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Prevalence and Clinical Implication of Metabolic Syndrome in Chronic Heart Failure

– Report From MetS-CHF Study –

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Background: Metabolic syndrome (MetS) is a pathological condition with a clustering of metabolic components and is a well-known risk and prognostic factor for ischemic heart disease (IHD). However, the prevalence and clinical significance of MetS remain to be fully elucidated in chronic heart failure (CHF), an important clinical syndrome caused by various cardiac abnormalities.

Methods and Results: The present nationwide, large-scale clinical study enrolled 3,603 patients with stage C/D CHF from 6 institutes in Japan. First, the prevalence of MetS in CHF patients was demonstrated to be 45% in males and 19% in females, which is more than double compared with the general population in Japan. The CHF patients with MetS were characterized by younger age, higher prevalence of current smoking and drinking, IHD, and hypertensive heart disease, whereas the prevalence of HF with preserved ejection fraction and MetS was higher in elderly female patients. Next, the contribution of the metabolic components (waist circumference, hypertension, glucose intolerance/diabetes mellitus and dyslipidemia) was found to be comparable between the ischemic and the non-ischemic CHF patients.

Conclusions: The prevalence of MetS in CHF patients is more than double compared with the general population in Japan and suggest that the metabolic components may have a substantial effect on the development of both ischemic and non-ischemic CHF. (*Circ J* 2010; **74:** 2612–2621)

Key Words: Chronic heart failure; Metabolic syndrome; Obesity; Sex

Over the past decades, the prevalence of obesity, lifestyle diseases (eg, diabetes mellitus, dyslipidemia, hypertension, and metabolic syndrome (MetS)) and resultant cardiovascular disease has been rapidly increasing in Japan because of the westernization of lifestyle.[1] MetS is a pathological condition with clustering of metabolic components, including dysglycemia, elevated blood pressure, elevated triglyceride levels, low high-density lipoprotein (HDL) cholesterol levels and obesity.[2] It has been repeatedly demonstrated that MetS is substantially involved in the increased risk of atherosclerotic diseases with resultant poor prognosis after acute coronary syndrome.[3–9] Although recent studies have reported the relationship between MetS and congestive heart failure,[10,11] the prevalence and clinical significance of MetS in chronic heart failure (CHF) remain to be fully elucidated. CHF is a complex clinical syndrome that can result from any structural or functional cardiac disorders, including coronary artery disease, hypertensive heart disease, myocardial disease and valvular heart disease.[12] CHF is a clinical syndrome in which not only heart failure with

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preserved ejection fraction (HFPEF), but also heart failure with reduced ejection fraction (HFREF), is substantially involved.[13,14] Indeed, HFPEF and HFREF respectively account for approximately half of the CHF patients.[15,16]

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We have been conducting a nationwide clinical study supported by the Japanese government on the current status of CHF in Japan with special reference to MetS (MetS-CHF Study). This is the first report of our study, which addresses the prevalence and clinical significance of MetS in Japanese patients with CHF.

Methods

The ethical committees of each institute approved the study protocol and all patients provided written informed consent.

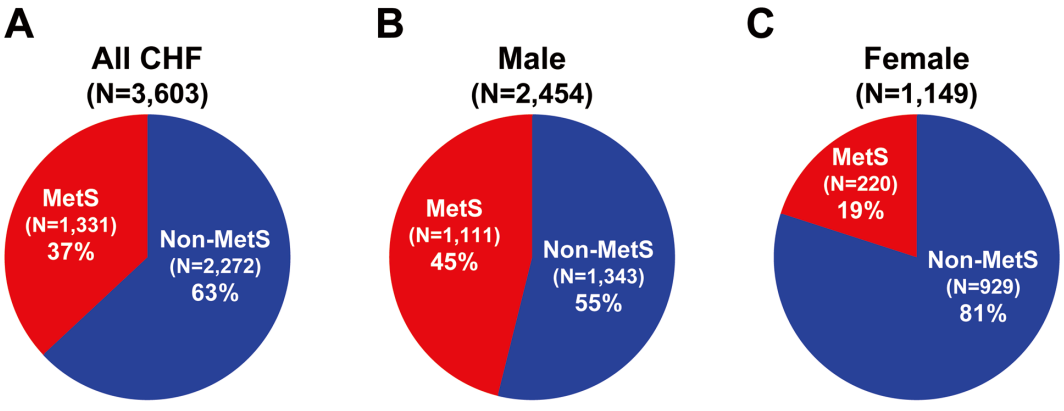
Study Population

Between September 2006 and December 2008 we enrolled 3,603 CHF patients in stages C/D according to the ACC/AHA Guidelines[12] from 6 institutes in Japan. For each patient, we prospectively collected from the participating hospitals

Table 1. Baseline Characteristics of Patients With Symptomatic CHF

	Male (n=2,454)	Female (n=1,149)	P value
Age (years)	67.9±0.2	71.1±0.4	<0.001
Cigarette smoking, n (%)			
Never	811 (48.9%)	856 (79.8%)	<0.001
Former	343 (20.7%)	153 (14.2%)	NS
Current	505 (30.4%)	64 (6.0%)	<0.001
Alcohol intake, n (%)			
Never	722 (30.7%)	760 (80.9%)	<0.001
Former	220 (11.2%)	35 (3.7%)	<0.001
Current	1,027 (52.1%)	144 (15.3%)	<0.001
BMI (kg/m^2)	23.1±0.1	22.1±0.2	<0.001
Waist circumference (cm)	86.7±0.2	81.9±0.4	<0.001
Blood pressure (mmHg)			
Systolic	125.7±0.4	126.3±0.6	NS
Diastolic	72.2±0.3	70.7±0.4	<0.001
Heart rate (beats/min)	71.8±0.3	74.7±0.4	<0.001
NYHA class			
I	490 (20.0%)	133 (11.6%)	<0.001
II	1,683 (68.9%)	814 (70.9%)	NS
III	246 (10.1%)	187 (16.3%)	<0.001
IV	24 (1.0%)	14 (1.2%)	NS
Stage C/D	2,381 (97.4%)/63 (2.6%)	1,113 (97.0%)/35 (3.0%)	NS
LVEF (%)	54.4±0.3	59.5±0.5	<0.001
HFREF (EF<50%)	797 (36.2%)	269 (25.7%)	<0.001
HFPEF (EF≥50%)	1,402 (63.8%)	777 (74.3%)	<0.001
SAS	5.7±0.04	4.6±0.06	<0.001
HT	1,876 (76.4%)	864 (75.2%)	NS
DM or fasting glucose ≥110 mg/dl	1,253 (51.1%)	526 (45.8%)	<0.01
Dyslipidemia	1,754 (71.7%)	816 (71.0%)	NS
IHD	1,264 (51.5%)	352 (30.6%)	<0.001
HHD	230 (9.4%)	126 (11.0%)	NS
CM	508 (20.7%)	216 (18.8%)	NS
VHD	494 (20.1%)	428 (37.2%)	<0.001
CHD	29 (1.2%)	32 (2.8%)	<0.001
Medications			
ACEI/ARB	1,793 (73.1%)	765 (66.6%)	<0.001
β-blocker	1,237 (50.4%)	507 (44.1%)	<0.001
Statin	876 (35.7%)	381 (33.2%)	NS

Values are mean±SEM.
CHF, chronic heart failure; BMI, body mass index; LVEF, left ventricular ejection fraction; HFREF, heart failure with reduced ejection fraction; EF, ejection fraction; HFPEF, heart failure with preserved ejection fraction; SAS, specific activity scale; HT, hypertension; DM, diabetes mellitus; IHD, ischemic heart disease; HHD, hypertensive heart disease; CM, cardiomyopathy; VHD, valvular heart disease; CHD, congenital heart disease; ACEI, angiotensin-converting enzyme inhibitor; ARB, angiotensin-receptor blocker.



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	General Population			CHF Patients
	Tanno and Sobetsu Study (Ref. 18)	Hisayama Study (Ref. 19)	Kanazawa Study (Ref. 20)	MetS-CHF Study
Male	18%	21%	16~21%	45%
Female	6%	8%	3~10%	19%

Figure 1. Prevalence of metabolic syndrome (MetS) in patients with chronic heart failure (CHF) was 37% of all patients with CHF (**A**), 46% of male patients (**B**) and 20% of female patients (**C**). Compared with the prevalence in the general population in the Tanno-Sobetsu,[18] Hisayama[19] and Kanazawa[20] studies, the prevalence of MetS was more than double (**D**).

the baseline demographic data, including age, sex, height, weight, waist circumference, coronary risk factors (blood pressure, lipid profile, fasting plasma glucose, smoking status), medications, comorbidities (previous myocardial infarction or stroke, dialysis, and atrial fibrillation) by use of a web data collection system (Tohoku Fujitsu, Sendai, Japan).

Definition of MetS

According to the new definition by the Japanese Committee for the Diagnostic Criteria of MetS in April 2005, we defined MetS as the presence of 2 or more abnormalities in addition to waist circumference (≥85 cm in males and ≥90 cm in females). Other abnormalities examined were dyslipidemia, hypertension, and glucose intolerance/diabetes mellitus. Dyslipidemia was defined as use of lipid-lowering drugs and/or elevated lipid levels (plasma triglycerides ≥150 mg/dl or HDL <40 mg/dl in men or 50 mg/dl in women). Glucose intolerance/diabetes mellitus was defined as use of antidiabetic drugs and/or fasting glucose ≥110 mg/dl. Hypertension was defined as use of antihypertensive drugs and/or systolic blood pressure ≥130 mmHg and/or diastolic blood pressure ≥80 mmHg.

Definition of CHF

In the present study, we included patients with stages C/D CHF defined by the ACC/AHA 2005 Guidelines (ie, they had developed symptoms of HF, at least NYHA class II).[12] According to the ESC 2007 Guideline, we further divided them into 2 groups: HFPEF (LV ejection fraction (EF) ≥50%, n=2,179) and HFREF (LVEF <50%, n=1,066).[17]

Data Collection

Baseline demographic data (age, sex, height, body weight, and waist), CHF stage, medications, including angiotensin-converting enzyme inhibitors (ACEI), angiotensin-receptor blockers (ARB), β-blockers, and statins, risk factors (hypertension, glucose intolerance/diabetes mellitus and dyslipidemia), blood pressure, pulse rate, blood data (lipid profile and glucose), and comorbidities (ischemic heart disease (IHD), hypertensive heart disease, cardiomyopathy, valvular heart disease, and congenital heart disease) were collected from the medical records. LVEF was measured by echocardiography.

Statistical Analysis

Continuous variables are expressed as mean±SEM. Comparisons between 2 groups were conducted with unpaired t-test for continuous variables and chi-test for categorical variables. Statistical analyses were performed using Prism 4 (GraphPad Software, La Jolla, CA, USA). $P<0.05$ was considered to be statistically significant.

Results

Characteristics of CHF Patients

Among the 3,603 consecutive patients with stage C/D CHF, there were 2,454 men (68%, 68±0.2 years) and 1,149 women (32%, 71±0.4 years) (**Table 1**). In total, 1,331 patients had MetS (37%) and 2,272 did not (63%) (**Figure 1A**, **Table 2**). Of the 2,454 male patients with CHF, 1,111 had MetS (45%) and 1,343 did not (55%) (**Figure 1B**, **Table 3**), and of the

Table 2. Comparison of Non-MetS and MetS Patients With Symptomatic CHF

	Total		
	Non-MetS (n=2,272)	MetS (n=1,331)	P value
Sex, n (%)			
Male	1,343 (59.1%)	1,111 (83.5%)	<0.001
Female	929 (40.9%)	220 (16.5%)	<0.001
Age (years)	69.7±0.3	67.6±0.3	<0.001
Cigarette smoking, n (%)			
Never	1,129 (63.6%)	538 (56.2%)	<0.001
Former	323 (18.2%)	173 (18.1%)	NS
Current	323 (18.2%)	246 (25.7%)	<0.001
Alcohol intake, n (%)			
Never	1,008 (55.7%)	474 (43.2%)	<0.001
Former	162 (9.0%)	93 (8.5%)	NS
Current	640 (35.3%)	531 (48.3%)	<0.001
BMI (kg/m^2)	21.2±0.1	25.5±0.2	<0.001
Waist circumference (cm)			
Male	81.2±0.2	92.8±0.2	<0.001
Female	77.9±0.3	97.1±0.5	<0.001
Blood pressure (mmHg)			
Systolic	123.6±0.4	129.8±0.5	<0.001
Diastolic	70.3±0.3	74.2±0.3	<0.001
Heart rate (beats/min)	72.8±0.3	72.6±0.4	NS
NYHA class			
I	354 (15.6%)	269 (20.3%)	<0.001
II	1,576 (69.6%)	921 (69.5%)	NS
III	303 (13.4%)	130 (9.8%)	<0.001
IV	32 (1.4%)	6 (0.4%)	<0.001
Stage C/D	2,193 (96.7%)/75 (3.3%)	1,301 (98.3%)/23 (1.7%)	<0.01
LVEF (%)	55.7±0.4	56.7±0.4	NS
HFREF (EF <50%)	700 (34.0%)	366 (30.8%)	NS
HFPEF (EF ≥50%)	1,357 (66.0%)	822 (69.2%)	NS
SAS	5.2±0.05	5.6±0.06	<0.001
HT	1,525 (67.1%)	1,215 (91.3%)	<0.001
DM or fasting glucose ≥110 mg/dl	890 (39.2%)	889 (66.8%)	<0.001
Dyslipidemia	1,402 (61.7%)	1,168 (87.8%)	<0.001
IHD	882 (38.8%)	734 (55.1%)	<0.001
HHD	192 (8.5%)	164 (12.3%)	<0.001
CM	477 (21.0%)	247 (18.6%)	NS
VHD	714 (31.4%)	208 (15.6%)	<0.001
CHD	49 (2.2%)	12 (0.9%)	<0.01
Medications			
ACEI/ARB	1,534 (67.5%)	1,024 (76.9%)	<0.001
β-blocker	1,058 (46.6%)	686 (51.5%)	<0.01
Statin	638 (28.1%)	619 (46.6%)	<0.001

Values are mean ± SEM.
MetS, metabolic syndrome. Other abbreviations see in Table 1.

1,149 female patients with CHF, 220 had MetS (19%) and 929 did not (81%) (**Figure 1C**, **Table 3**). The prevalence of MetS in the general Japanese population has been previously reported as approximately 20% in men and approximately 10% in women in the Tanno-Sobetsu Study, the Hisayama Study (males 58±11 years, females 59±11 years), and the Kanazawa Study (males 68±8 years, females 66±9 years),[7,18–20] so our results show a prevalence of MetS in Japanese CHF patients as more than double that of the general population (**Figure 1D**).

As shown in **Table 1**, the present stage C/D CHF patients were characterized by a higher prevalence of hypertension and dyslipidemia, followed by glucose intolerance/diabetes mellitus, in both sexes. Furthermore, the male CHF patients

Table 3. Comparison of Non-MetS and MetS Patients With Symptomatic CHF

	Male			Female		
	Non-MetS (n=1,343)	MetS (n=1,111)	P value	Non-MetS (n=929)	MetS (n=220)	P value
Age (years)	68.9±0.3	66.6±0.3	<0.001	70.8±0.4	72.6±0.7	<0.05
Cigarette smoking, n (%)						
Never	441 (48.6%)	370 (49.3%)	NS	688 (79.4%)	168 (81.6%)	NS
Former	195 (21.4%)	148 (19.7%)	NS	128 (14.8%)	25 (12.1%)	NS
Current	272 (30.0%)	233 (31.0%)	NS	51 (5.8%)	13 (6.3%)	NS
Alcohol intake, n (%)						
Never	402 (37.9%)	320 (35.3%)	NS	606 (81.0%)	154 (80.6%)	NS
Former	131 (12.3%)	89 (9.8%)	NS	31 (4.2%)	4 (2.1%)	NS
Current	529 (49.8%)	498 (54.9%)	NS	111 (14.8%)	33 (17.3%)	NS
BMI (kg/m^2)	21.3±0.2	25.3±0.2	<0.001	21.1±0.2	26.5±0.5	<0.001
Blood pressure (mmHg)						
Systolic	122.6±0.6	129.4±0.5	<0.001	125.1±0.7	131.6±1.4	<0.001
Diastolic	70.2±0.3	74.6±0.4	<0.001	70.4±0.04	72.2±0.9	NS
Heart rate (beats/min)	71.5±0.4	72.2±0.4	NS	74.7±0.6	74.7±1.0	NS
NYHA class						
I	240 (18.0%)	250 (22.6%)	<0.01	114 (12.3%)	19 (8.6%)	NS
II	929 (69.5%)	754 (68.2%)	NS	647 (69.7%)	167 (75.9%)	NS
III	149 (11.1%)	97 (8.8%)	NS	154 (16.6%)	33 (15.0%)	NS
IV	19 (1.4%)	5 (0.4%)	<0.001	13 (1.4%)	1 (0.5%)	NS
Stage C/D	1,296 (96.7%)/ 44 (3.7%)	1,085 (98.3%)/ 19 (1.7%)	<0.05	897 (96.7%)/ 31 (3.3%)	216 (98.2%)/ 4 (1.8%)	NS
LVEF (%)	53.3±0.5	55.8±0.5	<0.001	59±0.5	61.4±1.0	NS
HFREF (EF <50%)	468 (38.7%)	329 (33.2%)	<0.01	232 (27.3%)	37 (18.8%)	<0.05
HFPEF (EF ≥50%)	740 (61.3%)	662 (66.8%)	<0.01	617 (72.7%)	160 (81.2%)	<0.05
SAS	5.6±0.06	5.8±0.06	<0.05	4.6±0.07	4.5±0.1	<0.001
HT	870 (64.8%)	1,006 (90.5%)	<0.001	655 (70.5%)	209 (95.0%)	<0.001
DM or fasting glucose ≥110 mg/dl	506 (37.7%)	747 (67.2%)	<0.001	384 (41.3%)	142 (64.5%)	<0.001
Dyslipidemia	787 (58.6%)	967 (87.0%)	<0.001	615 (66.2%)	201 (87.3%)	<0.001
IHD	632 (47.1%)	632 (56.9%)	<0.001	250 (27.0%)	102 (46.4%)	<0.001
HHD	104 (7.7%)	126 (11.3%)	<0.01	88 (9.5%)	38 (17.3%)	0.001
CM	294 (21.9%)	214 (19.3%)	NS	183 (19.8%)	33 (15.0%)	NS
VHD	332 (24.7%)	162 (14.6%)	<0.001	382 (41.3%)	46 (20.9%)	<0.001
CHD	19 (1.4%)	10 (0.9%)	NS	30 (3.2%)	2 (1%)	NS
Medications						
ACEI/ARB	935 (69.6%)	858 (77.2%)	<0.001	599 (64.5%)	166 (75.5%)	<0.01
β-blocker	666 (49.6%)	571 (51.4%)	NS	392 (42.2%)	115 (52.3%)	<0.01
Statin	364 (27.1%)	512 (46.1%)	<0.001	274 (29.5%)	107 (48.6%)	<0.001

Values are mean±SEM.
Abbreviations see in Tables 1,2.

were characterized by higher prevalence of larger body mass index, glucose intolerance/diabetes mellitus, and IHD, whereas the female patients were in a higher NYHA class, had lower exercise tolerance, and higher prevalence of both preserved LVEF and valvular heart disease.

MetS in CHF

In both male and female patients with CHF, those with MetS were characterized by younger age, higher prevalence of current smoking and drinking, IHD, and hypertensive heart disease, lower NYHA class, better exercise tolerance, and more likelihood of taking medications such as ACEI/ARB, β-blockers or statins (Tables 2,3, Figure 2). The prevalence of HFPEF was significantly higher in the MetS group compared with the non-MetS group (Table 3, Figure 3).

When compared with the patients with HFREF, those with HFPEF were characterized by higher prevalence of elderly and female patients, obesity, hypertensive and valvular heart disease, and less likelihood of taking medications such as ACEI/ARB, β-blockers or statins (Table 4).

Metabolic Components in CHF

In the present study, the contribution of single or combined metabolic components was observed in both the ischemic

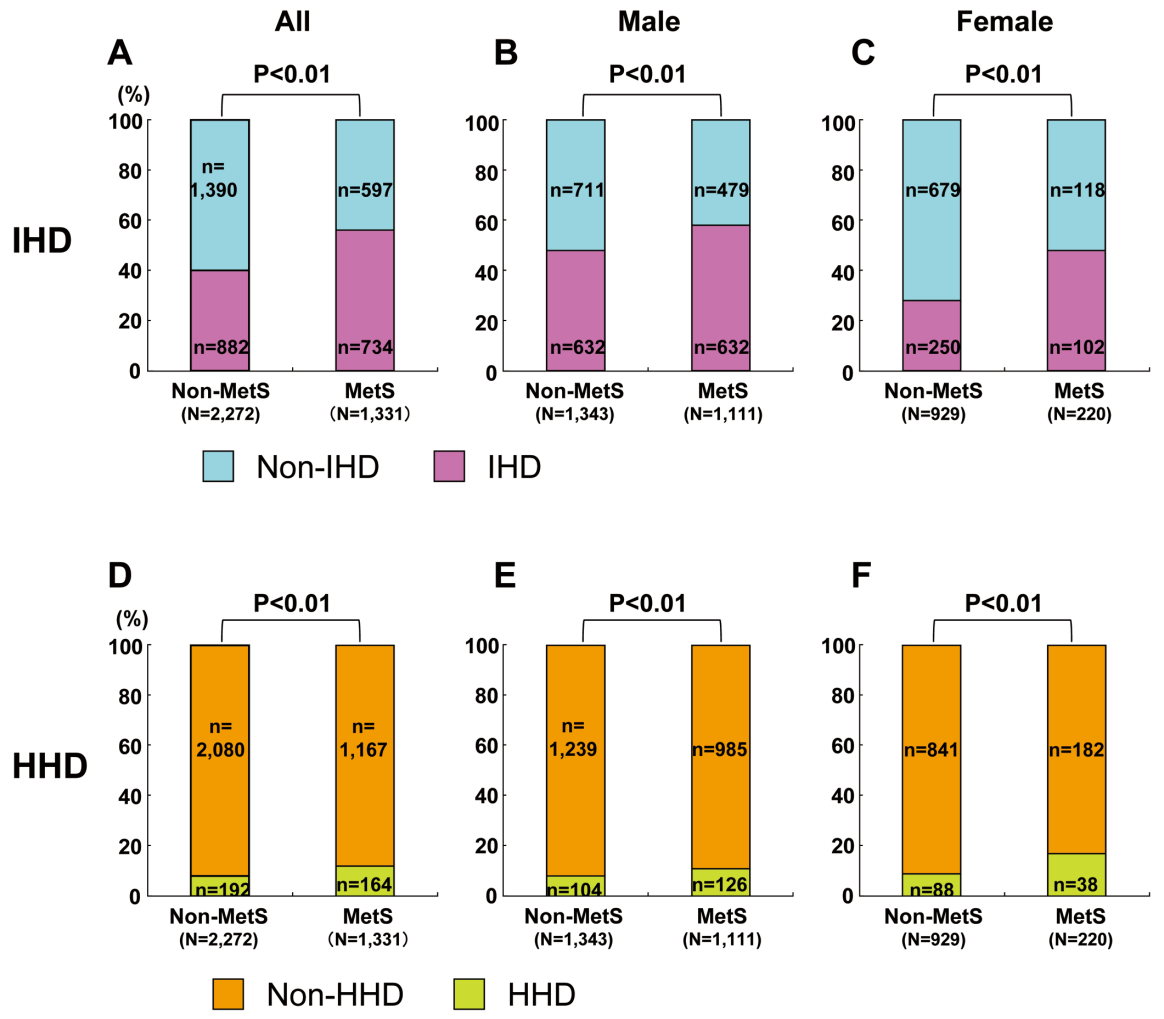

Figure 2. Effect of metabolic syndrome (MetS) on ischemic heart disease (IHD) and hypertensive heart disease (HHD). IHD was significantly more prevalent in CHF patients with MetS than in those without it for all patients (**A**), and in male (**B**) or female patients (**C**). Similarly, for HHD for all patients (**D**), and male (**E**) and female patients (**F**).

and non-ischemic CHF patients (Figure 4A). Although the prevalence of ischemic CHF was significantly higher in most of the subgroups with more than 3 metabolic components, the contribution of other single or combined metabolic components was either comparable between the 2 groups or stronger in the non-ischemic CHF group (Figure 4A). Although the prevalence of combined metabolic components varied, these components were comparably associated with both HFPEF and HFREF (Figure 4B).

Discussion

The novel findings of the present study are that (a) the prevalence of MetS in CHF was more than double that of the general Japanese population, (b) MetS was associated with ischemic or hypertensive heart disease-related heart failure, (c) HFPEF was characterized by a higher prevalence of elderly and female patients with MetS, and (d) the prevalence of the metabolic components was comparable between the ischemic and non-ischemic CHF patients. To the best of our knowledge, this is the first study to provide evidence for a relationship between MetS and CHF.

Prevalence of MetS in CHF

It has been reported that the prevalence of MetS in the general Japanese population is 10–20% in men and 2–8% in women, as defined by the current Japanese criteria.[7,18,19] In contrast, the present study demonstrated a prevalence of MetS (45% in men and 19% in women) that is more than 2-fold that of the general population, suggesting that the presence of MetS is an important therapeutic target of CHF treatment. It is conceivable that the increased prevalence of MetS in CHF patients is both the cause and the result of CHF, as activation of both the sympathetic nervous system and renin–angiotensin system causes the metabolic components.[21] In order to address this important issue, we are now performing a cohort study in which we follow-up MetS patients without CHF to examine the development of CHF in them.

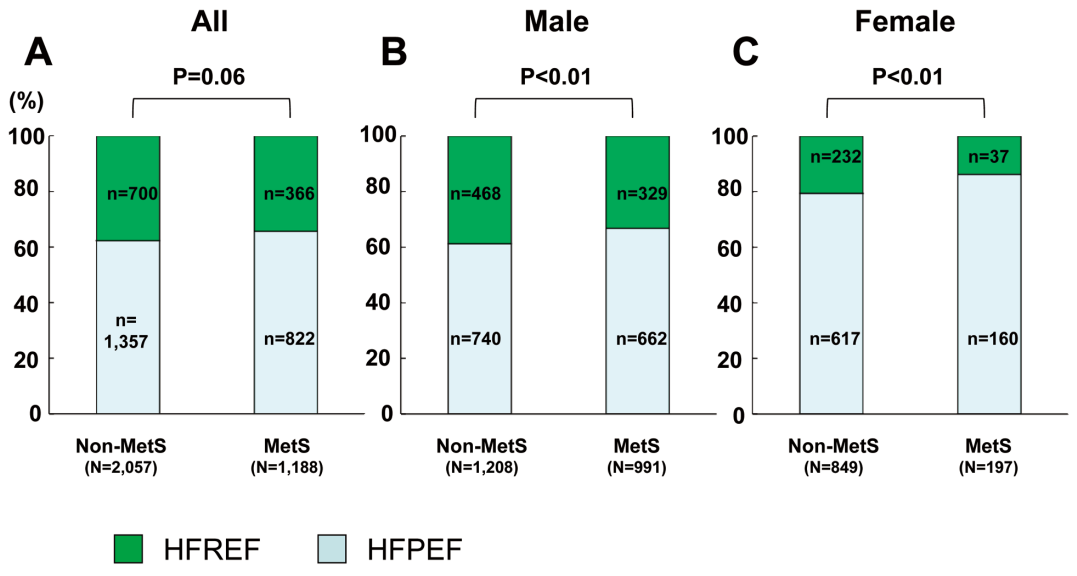

Figure 3. Effect of metabolic syndrome (MetS) on left ventricular ejection fraction. The prevalence of heart failure with preserved ejection fraction (HFPEF) was significantly greater for males (**B**) and females (**C**) with MetS than in those without MetS and tended to be so for all patients with chronic heart failure (**A**). HFREF, heart failure with reduced ejection fraction.

Role of MetS in Ischemic and Hypertensive Heart Disease

MetS has been identified as a risk and prognostic factor for IHD and stroke.[8,22,23] In the present study, MetS was highly associated with IHD in both male and female patients with CHF. Thus, the prevention of IHD is extremely important for preventing the development of CHF, both by life-style modification and the use of anti-atherosclerotic drugs in order to achieve stabilization and regression of systemic atherosclerosis. Furthermore, because hypertension is associated with obesity,[24] it is also important to treat obesity for blood pressure control in order to prevent the development of hypertensive heart disease.

Comparison of HFPEF and HFREF

It has been demonstrated that heart failure can also occur in patients with preserved LVEF, which is often observed in hypertensive heart disease mainly caused by LV diastolic dysfunction.[14] It is now widely accepted that HFPEF is a major cardiovascular disorder with poor prognosis, accounting for approximately 50% of patients with heart failure symptoms,[15,16] and our study demonstrated that 67% of CHF patients had HFPEF (**Table 4**). The present results also indicate the different clinical characteristics of HFPEF and HFREF patients, and the former were characterized by a higher prevalence of elderly and female patients, obesity, and hypertensive and valvular heart disease. Although it has been previously demonstrated that the major determinants of diastolic dysfunction are enhanced myocardial stiffness and impaired relaxation capacity,[25] further studies are needed to clarify the association between these clinical factors and LV dysfunction.

Metabolic Components in Ischemic and Non-Ischemic CHF

In the present study, among the metabolic components in the CHF patients, the prevalence of both hypertension and dyslipidemia was higher, followed by glucose intolerance/diabetes mellitus, probably because of environmental and genetic factors. In order to prevent the development of CHF, all components of MetS should be controlled (ie, blood pressure by anti-hypertensive drugs, lipid-lowering by HMG-CoA reductase inhibitors, and glucose control by diet therapy, exercise and antidiabetic drugs), which is known to ameliorate vascular function and stabilize atheroma.[26–33] In contrast, smoking and alcohol intake may not be highly related to the development of CHF compared with hypertension or dyslipidemia, so smoking cessation and moderate alcohol intake are recommended in the early stage of CHF.[9]

In the present study, MetS was related to the development of HFPEF (LVEF≥50%) in both male and female patients with CHF. Although the precise mechanisms are unknown, coronary microvascular dysfunction with preserved systolic function might be linked to this phenomenon.[34,35]

The present study also demonstrated that there are single or combined metabolic components in both non-ischemic CHF and ischemic CHF patients, a consistent finding with a previous report regarding the lipid levels and heart failure incidence in Caucasians.[36] Therefore, these metabolic components should be regarded as important therapeutic targets for CHF caused by both ischemic and non-IHD.

Study Limitations

First, although we were able to collect the data for a relatively large number of CHF patients, their prognoses need to be elucidated. As we are currently performing a follow-up study for them, we will report the results separately in the future. Second, we used the 2005 definition of the Japanese Committee for the Diagnostic Criteria of MetS, so we were unable to compare the present data with that of non-Japanese studies. We plan to use other diagnostic criteria, such as the National Cholesterol Education Program-Adult Treatment

Table 4. Comparison of HFPEF and HFREF Patients With Symptomatic CHF

	Total		
	HFPEF (n=2,179)	HFREF (n=1,066)	P value
Sex, n (%)			
Male	1,402 (64.3%)	797 (74.8%)	<0.001
Female	777 (35.7%)	269 (25.2%)	<0.001
Age (years)	69.6±0.3	67.7±0.4	<0.001
Non-MetS	1,357 (62.3%)	700 (65.7%)	0.06
MetS	822 (37.7%)	366 (34.3%)	0.06
Cigarette smoking, n (%)			
Never	453 (41.2%)	470 (60.4%)	<0.01
Former	307 (27.9%)	133 (17.1%)	<0.01
Current	339 (30.8%)	175 (22.5%)	<0.01
Alcohol intake, n (%)			
Never	925 (52.2%)	435 (49.7%)	<0.001
Former	149 (8.4%)	85 (9.7%)	<0.001
Current	699 (39.4%)	356 (40.6%)	<0.001
BMI (kg/m^2)	23.1±0.1	22.4±0.2	<0.01
Waist circumference (cm)			
Male	86.9±0.3	85.9±0.3	<0.001
Female	82.1±0.4	80.9±0.8	<0.001
Blood pressure (mmHg)			
Systolic	128.1±0.4	120.7±0.6	<0.001
Diastolic	72.2±0.3	70.5±0.4	<0.001
Heart rate (beats/min)	72.3±0.3	73.8±0.5	<0.05
NYHA class			
I	429 (19.7%)	134 (12.6%)	<0.001
II	1,510 (69.5%)	743 (69.9%)	NS
III	215 (9.9%)	173 (16.3%)	<0.001
IV	19 (0.9%)	13 (1.2%)	NS
Stage C/D	2,125 (97.7%)/49 (2.3%)	1,027 (96.5%)/37 (3.5%)	<0.05
LVEF (%)	65.3±0.2	37.2±0.3	<0.001
SAS	5.4±0.05	5.0±0.06	<0.001
HT	1,725 (53.2%)	729 (68.4%)	<0.001
DM or fasting glucose ≥110 mg/dl	1,042 (47.8%)	554 (52.0%)	<0.05
Dyslipidemia	1,499 (68.8%)	802 (75.2%)	<0.001
IHD	894 (41.0%)	501 (47.0%)	<0.001
HHD	258 (11.8%)	73 (6.8%)	<0.001
CM	319 (14.6%)	365 (34.2%)	<0.001
VHD	695 (31.9%)	169 (15.9%)	<0.001
CHD	48 (2.2%)	6 (0.6%)	<0.01
Medications			
ACEI/ARB	1,483 (68.1%)	835 (78.3%)	<0.001
β-blocker	880 (40.9%)	711 (66.7%)	<0.001
Statin	702 (32.2%)	403 (37.8%)	<0.01

Values are mean±SEM.
Abbreviations see in Tables 1,2.

Panel Ⅲ (NCEP/ATPⅢ),[37] American Heart Association/National Heart, Lung, and Blood Institute (AHA/NHLBI),[38] and International Diabetes Federation (IDF),[39] in future analyses. Third, although MetS is the association and clustering of metabolic components, we were unable to exclude CHF patients complicated by severe hypertension, severe dyslipidemia, or severe diabetes mellitus. This issue also remains to be examined in future studies. Last, the present study lacks an appropriate control group in the same population, which why we used the data from the Kanazawa Study of the Japanese general population in 2007 that demonstrated a prevalence of MetS of 16–21% in 50- to 80-year-old males and in females, prevalence of 3% in the 50s, 5% in the 60s, 8% in the 70s, and 10% in the 80s.[20]

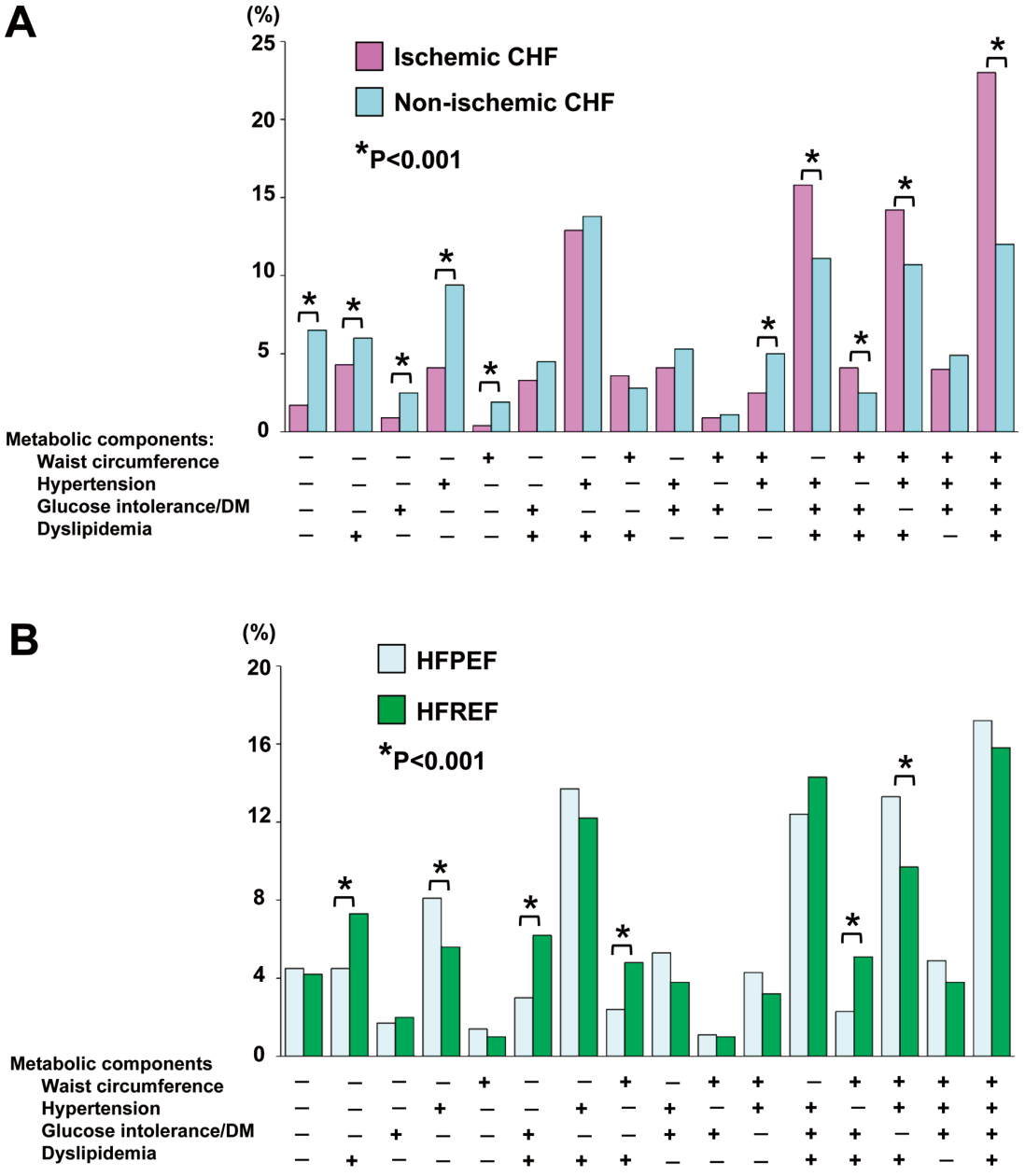

Figure 4. Accumulation of metabolic components in patients with chronic heart failure (CHF). (**A**) When the number of metabolic components was greater than 3, their contribution to ischemic heart failure was greater, whereas the contribution of other single or combined metabolic components was comparable between the 2 groups or stronger in the non-ischemic heart failure group. (**B**) Although the prevalence of combined metabolic components varied, the components were equally associated with both heart failure with preserved ejection fraction (HFPEF) and heart failure with reduced ejection fraction (HFREF). DM, diabetes mellitus.

Conclusion

We found that the prevalence of MetS in CHF patients was more than double compared with the general population in Japan, with a greater involvement of ischemic or hypertensive heart disease and a higher prevalence in elderly and female patients. Because the metabolic components might have a substantial effect on the development of both ischemic and non-ischemic CHF, MetS should be regarded as a new therapeutic target for this disorder.

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Disclosures

None.

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