history of stroke, cardiac disease, and kidney disease, lifestyle habits such as smoking, alcohol intake, and regular exercise such as walking, dietary habits, and medications for hypertension, DM, and dyslipidemia. The data were verified and created the standard analysis file (SAF) by Okinawa Heart and Renal Association (OHRA).

The participants who underwent screening are eligible for public support for the standard health checks. The baseline variables were height, weight, waist circumference, blood pressure, fasting blood glucose, hemoglobin A1c, triglyceride, serum high-density lipoprotein (HDL) cholesterol, low-density lipoprotein (LDL) cholesterol, glutamyl oxaloacetic transaminase, glutamate pyruvate transaminase, gamma-glutamyl transpeptidase, hemoglobin, uric acid, serum creatinine, dipstick urine test for proteinuria, hematuria, and glycosuria. Proteinuria was coded as (−), (±), (1+), (2+), and (3+ and over) and positive proteinuria was defined as 1+ and over. The serum creatinine was measured using the enzymatic method. The glomerular filtration rate was calculated using the formula of the Japanese Society of Nephrology (16). The reference levels for explaining participants as abnormal were set at 150 mg/dL (triglyceride), 40 mg/dL (HDL cholesterol), 150 mg/dL (LDL cholesterol), 7.0 mg/dL (uric acid), 110 mg/dL (fasting blood glucose), and 6.1% [hemoglobin (Hb) A1C], respectively. Blood pressure was measured in all participants using a standard sphygmomanometer. Hypertension was defined as 140/90 mmHg and over or on antihypertensive medication. DM was defined as HbA1c ≥ 6.1% Japan Diabetes Society (JDS) or on medication for DM. Obesity was defined as a body mass index (BMI) ≥25 kg/m^2. The value for HbA1c was estimated as a National Glycohemoglobin Standardization Program (NGSP) equivalent value calculated with the following formula: HbA 1c (%) = HbA1c (JDS) (%) +0.4%. A diagnosis of MetS was made according to Japanese criteria: waist circumference (men ≥85 cm, women ≥90 cm) plus two or three abnormal values in blood sugar metabolism [fasting blood glucose ≥100 mg/dL or HbA1c ≥5.2% by 2012 (JDS), HbA1c ≥5.6% by NGSP since 2013], lipid (triglyceride ≥150 mg/dL, or HDL cholesterol<40 mg/dL), and blood pressure (systolic ≥130 mmHg, or diastolic ≥85 mmHg) (17). HbA1c (NGSP) was obtained as HbA1c (JDS, %) plus 0.4%. Those who have a waist circumference (men ≥85 cm, women ≥90 cm) plus one of the abnormalities in blood glucose metabolism, lipid, or blood pressure were grouped into the preliminary MetS (pre-MetS). The rest of the participants were considered to not have MetS. Participants without waist circumference data (N=22,430, 3.4% of the total) were excluded from the analysis.

We further examined the one-year changes of MetS such as MetS (-/-), MetS (-/+), MetS (+/-), and MetS (+/+). Among the screened subjects who were re-examined next year (N=414,358), the prevalence of MetS (-/-), MetS (-/+), MetS (+/-), and MetS (+/+) was 80.7% (N=332,938), 5.3% (N=22,263), 5.3% (N=22,761) and 8.7% (N=36,396), respectively.

National database of death certificate

With the permission of the Ministry of Health and Welfare, we obtained the database of the death certificates between 2008 and 2015 (total registered were about 10 million). The dataset included sex, birthdate, place of death, data of death and causes of death by ICD-10. The database was solely used and managed by Chiho Iseki (OHRA) and the principal analyses to identify those who died among screened subjects were completed by March 2018. Afterwards, further analyses were done using a SAF without any personal identifier.

By using two registries, we identified candidates who died after participating in the screening program in each district. Identifiers such as sex, birthdate, date of death and the

Table 1. Demographics of the Screened Subjects (n=664,926). Specific Health Check was Performed between April 1, 2008 to March 31, 2015.

Variables	Total (n=664,926)				Men (n=284,320)				Women (n=380,606)			
	Count	Median	25%	75%	Count	Median	25%	75%	Count	Median	25%	75%
Age, years	664,508	64	58	69	284,105	65	58	69	380,403	64	58	69
Body height, cm	664,434	157	151.1	163.9	284,066	164.7	160.5	169.0	380,368	152.2	148.4	156.0
Body weight, kg	664,445	57.1	50.4	65.0	284,075	64.3	58.4	70.9	380,370	52.4	47.4	58.0
Body mass index, kg/m^2	664,431	23.1	21.0	25.4	284,068	23.7	21.9	25.8	380,363	22.6	20.5	25.0
Waist circumference, cm	637,464	84	78	90	275,648	85.5	80.2	91.0	361,816	83.0	76.0	89.0
Systolic blood pressure, mmHg	664,291	129	118	140	284,014	130	120	140	380,277	128	116	138
Diastolic blood pressure, mmHg	664,263	76	70	83	284,002	79	70	86	380,261	74	68	81
AST, U/L	660,943	22	19	27	282,674	23	20	28	378,269	22	19	25
GPT, U/L	660,940	19	15	25	282,674	21	16	29	378,266	17	14	22
γ-GTP, U/L	664,272	24	17	40	283,904	34	23	57	380,368	20	15	29
Triglyceride, mg/dL	664,423	103	74	148	284,043	114	80	168	380,380	96	70	135
HDL-cholesterol, mg/dL	664,449	59	50	71	284,076	54	46	65	380,373	63	54	74
LDL-cholesterol, mg/dL	664,374	124	104	145	284,026	119	99	140	380,348	127	108	148
Fasting blood glucose, mg/dL	455,411	94	88	102	194,213	97	90	107	261,198	92	86	99
Hemoglobin, g/dL	233,562	13.6	12.7	14.5	92,097	14.6	13.8	15.4	141,465	13.1	12.4	13.7
HbA1c (NGSP), %	636,289	5.3	5.0	5.6	272,609	5.3	5.0	5.6	363,680	5.2	5.0	5.5
Serum creatinine, mg/dL	565,684	0.7	0.6	0.8	242,864	0.80	0.70	0.90	322,820	0.60	0.53	0.70
eGFR, mL/min/1.73m^2	565,684	74.7	64.3	85.8	242,864	73.8	64.3	85.0	322,820	75.0	64.2	89.0
Uric Acid, mg/dL	500,511	5.2	4.3	6.2	215,728	6.0	5.2	6.9	284,783	4.6	3.9	5.3
Proteinuria, ≥1+(%)	662,760	5.7			283,322	8.0			379,438	3.9		
Hematuria, ≥1+(%)	394,620	16.4			170,120	9.4			224,500	21.7		
Glycosuria, ≥1+(%)	662,782	2.7			283,295	4.8			379,487	1.1		
Lifestyle												
Smoking, %	664,332	15.6			284,024	27.6			380,308	6.6		
Drinking, %	628,095	46.5			267,032	70.3			361,063	28.9		
Walking, %	513,804	49.4			215,608	51.5			298,196	47.9		
Exercise, %	515,664	40.9			216,253	45.1			299,411	37.8		
Medication												
Hypotensives, %	664,341	29.7			284,028	32.8			380,313	27.4		
Lipid lowering, %	664,333	14.9			284,022	10.8			380,311	18.0		
Diabetes mellitus, %	664,331	5.5			284,023	7.5			380,308	4.0		
Past history												
Stroke, %	628,350	3.7			267,840	5.0			360,510	2.7		
Heart disease, %	628,006	5.7			267,724	7.4			360,282	4.5		
Kidney disease, %	628,342	0.8			267,815	1.0			360,527	0.7		

AST: aspartate aminotransferase, GPT: glutamyl transpeptidase, NGSP: National Glycohemeglobin Standardization Program

place of death were used and confirmed at each center that had performed the screening. We then further verified the candidates with the collaboration of the regional National Health Insurance agency and public health nurses. All other participants were considered to be alive by the end of 2015.

Statistical analysis

The data were analyzed using the SAS/STAT software program (version 6.03, SAS Institute, Tokyo, Japan). An multivariable logistic analysis on death was done after adjusting for age, sex, BMI, estimated glomerular filtration rate (eGFR), proteinuria, and other pertinent variables. The hazard ratio (HR) and 95% confidence interval (CI) were calculated on the risk of death by the presence of metabolic syndrome. A p value of less than 0.05 was considered to be statistically significant in all analyses.

Results

A total of 664,926 screened subjects from 7 districts are summarized in Table 1. The measurement of serum creatinine was not mandatory; however, it was available in 85.1% of the total cohort (N=565,684). The median eGFR was 74.7 mL/min/1.73 m^2 and the median BMI was 23.1 kg/m^2 (23.7 kg/m^2 in men and 22.6 kg/m^2 in women). Proteinuria was positive in 5.7%. The estimated prevalence of CKD defined as eGFR<60 mL/min/1.73 m^2 and/or proteinuria was 19.0%, 23.8% in men and 15.3% in women.

We identified 8,051 (1.2 % of the total) deaths (Table 2). Among those without waist circumference data (n=22,430, 3.4% of the total), we identified 190 deaths (0.8%). The number of deaths according to the absence or presence of MetS are summarized n men and women (Supplementary

Table 2. Causes of Death among Subjects Participated at the 2008 Screening and Confirmed Death by the End of 2014 (n=8,051). Specific Health Check was Performed between April 1, 2008 to March 31, 2015.

Causes of death, ICD-10	Total	Men	Women
Infection, A00-B99	141	78	63
Neoplasm, C00-D48	4,159	2,611	1,548
Hematology & Immunology, D50-D89	26	17	9
Endocrine, Nutrition and Metabolism, E00-E90	64	48	16
Psychology, Behavior, F00-F99	16	12	4
Nervous system, G00-G99	121	71	50
Circulatory, I00-I99	1,616	1,044	572
Respiratory, J00-J99	437	320	117
Gastrointestinal, K00-K93	272	193	79
Skin and dermal, L00-L99	4	1	3
Musculoskeletal, M00-M99	52	16	36
Genitourinary, N00-N99	44	32	12
Pregnancy related, O00-O99	1	0	1
Congenial anomaly, Q00-Q99	4	2	2
Miscellaneous, R00-R99	131	86	45
Accident, toxic, S00-T98	920	593	327
Unknown	43	27	16
Total	8,051	5,151	2,900

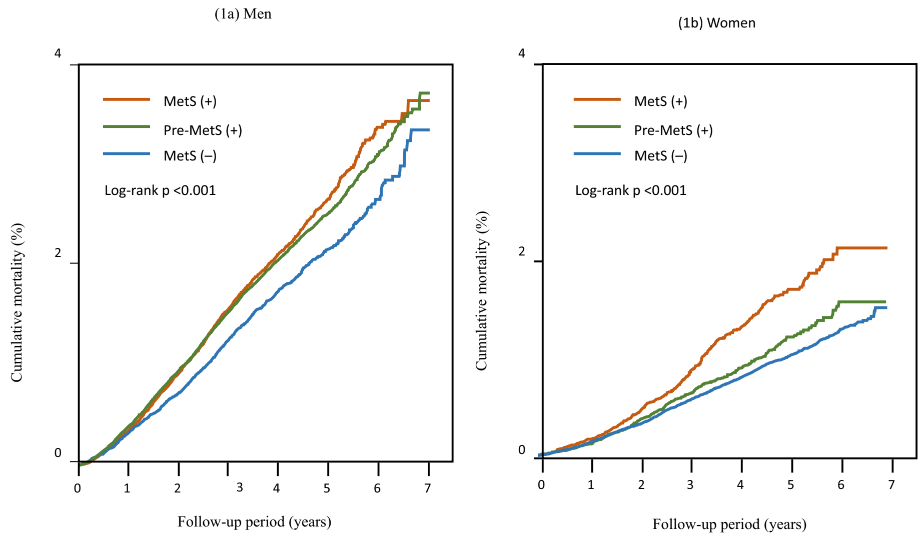

Figure 1. 1a(men) and 1b (women) show the all-cause mortality rate (%) among MetS (-), pre-MetS (+), and MetS (+).

material 1). The prevalence of MetS was highest in the 70 to 74 years of age group for both men and women. The leading cause of death was due to the presence of a neoplasm in both genders. It was 51.7% of the total, 50.7% in men and 53.4% in women. The second cause of death was circulatory; 20.4% of the total, 21.1% in men and 19.2% in women. The baseline characteristics of those who confirmed death were also summarized by gender (Supplementary material 2).

The cumulative survival curves are shown for all-cause mortality in Fig. 1a (men) and Fig. 1b (women). The subjects with MetS showed a higher mortality rate than those without MetS among both men and women. In addition, the cumulative survival curves for cardiovascular death are shown in Fig. 2a (men) and Fig. 2b (women). The subjects with MetS showed a higher cardiovascular mortality rate in both men and women (Supplementary material 3).

The death risk by MetS was summarized in Table 3. The crude death rate was 1.6% for metabolic syndrome, 1.3% for preliminary metabolic syndrome, and 1.1% for those without metabolic syndrome. In the metabolic syndrome group, the adjusted hazard ratio (95% confidence interval) was 1.08 (1.02-1.15) for all-cause and 1.39 (1.22-1.58) for cardiovascular disease when the reference was for those without metabolic syndrome. There was no significant impact of MetS on cancer-related death.

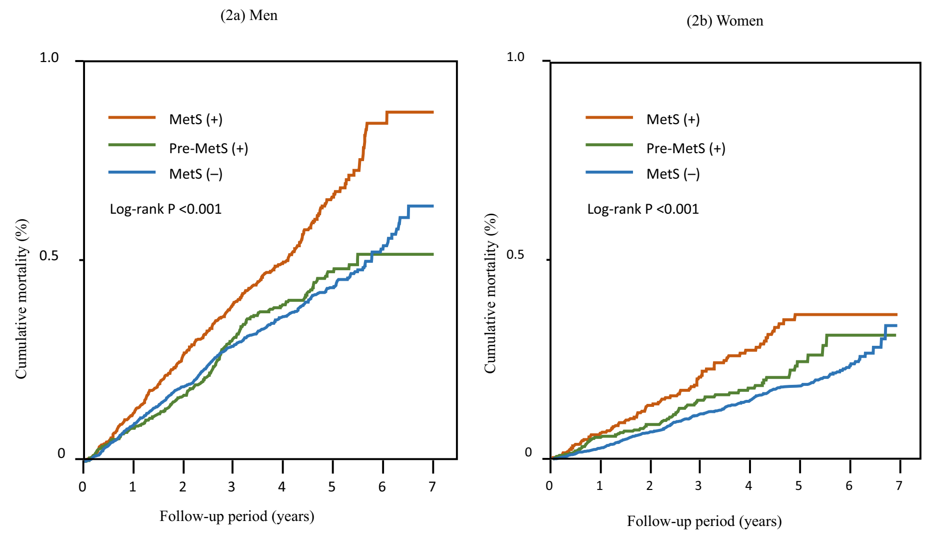

Figure 2. 2a (men) and 2b (women) show the cardiovascular mortality rate (%) among MetS (-), pre-MetS (+), and MetS (+).

Table 3. Death Rate and Effect of Metabolic Syndrome on Survival.

	Metabolic syndrome (-)	Preliminary metabolic syndrome	Metabolic syndrome (+)
Number of participant	444,122	95,559	102,989
Number of all-cause death (%)	5,013 (1.1%)	1,222 (1.3%)	1,628 (1.6%)
Death Rate, per 1,000 person-year	3.0	3.5	4.6
Un-adjusted hazard ratio (95% CI)	1.00 (reference)	1.18 (1.11-1.25)	1.53 (1.45-1.62)
Adjusted for age and sex	1.00 (reference)	0.88 (0.83-0.94)	1.10 (1.04-1.17)
Adjusted for age, sex, and others*	1.00 (reference)	0.91 (0.85-0.97)	1.08 (1.02-1.15)
Number of cardiovascular death (%)	924 (0.2%)	264 (0.3%)	398 (0.4%)
Death Rate, per 1,000 person-year	0.6	0.8	1.1
Un-adjusted hazard ratio (95% CI)	1.00 (reference)	1.37 (1.20-1.58)	2.00 (1.78-2.25)
Adjusted for age and sex	1.00 (reference)	1.04 (0.91-1.20)	1.46 (1.29-1.65)
Adjusted for age, sex, and others*	1.00 (reference)	1.08 (0.94-1.25)	1.39 (1.22-1.58)
Number of cancer-related death (%)	2,612 (0.6%)	654 (0.7%)	799 (0.8%)
Death rate, per 1,000 person-year	1.6	1.9	2.2
Un-adjusted hazard ratio (95% CI)	1.00 (reference)	1.21 (1.11-1.32)	1.46 (1.34-1.58)
Adjusted for age and sex	1.00 (reference)	0.91 (0.84-0.998)	1.05 (0.97-1.14)
Adjusted for age, sex, and others*	1.00 (reference)	0.94 (0.86-1.03)	1.06 (0.97-1.15)

CI: confidence interval

Others* denotes for smoking, alcohol intake, past medical history such as stroke, heart disease and kidney disease.

The Death Risks were summarized with the change of metabolic syndrome status (Table 4). There was a significantly higher mortality risk among those with MetS (+/+) than those with MetS (-/-). Those with MetS (+/+) showed a significantly higher mortality risk of CVD in both genders. (Supplementary material 4, Fig. 3). However, cancer-related death only increased in men with MetS (+/-). (Supplementary Table 4). In contrast, the mortality risk of CVD among those with MetS (+/-) did not significantly increase in both genders (Supplementary material 4, Fig. 3).

Discussion

This study is the first to examine the impact of MetS on mortality from the participants of the Specific Health Check and Guidance Program in Japan. Both studies using cross-sectional and subsequent data suggested the presence of MetS to be associated with high risk of mortality, in particular CVD deaths. Furthermore, an improvement in MetS symptoms was associated with a reduced risk for CVD death. The present results may support the notion the early detection and early intervention for those individuals with MetS should be encouraged to undergo lifestyle modifica-

Table 4. Death Risks were Summarized with the Change of Metabolic Syndrome Status.

The change of metabolic syndrome status	MetS (-/-)	MetS (-/+)	MetS (+/-)	MetS (+/+)
Number of participant	332,938	22,263	22,761	36,396
Number of all-cause death (%)	2,532 (0.8%)	245 (1.1%)	260 (1.1%)	416 (1.1%)
Death Rate, per 1,000 person-year	1.8	2.7	2.8	2.9
Un-adjusted hazard ratio (95% CI)	1.00 (reference)	1.51 (1.33-1.73)	1.59 (1.40-1.81)	1.66 (1.50-1.84)
Adjusted for age and sex	1.00 (reference)	1.67 (1.02-1.33)	1.23 (1.09-1.40)	1.23 (1.10-1.36)
Adjusted for age, sex, and others*	1.00 (reference)	1.15 (1.01-1.32)	1.20 (1.05-1.38)	1.18 (1.06-1.32)
Number of cardiovascular death (%)	486 (0.2%)	63 (0.3%)	45 (0.2%)	109 (0.3%)
Death rate, per 1,000 person-year	0.3	0.6	0.5	0.8
Un-adjusted hazard ratio (95% CI)	1.00 (reference)	2.02 (1.55-2.62)	1.43 (1.05-1.94)	2.25 (1.83-2.77)
Adjusted for age and sex	1.00 (reference)	1.60 (1.23-2.09)	1.14 (0.84-1.55)	1.71 (1.39-2.12)
Adjusted for age, sex, and others*	1.00 (reference)	1.50 (1.13-1.99)	1.16 (0.85-1.60)	1.57 (1.26-1.97)
Number of cancer-related death (%)	1,358 (0.4%)	120 (0.5%)	147 (0.7%)	202 (0.6%)
Death Rate, per 1,000 person-year	1.0	1.3	1.6	1.4
Un-adjusted hazard ratio (95% CI)	1.00 (reference)	1.39 (1.15-1.67)	1.69 (1.42-2.00)	1.51 (1.31-1.76)
Adjusted for age and sex	1.00 (reference)	1.06 (0.88-1.28)	1.30 (1.09-1.54)	1.11 (0.95-1.29)
Adjusted for age, sex, and others*	1.00 (reference)	1.07 (0.88-1.30)	1.28 (1.07-1.53)	1.10 (0.94-1.29)

CI: confidence interval

Others* denotes for smoking, alcohol intake, past medical history such as stroke, heart disease and kidney disease.

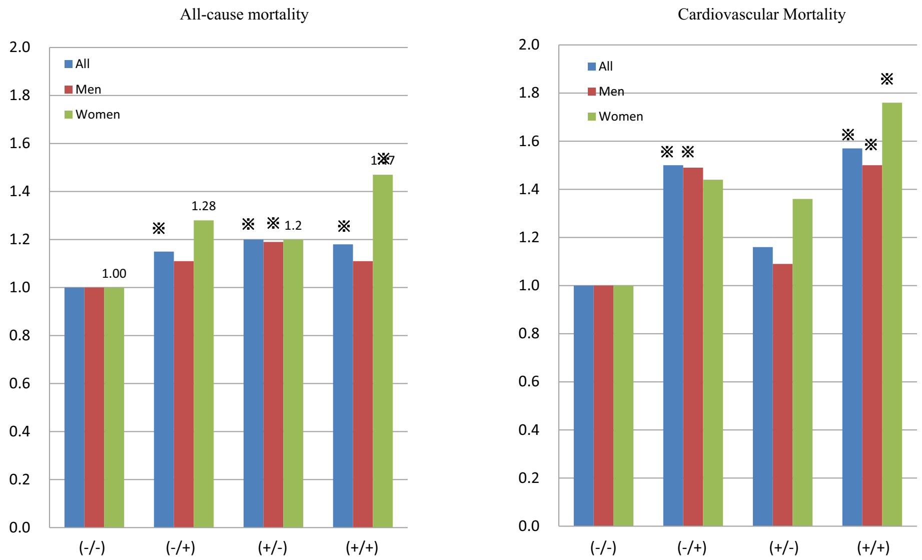

Figure 3. Death risks for all-cause cardiovascular disease are summarized with the change of MetS status such as (-/-), (-/+), (+/-), and (+/+) among all, men, and women. *p<0.05 (compared to MetS (-/-).

tion.

The association between MetS and all-cause and cardiovascular mortality has been reported in previous studies (18). However, the strength of the association varies by the characteristics of studied population such as age, gender and ethnicity and it is not well investigated in the Japanese population. The present study showed a significant association between MetS, and all-cause and cardiovascular mortality in both genders in the population including a wide-range of ages. Recently, Watanabe et al. reported that MetS was also related to the cancer deaths, particularly in women (2). However, we could not confirm any significant influence of MetS on the cancer-related death risk even after using the data of two visits. Further investigation on this point is warranted.

We have been studying the screened subject concerning CKD and its related medical conditions both cross-sectional (4-8) and longitudinal studies (9-13). Obesity is often associated with conventional risk factors of cardiovascular disease such as DM, hypertension, dyslipidemia, sleep apnea, and hyperuricemia. Therefore, CKD is common in obese people, and the higher the BMI, the higher the incidence of end-stage renal disease (ESRD). Obesity is increasing in developing countries such as the Asian region (19, 20). DM is the leading cause of ESRD in many countries and recently also in China (21). The current study showed that MetS including obesity is a common risk for CVD and mortality in a community-based population.

In people with obesity, ESRD risk competes with the death risk as a higher BMI was associated with a lower mortality. Further analyses with data concerning nutritional status would be necessary. Since half of the deaths in this cohort were related to malignancies, it is possible that people with emaciation (BMI<18.5 kg/m^2) were associated with protein-energy wasting (PEW) (22). The mortality rate is lower in women, even among those in the 60 to 74 year old age group, thus suggesting factors other than the effect of sex hormone. Gender difference also exists in the relationship between BMI and incidence and prevalence of CKD and ESRD (23-25). In Japan, the ESRD incidence in men is higher than that in women probably reflecting differences in lifestyle related factors such as diet, exercise, smoking, and alcohol intake. The current study also showed a slight gender-difference in the association between the metabolic status and mortality. This point should be investigated further.

Strengths and limitations

The strength of the present study is that subjects were all participants of a large nation-wide screening program. They were examined using same set of clinical and laboratory tests and the same format questionnaire of lifestyle-related variables. We obtained permission from each district through the steering committee members and had the support of the co-medical staff. Identifying those who died during the study period was done using the National death certificate database and confirmed in each district. We believe that this cohort is fairly well represents the status of the whole nation, if not perfectly. Furthermore, we evaluated the impact of MetS using follow-up screening.

There are several limitations associated with study. First, we used the Japanese criteria for the diagnosis of MetS. Waist circumference was measured in 95.9% of the total (men 96.9%, women 95.1%). It is the mandatory data for the current Japanese criteria of MetS. It is quite different from that of the National Cholesterol Education Program (NCEP) ATP III which defines abdominal obesity as a waist circumference of ≥102 cm in men and ≥88 cm in women (26). We identified a better correlation between CKD and MetS with the modified NCEP criteria. Secondly, this screening program is a voluntary one and is self-selected. The relationship between deaths related to malignancy remained unknown. However, we believe that only a few, if any of the screened people have self-evident illness such as advanced cancer. Thirdly, there are obvious regional differences in incidence and prevalence of CVD, ESRD, and death rate. In this study, we obtained data from only 7 out of 47 districts from the north to south of Japan. Further studies are necessary to elucidate the factors related to regional difference in the death rate. Fourth, the participants of this screening are restricted to middle to old aged (40 to 74 years old) person. The policy was based on the assumptions of the benefit of early detection and, thereafter modification of lifestyle related diseases such as DM, hypertension, dyslipidemia, CVD and probably CKD. Actually, lifestyle changes to non-smoking, healthy weights, moderate alcohol drinking, physical activity and healthy eating habits were associated with a low incidence of proteinuria (27). In Norway, the CKD prevalence remained stable despite modest increases in DM and obesity, probably explained with marked improvements in blood pressure, lipid levels, and physical activity (28). We previously reported the benefit of dipstick proteinuria screening for the management of CKD (29). Similarly, we need further analysis to elucidate whether the early detection and intervention of those who were diagnosed to have MetS is truly effective.

Conclusions

The present study showed a significant relationship between the presence of MetS and the subsequent mortality risk both all-cause and CVD among the screened participants of the Specific Health Check and Guidance program in Japan. Early detection and proper management of MetS may prolong a person's lifespan, however, the benefits of intervention to address the problem of MetS remain to be elucidated in a future study.

The authors state that they have no Conflict of Interest (COI).

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