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発表者氏名	論文タイトル名	発表誌名	巻号	ページ	出版年

木内貴弘 石川ひろの	東京大学大学院医学系研究科医療コミュニケーション学教室のヘルスコミュニケーション学教育の概要	日本ヘルスコミュニケーション研究雑誌	1巻 1号	P6 ～ P12	2010
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IV.研究成果の刊行物・別刷

Prognostic Effects of Combined Treatment With Calcium Channel Blockers and Statins in Patients With Coronary Narrowing

From the Japanese Coronary Artery Disease Study

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SUMMARY

Calcium channel blockers (CCB) and statins are frequently prescribed for patients with coronary artery disease (CAD) complicated by hypertension and/or hypercholesterolemia. CCB have pleiotropic actions beyond their blood pressure-lowering effect, while statins have pleiotropic actions beyond their cholesterol-lowering effect. We assessed the hypothesis that combined treatment with CCB and statins has additional prognostic benefits resulting from potential additive or synergistic pleiotropic actions of both classes of drugs in the Japanese CAD (JCAD) study population. The JCAD study consisted of 13,812 patients with angiographically demonstrable significant coronary narrowing in at least 1 of 3 major coronary arteries who were followed-up for a mean of 2.7 years (follow-up rate, 88.4%). The primary endpoint of the present study was all cardiovascular events. We compared the event rate between patients receiving neither CCB nor statins and those receiving each drug alone or as a combination treatment using propensity score matching analysis. The rate of all events was 62.8 per 1,000 patient-years in the JCAD study. Kaplan-Meier analysis with the log-rank test showed no statistically significant difference in the event rate in each comparison. In conclusion, there may be no additional prognostic benefit beyond the blood-pressure-lowering and cholesterol-lowering effects in the combined treatment with CCB and statins for angiographically documented CAD patients. (Int Heart J 2010; 51: 299-302)

Key words: Blood pressure, Calcium channel blockers, Cholesterol, Coronary artery disease, Propensity score matching analysis, Statins

The merits of combination therapy have recently drawn considerable attention, particularly in the field of cardiovascular diseases.[1,2] Combination treatment is superior to monotherapy in terms of additional benefits and limited side effects. Combination therapy can be classified into two groups: a combination of drugs with similar pharmacologic effects, such as the combined therapy of a renin-angiotensin system inhibitor (RASI) and a calcium channel blocker (CCB) for hypertensives; or a combination of drugs with different pharmacologic effects, such as combined therapy of an RASI and statin for patients with hypertension and hypercholesterolemia. More recently, a large number of single-pill combination drugs have been developed.[3-5] If combined treatment provides beneficial effects on the prognosis of patients, the usefulness of combination drugs would be strengthened in addition to their advantages with regard to drug adherence and prescription costs. In an earlier study, we assessed the treatment effects of combined RASI and statins.[6] The combined treatment provided additional beneficial effects on the prognosis of coronary artery disease (CAD) patients beyond the blood-pressure-lowering and cholesterol-lowering effects.[6] CCB, which are one of the most frequently prescribed classes of drugs for hypertension, are reported to have pleiotropic actions, which is also the case for RASI and statins.[7,8] Therefore, in the present study, we evaluated whether combined therapy consisting of CCB and statins also has a favorable prognostic effect via pleiotropic actions after adjustment for baseline covariates such as blood pressure and LDL-cholesterol level in the Japanese Coronary Artery Disease (JCAD) Study population.[6,9,10]

METHODS

Study population: The protocol and major outcomes of the JCAD study have been published previously.[9,10] Briefly, we consecutively enrolled patients with angiographically demonstrable narrowing > 50% in ≥ 1 of 3 major coronary arteries. Initially, 15,628 patients were registered and 13,812 patients were followed-up for a mean of 2.7 years (follow-up rate, 88.4%). Clinical events to be registered in the database were defined as all-cause deaths, including cardiac, cerebral, vascu-

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Received for publication July 5, 2010.

Accepted July 22, 2010.

lar, and other deaths, and cerebral, cardiac, and vascular events. Cerebral events included cerebral hemorrhage, cerebral infarction, and transient ischemic attack. Cardiac events consisted of fatal and nonfatal myocardial infarction, unstable angina, congestive heart failure, coronary bypass graft surgery, resuscitated cardiac arrest, and cardiopulmonary arrest on arrival. Angiographic restenosis incidentally found during routine follow-up coronary angiography without clinical symptoms was excluded from event registration. Aortic dissection and rupture of an aortic aneurysm were classified as vascular events. The primary endpoint of the present study was all composite cardiovascular events. The data were derived from a *post-hoc* analysis of an observational, nonrandomized trial. Informed consent was obtained from each patient and the study protocol conformed to the ethical guidelines of the 1975 Declaration of Helsinki as reflected in *a priori* approval by the institution's human research committee. In this subanalysis, risk of any cardiovascular event in patients receiving neither CCB nor statins was compared with those of patients receiving either one or both drugs.

Statistical analysis: Numerical data are presented as the mean value ± SD. The unpaired Student's *t*-test was used to compare parametric values, while comparisons of variables between the 2 groups were conducted using the Wilcoxon test for non-parametric unpaired values. Proportional data were analyzed using the chi-square test. Propensity score matching analysis was used to match baseline characteristics between the 2 groups.[11] Kaplan-Meier hazard ratios were used to examine the incidence over time, and the log-rank test was used to assess group differences. A two-sided $P < 0.05$ was regarded as statistically significant.

Results

The rate of all events was 62.8 per 1,000 patient-years in the JCAD study. Baseline covariates potentially influencing the cardiovascular event rate were adjusted between the control and each treatment group by the propensity score matching method. However, systolic blood pressure was slightly but significantly lower (2.5 mmHg mean) in the control group than in the CCB monotherapy group, whereas fasting blood glucose level was significantly higher (2.6 mg/dL mean) in the control group (Table I). Plasma total cholesterol levels were significantly lower (5.0 mg/dL mean) in the control group than in the statin monotherapy group (Table II). Systolic blood pressure was significantly lower (2.0 mmHg mean) in the control group than in the combination treatment group. Plasma total cholesterol levels were also significantly lower (4.6 mg/dL mean) in the control group (Table III). The Figure shows the relative risk

Table I. Baseline Characteristics of Patients After Propensity Score Matching

Variable	No CCB, No Statin	CCB, No Statin	*P*
Patients receiving a CCB, but no statin			
No. of patients	2,887	2,887	
Age (years)	66.4 ± 9.5	66.4 ± 9.5	0.5721
Men	80.9%	80.4%	0.6412
Hypertension	54.1%	54.2%	0.8949
Hyperlipidemia	36.4%	36.9%	0.7226
Impaired glucose tolerance	38.5%	39.2%	0.5708
Body mass index ≥ 25 (kg/m^2)	28.9%	29.4%	0.6641
Tobacco use	40.1%	39.2%	0.4843
Alcohol intake	38.9%	39.3%	0.7874
Family history of coronary artery disease	14.6%	13.4%	0.1976
Heart failure	11.1%	11.2%	0.8670
Left main coronary narrowing	4.8%	4.5%	0.6620
Number of coronary arteries narrowing	1.8 ± 0.8	1.8 ± 0.8	0.6416
Systolic blood pressure (mmHg)	131.3 ± 20.9	133.8 ± 19.9	< 0.0001
Diastolic blood pressure (mmHg)	74.1 ± 12.5	74.2 ± 12.0	0.8300
Total cholesterol (mg/dL)	188.2 ± 34.7	189.0 ± 34.0	0.5160
Fasting blood glucose (mg/dL)	122.0 ± 47.3	119.4 ± 45.8	0.0339

Values are expressed as the mean ± SD or percentage of each characteristic. Hypertension was defined as systolic blood pressure ≥ 140 mmHg or diastolic blood pressure ≥ 90 mmHg; hyperlipidemia was defined as total cholesterol ≥ 220 mg/dL or low-density-lipoprotein cholesterol ≥ 140 mg/dL or triglycerides ≥ 150 mg/dL. CCB indicates calcium channel blocker.

Table II. Baseline Characteristics of Patients After Propensity Score Matching

Variable	No CCB, No Statin	CCB, No Statin	*P*
Patients receiving a statin, but no CCB			
No. of patients	1,610	1,610	
Age (years)	64.0 ± 9.6	64.0 ± 9.6	0.6906
Men	77.5%	77.8%	0.8324
Hypertension	47.1%	48.5%	0.4171
Hyperlipidemia	74.9%	75.0%	0.9352
Impaired glucose tolerance	40.8%	40.2%	0.7196
Body mass index ≥ 25 (kg/m^2)	31.1%	31.8%	0.6763
Tobacco use	43.2%	42.5%	0.6952
Alcohol intake	37.9%	38.3%	0.7995
Family history of coronary artery disease	15.8%	16.7%	0.5039
Heart failure	12.5%	12.7%	0.8318
Left main coronary narrowing	3.8%	4.5%	0.3300
Number of coronary arteries narrowing	1.7 ± 0.8	1.8 ± 0.8	0.3309
Systolic blood pressure (mmHg)	130.0 ± 20.8	128.7 ± 19.2	0.0942
Diastolic blood pressure (mmHg)	74.0 ± 12.5	74.1 ± 12.0	0.8788
Total cholesterol (mg/dL)	201.4 ± 36.0	206.4 ± 39.1	0.0040
Fasting blood glucose (mg/dL)	124.1 ± 48.5	123.8 ± 50.0	0.8325

Values are expressed as the mean ± SD or percentage of each characteristic. Hypertension was defined as systolic blood pressure ≥ 140 mmHg or diastolic blood pressure ≥ 90 mmHg; hyperlipidemia was defined as total cholesterol ≥ 220 mg/dL or low-density-lipoprotein cholesterol ≥ 140 mg/dL or triglycerides ≥ 150 mg/dL. CCB indicates calcium channel blocker.

Table III. Baseline Characteristics of Patients After Propensity Score Matching

Variable	No CCB, No Statin	CCB, No Statin	*P*
Patients receiving a CCB and a statin			
No. of patients	1,589	1,589	
Age (years)	64.7 ± 9.5	64.8 ± 9.3	0.8286
Men	75.7%	75.3%	0.8045
Hypertension	55.8%	56.6%	0.6167
Hyperlipidemia	72.3%	72.0%	0.8743
Impaired glucose tolerance	42.0%	39.8%	0.2199
Body mass index ≥ 25 (kg/m^2)	34.1%	33.5%	0.7357
Tobacco use	39.4%	38.9%	0.7712
Alcohol intake	37.6%	37.4%	0.9125
Family history of coronary artery disease	15.1%	15.5%	0.7303
Heart failure	9.6%	9.4%	0.9037
Left main coronary narrowing	4.3%	4.5%	0.7947
Number of coronary arteries narrowing	1.8 ± 0.8	1.8 ± 0.8	0.4710
Systolic blood pressure (mmHg)	131.7 ± 21.2	133.7 ± 19.7	0.0023
Diastolic blood pressure (mmHg)	74.5 ± 12.7	75.2 ± 12.4	0.1775
Total cholesterol (mg/dL)	200.5 ± 36.6	205.1 ± 39.8	0.0195
Fasting blood glucose (mg/dL)	124.7 ± 50.9	121.4 ± 47.0	0.2381

Values are expressed as the mean ± SD or percentage of each characteristic. Hypertension was defined as systolic blood pressure ≥ 140 mmHg or diastolic blood pressure ≥ 90 mmHg; hyperlipidemia was defined as total cholesterol ≥ 220 mg/dL or low-density-lipoprotein cholesterol ≥ 140 mg/dL or triglycerides ≥ 150 mg/dL. CCB indicates calcium channel blocker.

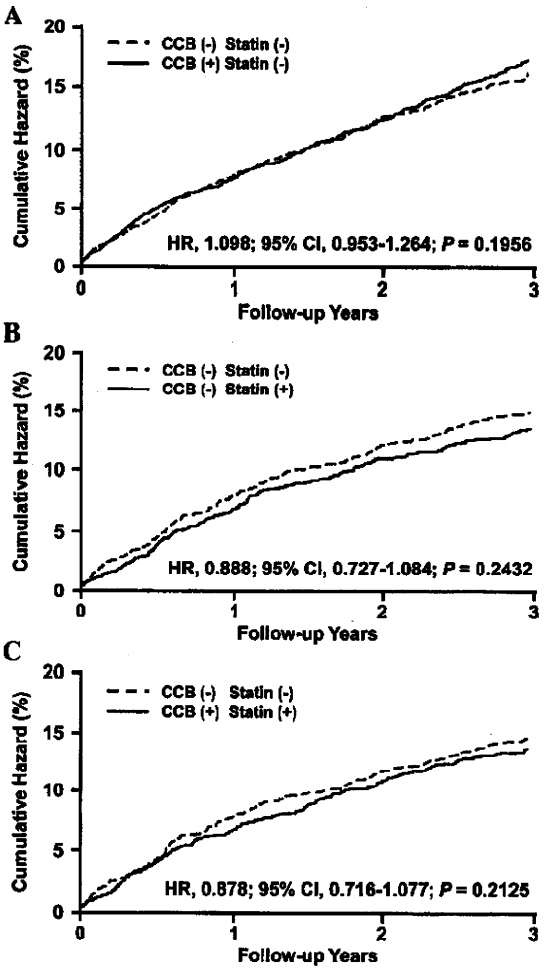

Figure. Cumulative hazards of all cardiovascular events in patients not receiving CCB and statins and those receiving (A) CCB but no statins, (B) statins but no CCB, and (C) both CCB and statins. CCB indicates calcium channel blocker; CI, confidence interval; and HR, hazard ratio.

reduction of all cardiovascular events with each therapy compared with that of the control group. There was no statistically significant difference in the incidence of all cardiovascular events between the control and each treatment group. Cumulative hazard analysis of endpoints of subcategories revealed similar results for the composite endpoint (data not shown).

Discussion

The major finding of the present study was that combination treatment consisting of CCB and statins has no additional prognostic benefits in CAD patients through pleiotropic actions beyond the blood-pressure-lowering and cholesterol-lowering effects. In contrast, our earlier study has demonstrated that RAS inhibitors combined with statins decreased the frequency of cardiovascular events in the same study population as in the present study.[6] These different findings may be interpreted as follows. First, the pleiotropic actions of CCB may be minimal, if any, after adjustment for blood pressure. In contrast, such effects of RAS inhibitors are well recognized.[12,13] Second, in both studies, baseline covariates including risk factors, blood pressure, and plasma total cholesterol and fasting blood glucose levels were adjusted between the control and each treatment group.[11] As a result, pleiotropic actions of CCB beyond lowering blood pressure and those of statins beyond decreasing plasma cholesterol levels could be successfully assessed.[7,8,14] However, in the comparison between the control and the CCB and statin combination treatment group, systolic blood pressure and plasma cholesterol levels were significantly lower in the control group. The small but significant difference may have attenuated the beneficial effect of the CCB and statin combination treatment. In contrast, systolic blood pressure of the RAS inhibitor and statin combination group was significantly lower (1.4 mmHg mean) than that in the control group.[6] Thus, there is a possibility that a small difference in systolic blood pressure significantly affected the frequency of cardiovascular events in our patients, which was the case in previous clinical studies.[1,2]

Although we did not demonstrate additional benefits with CCB and statin combination treatment as a result of the pleiotropic actions of these drugs in CAD patients, prospective ran-

domized studies comprising various patient populations will be necessary in future.

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Heart Vessels (2010) 25:453–459
DOI 10.1007/s00380-010-0012-5

ORIGINAL ARTICLE

Treatment effects of renin-angiotensin system inhibitor and calcium channel blocker in patients with coronary artery narrowing (from the Japanese Coronary Artery Disease Study)

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Received: 26 March 2009 / Accepted: 24 December 2009 / Published online: 5 October 2010

Abstract Low-dose antihypertensive drugs in combination are prescribed frequently in clinical practice. Combination treatment is superior to monotherapy with higher doses of each drug in terms of blood pressure reduction and side effects. However, it is unclear whether combination treatment provides additional prognostic benefit beyond the blood pressure lowering effects. We assessed the usefulness of the combined treatment of a renin-angiotensin system inhibitor (RASI) and a calcium channel blocker (CCB) for all cardiovascular events in the Japanese Coronary Artery Disease (JCAD) Study population. In the JCAD Study, which is an observational and non-randomized trial, 13,812 patients with angiographically shown narrowing >50% in ≥1 of 3 major coronary arteries were followed up for a mean of 2.7 years. The primary endpoint of the study was all cardiovascular events. In the present study, baseline covariates possibly influencing the event rate were adjusted between the different treatment groups. There was no statistically significant difference in the event rate between the RASI monotherapy and combined treatment groups, although Kaplan-Meier analysis showed a 23% ($p = 0.0003$) relative risk reduction with an RASI monotherapy compared with the control group. In conclusion, there may be no additional benefit beyond blood pressure lowering effects in the combination of an RASI and a CCB in patients with angiographically documented CAD.

Keywords Calcium channel blocker · Combination therapy · Coronary artery disease · Renin-angiotensin system inhibitor

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Introduction

It is well known that the use of antihypertensive agents in combination provides a synergistic or at least an additive blood pressure reduction, which is greater than higher doses of either drug used as monotherapy [1–4]. Combination low-dose drug treatment also reduces side effects [1, 2]. The combination of a renin-angiotensin system inhibitor (RASI) and a calcium channel blocker (CCB) is frequently used in clinical practice [5]. Since both an RASI and a CCB possibly provide cardiovascular protection by improving vascular function [6–8], it is postulated that combination therapy might provide prognostic benefit beyond the blood pressure lowering effects. Thus, we compared the prognostic effects of an RASI and a CCB alone or in combination beyond the blood pressure lowering effects after adjustment for baseline covariates, including t blood pressure, in the Japanese Coronary Artery Disease (JCAD) Study population [9].

Materials and methods

The protocol and major outcomes of the JCAD study were previously published [9]. Briefly, we consecutively enrolled patients with angiographically demonstrable narrowing >50% in ≥1 of 3 major coronary arteries. Initially, 15,628 patients were registered, and 13,812 patients were followed up for a mean of 2.7 years (follow-up rate 88.4%). Clinical events to be registered in the database were defined as all-cause deaths, including cardiac, cerebral, vascular and other deaths, and cerebral, cardiac and vascular events. Cerebral events included cerebral hemorrhage, cerebral infarction and transient ischemic attack. Cardiac events consisted of fatal and nonfatal myocardial infarction, unstable angina, congestive heart failure, coronary bypass graft surgery, resuscitated cardiac arrest and cardiopulmonary arrest on arrival. Angiographic restenosis incidentally found during routine follow-up coronary angiography without clinical symptoms was excluded from event registration. Aortic dissection and rupture of an aortic aneurysm were classified as vascular events. The primary endpoint of this present study was all cardiovascular events. The study data were derived from a post-hoc analysis of an observational, non-randomized trial.

Informed consent was obtained from each patient, and the study protocol conformed to the ethical guidelines of the 1975 Declaration of Helsinki as reflected in a priori approval by the institution's human research committee.

Statistical analysis

Numerical data are presented as the mean value ± SD. An unpaired Student's t test was applied for the comparison of parametric values, whereas comparisons of variables between the two groups were made by the Wilcoxon test for non-parametric unpaired values. Proportional data were analyzed by the chi-square test. Propensity score matching analysis was used to match baseline characteristics between the two groups [10]. Kaplan-Meier hazard ratios were used to examine the incidence over time, and the log-rank test was used to assess group differences. Two-sided $p < 0.05$ was regarded as statistically significant.

Results

As shown in Table 1, baseline covariates potentially influencing the cardiovascular event were adjusted between the two groups by the propensity score matching method. However, systolic blood pressure was slightly but significantly higher (1.3 mmHg in mean) in the control group than in the RASI monotherapy group (Table 1a), and was slightly but significantly lower (1.9 mmHg in mean) in the control group than in the combination treatment group (Table 1c). It was also significantly lower (3.1 mmHg in mean) in the RASI monotherapy group than in the combination treatment group (Table 1d). Kaplan-Meier analysis showed a 23% relative risk reduction of all cardiovascular events with RASI monotherapy compared with the control group. Log-rank test showed a statistically significant difference ($p = 0.0003$) in the event rate between the two groups (Fig. 1a). Meanwhile, there was no statistically significant difference in the incidence of all cardiovascular events between the control and the CCB monotherapy groups (Fig. 1b). Furthermore, no statistically significant difference in the incidence of all cardiovascular events was observed between the control and combination treatment groups (Fig. 1c). There was also no statistically significant difference in the incidence of all cardiovascular events between the RASI monotherapy and combination treatment groups (Fig. 1d).

Cumulative hazard analysis of endpoints of subcategories revealed similar results of the composite endpoint. Cerebral events in the RASI monotherapy group were significantly lower than in the combination treatment group (Table 2).

Table 3 shows follow-up blood pressure levels in each group. There were slight but significant differences in the systolic blood pressure levels between the combination treatment group and the untreated control or RASI monotherapy group over the 3-year follow-up periods.

Discussion

In this study, baseline covariates, including coronary risk factors such as hypertension, hyperlipidemia, impaired glucose tolerance and tobacco use, were adjusted between

Table 1 Baseline characteristics of patients after propensity score matching

Variables	No RASI, no CCB	RASI, but no CCB	*p* value
(a) Patients receiving an RASI, but no CCB			
No. of patients	2,447	2,447	
Age (years)	65.5 ± 10.3	64.5 ± 10.0	0.9205
Men	79.1%	78.5%	0.5998
Hypertension	48.6%	49.2%	0.6473
Hyperlipidemia	56.6%	55.9%	0.6040
Impaired glucose tolerance	38.9%	39.6%	0.5983
Body mass index ≥25 (kg/m^2)	30.9%	31.2%	0.8288
Tobacco use	43.1%	43.0%	0.9310
Alcohol intake	39.6%	39.7%	0.9534
Family history of coronary artery disease	15.6%	16.0%	0.6952
Heart failure	12.4%	12.0%	0.6620
Left main coronary narrowing	4.4%	4.0%	0.4765
Number of coronary arteries narrowed	1.8 ± 0.8	1.8 ± 0.8	0.9581
Systolic blood pressure (mmHg)	130.5 ± 20.1	129.2 ± 20.2	0.0039
Diastolic blood pressure (mmHg)	74.2 ± 12.1	74.2 ± 12.2	0.5275
Total cholesterol (mg/dl)	195.9 ± 39.0	196.8 ± 38.1	0.3549
Fasting blood sugar (mg/dl)	121.5 ± 48.9	122.4 ± 48.4	0.1442
Angiotensin-converting enzyme inhibitors	0%	71.6%	0.0000
Angiotensin receptor blockers	0%	30.3%	0.0000
Variables	No RASI, no CCB	CCB, but no RASI	*p* value
(b) Patients receiving a CCB, but no RASI			
No. of patients	2,659	2,659	
Age (years)	65.3 ± 9.9	65.3 ± 9.7	0.8263
Men	77.5%	77.5%	0.9476
Hypertension	50.2%	50.0%	0.8909
Hyperlipidemia	57.4%	57.6%	0.9116
Impaired glucose tolerance	38.2%	39.5%	0.3680
Body mass index ≥25 (kg/m^2)	31.1%	32.1%	0.4259
Tobacco use	37.8%	37.3%	0.6918
Alcohol intake	38.0%	38.6%	0.6517
Family history of coronary artery disease	15.9%	15.4%	0.6238
Heart failure	7.0%	7.0%	0.9572
Left main coronary narrowing	5.3%	5.2%	0.9510
Number of coronary arteries narrowed	1.8 ± 0.8	1.8 ± 0.8	0.7075
Systolic blood pressure (mmHg)	131.5 ± 20.1	131.9 ± 18.2	0.3305
Diastolic blood pressure (mmHg)	74.2 ± 12.0	74.3 ± 11.8	0.9703
Total cholesterol (mg/dl)	197.7 ± 39.1	197.9 ± 38.4	0.7003
Fasting blood sugar (mg/dl)	120.9 ± 47.4	120.0 ± 44.9	0.6105
Variables	No RASI, no CCB	RASI and CCB	*p* value
(c) Patients receiving an RASI and a CCB			
No. of patients	1,903	1,903	
Age (years)	65.5 ± 9.7	65.6 ± 9.5	0.6973
Men	75.8%	76.0%	0.8795
Hypertension	69.8%	69.8%	1.0000
Hyperlipidemia	58.5%	58.8%	0.8434
Impaired glucose tolerance	41.6%	42.3%	0.6694

Table 1 continued

Variables	No RASI, no CCB	RASI and CCB	*p* value
Body mass index ≥25 (kg/m^2)	34.7%	34.4%	0.8647
Tobacco use	38.3%	38.5%	0.8940
Alcohol intake	39.0%	38.5%	0.7393
Family history of coronary artery disease	15.7%	16.2%	0.6582
Heart failure	9.9%	9.7%	0.8701
Left main coronary narrowing	4.2%	4.6%	0.4763
Number of coronary arteries narrowed	1.8 ± 0.8	1.8 ± 0.8	0.2933
Systolic blood pressure (mmHg)	134.9 ± 20.9	136.8 ± 21.0	0.0375
Diastolic blood pressure (mmHg)	75.6 ± 12.3	75.7 ± 12.6	0.5903
Total cholesterol (mg/dl)	197.3 ± 38.6	197.2 ± 36.8	0.8362
Fasting blood sugar (mg/dl)	123.9 ± 49.8	121.2 ± 46.2	0.4278
Angiotensin-converting enzyme inhibitors	0%	71.4%	0.0000
Angiotensin receptor blockers	0%	31.1%	0.0000
Variables	RASI, but no CCB	RASI and CCB	*p* value
(d) Patients receiving an RASI and a CCB			
No. of patients	1,901	1,901	
Age (years)	65.2 ± 9.6	65.3 ± 9.5	0.9449
Men	76.9%	77.1%	0.8472
Hypertension	69.4%	69.9%	0.7778
Hyperlipidemia	56.8%	57.9%	0.4911
Impaired glucose tolerance	43.0%	42.6%	0.7932
Body mass index ≥25 (kg/m^2)	34.1%	34.0%	0.9454
Tobacco use	42.1%	41.8%	0.8695
Alcohol intake	40.9%	41.5%	0.7170
Family history of coronary artery disease	16.8%	17.1%	0.7623
Heart failure	12.5%	13.2%	0.5281
Left main coronary narrowing	3.5%	3.7%	0.7287
Number of coronary arteries narrowed	1.8 ± 0.8	1.8 ± 0.8	0.9997
Systolic blood pressure (mmHg)	133.6 ± 21.1	136.7 ± 21.4	0.0000
Diastolic blood pressure (mmHg)	75.8 ± 12.9	75.7 ± 12.7	0.7263
Total cholesterol (mg/dl)	195.2 ± 37.6	195.6 ± 36.5	0.9230
Fasting blood sugar (mg/dl)	124.0 ± 50.0	121.5 ± 46.8	0.2644
Angiotensin-converting enzyme inhibitors	70.2%	72.1%	0.1977
Angiotensin receptor blockers	31.8%	30.5%	0.3812

Values are the mean ± SD or percentage of each characteristic

Hypertension was defined as systolic blood pressure ≥140 mmHg or diastolic blood pressure ≥90 mmHg; hyperlipidemia was defined as total cholesterol ≥220 mg/dl or low density lipoprotein cholesterol ≥140 mg/dl or triglyceride ≥150 mg/dl

CCB calcium channel blocker, *RASI* renin-angiotensin system inhibitor

the control and treatment groups by the propensity score matching method [10]. As a result, additional effects beyond blood pressure lowering of an RASI and a CCB alone, or in combination were successfully evaluated. The findings of this study suggest that the usefulness of a combination of an RASI and a CCB beyond blood pressure lowing may not exist. This implies that the beneficial effects of the combination treatment with an RASI and a CCB compared with each monotherapy are largely due to the blood pressure lowering effects. In previous studies indicating the usefulness of combination therapy, blood pressure levels were significantly lower in the combination treatment groups [1–4]. Thus, there may be no additional beneficial effects of a combination of an RASI and a CCB. This may be explained, at least in part, by the difference between the clinical situation and experimental study where a more than tenfold dose of a CCB was used to unravel the vascular protective effect of the drug [7].

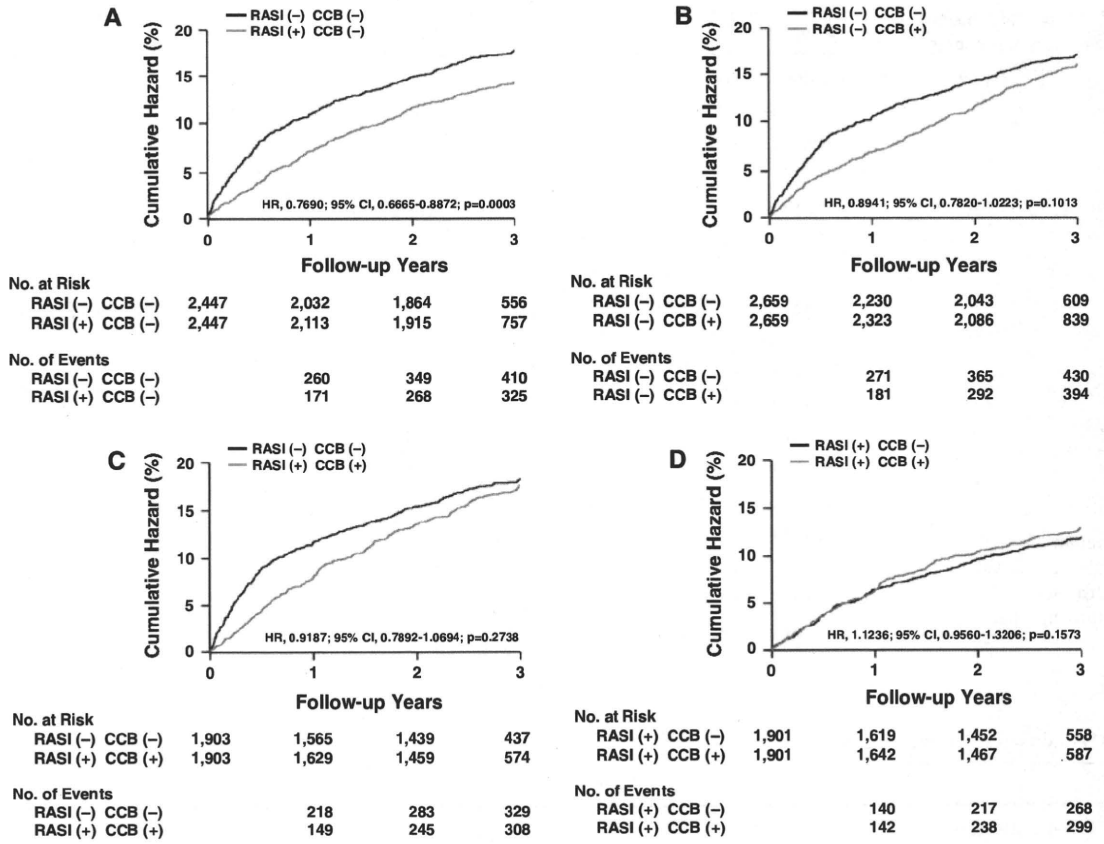

Fig. 1 Cumulative hazard of all cardiovascular events in patients not receiving an RASI and a CCB and those receiving an RASI but no CCB (**a**), a CCB but no RASI (**b**), and both an RASI and a CCB (**c**). Cumulative hazard of all cardiovascular events in patients receiving an RASI but no CCB and those receiving both an RASI and a CCB (**d**). *CCB* calcium channel blocker, *CI* confidence interval, *HR* hazard ratio, *RASI* renin-angiotensin system inhibitor

Although the RASI monotherapy was effective in terms of the prevention of cardiovascular events, the reason why the significantly favorable effect of an RASI disappeared with the addition of a CCB is unclear. The slight but significantly higher blood pressure in the combination treatment group as compared with the untreated control and RASI monotherapy groups may have counterbalanced the effectiveness of the combination treatment. Thus, there is a possibility that "reversal of cause and effect" may have been brought about in the present study.

In the blood pressure lowering arm of the Anglo-Scandinavian Cardiac Outcomes Trial (ASCOT) [11], 5,137 hypertensive patients with diabetes mellitus were randomized to amlodipine with addition of perindopril or atenolol with addition of thiazide, and were followed up for 5 years. The amlodipine-based treatment reduced the incidence of total cardiovascular events and procedures by 14% compared with the atenolol-based treatment. The mean systolic and diastolic pressures were 3.0 and 1.9 mmHg lower among those on the amlodipine-based treatment. Blood levels of glucose, creatinine and triglyceride throughout the study were significantly higher among patients on the atenolol-based treatment. The above-mentioned differences between the two treatment arms may explain the superiority of the combination of a CCB with an RASI to that of a beta-blocker with a diuretic.

In avoiding cardiovascular events by using combination therapy in patients living with systolic hypertension (ACCOMPLISH trial [12]), the benazepril-amlodipine combination treatment has been demonstrated to be superior to the benazepril-hydrochlorothiazide combination in reducing cardiovascular events in high-risk patients with hypertension (relative risk reduction, 19.6%; $p < 0.001$). Mean blood pressure after dose adjustment was significantly lower in the benezepril-amlodipine group compared with the benazepril-hydrochlorothiazide group. The mean difference in blood pressure between the two groups was 0.9 mmHg in the systolic and 1.1 mmHg in the diastolic readings. A small but significant difference in blood pressure may explain the superiority of the benezepril-amlodipine group resutls. Alternatively, the combination of a CCB with an RASI may provide unique beneficial effects

Table 2 Cumulative hazard of cardiac and cerebral events

Groups	No. of events	No. of patients	HR	95% CI	*p* value
Cardiac events					
RASI (−) CCB (−)	336	2,447	0.7487	0.6367–0.8804	0.0005
RASI (+) CCB (−)	260	2,447			
RASI (−) CCB (−)	337	2,659	0.8927	0.7651–1.0415	0.1485
RASI (−) CCB (+)	312	2,659			
RASI (−) CCB (−)	265	1,903	0.9054	0.7615–1.0766	0.2607
RASI (+) CCB (+)	250	1,903			
RASI (+) CCB (−)	216	1,901	1.0790	0.8975–1.2973	0.4185
RASI (+) CCB (+)	240	1,901			
Cerebral events					
RASI (−) CCB (−)	47	2,447	0.6779	0.4321–1.0634	0.0886
RASI (+) CCB (−)	33	2,447			
RASI (−) CCB (−)	49	2,659	0.9433	0.6344–1.4025	0.7731
RASI (−) CCB (+)	49	2,659			
RASI (−) CCB (−)	41	1,903	1.0364	0.6783–1.5834	0.8687
RASI (+) CCB (+)	45	1,903			
RASI (+) CCB (−)	23	1,901	1.9742	1.1864–3.3020	0.0077
RASI (+) CCB (+)	44	1,901			

CCB calcium channel blocker, *CI* confidence interval, *HR* hazard ratio, *RASI* renin-angiotensin system inhibitor

Table 3 Follow-up blood pressure levels

	Baseline	1 Year	2 Years	3 Years
Systolic blood pressure				
RASI (−) CCB (−)	131 ± 20 (n = 2,447)	131 ± 18 (n = 1,609)	131 ± 17 (n = 1,355)	131 ± 17 (n = 1,269)
RASI (+) CCB (−)	129 ± 20* (n = 2,447)	131 ± 18 (n = 2,051)	131 ± 17 (n = 1,747)	131 ± 17 (n = 1,650)
RASI (−) CCB (−)	132 ± 20 (n = 2,659)	131 ± 18 (n = 1,754)	131 ± 17 (n = 1,462)	131 ± 17 (n = 1,383)
RASI (−) CCB (+)	132 ± 18 (n = 2,659)	131 ± 17 (n = 2,249)	131 ± 17 (n = 1,900)	131 ± 16 (n = 1,829)
RASI (−) CCB (−)	135 ± 21 (n = 1,903)	133 ± 18 (n = 1,224)	131 ± 18 (n = 1,015)	131 ± 17 (n = 961)
RASI (+) CCB (+)	137 ± 21* (n = 1,903)	135 ± 18* (n = 1,621)	133 ± 18* (n = 1,395)	133 ± 17* (n = 1,341)
RASI (+) CCB (−)	134 ± 21 (n = 1,901)	132 ± 18 (n = 1,572)	132 ± 17 (n = 1,332)	132 ± 17 (n = 1,244)
RASI (+) CCB (+)	137 ± 21† (n = 1,901)	136 ± 18† (n = 1,611)	134 ± 18† (n = 1,388)	134 ± 17† (n = 1,335)
Diastolic blood pressure				
RASI (−) CCB (−)	74 ± 12 (n = 2,447)	75 ± 11 (n = 1,609)	74 ± 10 (n = 1,355)	74 ± 11 (n = 1,269)
RASI (+) CCB (−)	74 ± 12 (n = 2,447)	74 ± 11 (n = 2,051)	74 ± 11 (n = 1,747)	74 ± 10 (n = 1,650)
RASI (−) CCB (−)	74 ± 12 (n = 2,659)	74 ± 11 (n = 1,754)	74 ± 10 (n = 1,462)	74 ± 11 (n = 1,383)
RASI (−) CCB (+)	74 ± 12 (n = 2,659)	74 ± 10 (n = 2,249)	74 ± 10 (n = 1,900)	74 ± 10 (n = 1,829)
RASI (−) CCB (−)	76 ± 12 (n = 1,903)	75 ± 11 (n = 1,224)	74 ± 10 (n = 1,015)	75 ± 11 (n = 961)
RASI (+) CCB (+)	76 ± 13 (n = 1,903)	75 ± 11 (n = 1,621)	75 ± 11 (n = 1,395)	74 ± 11 (n = 1,341)
RASI (+) CCB (−)	76 ± 13 (n = 1,901)	75 ± 11 (n = 1,572)	75 ± 11 (n = 1,332)	75 ± 10 (n = 1,244)
RASI (+) CCB (+)	76 ± 13 (n = 1,901)	75 ± 11 (n = 1,611)	74 ± 11 (n = 1,388)	74 ± 11 (n = 1,335)

Values are the mean ± SD

CCB calcium channel blocker, *RASI* renin-angiotensin system inhibitor

* $p < 0.05$ versus RASI (−) CCB (−); † $p < 0.05$ versus RASI (+) CCB (−)

beyond the blood pressure lowering effects as compared to the combination of an RASI with a diuretic.

There are several limitations to the present study. First, it is likely that there is a bias related to individuals in this cohort treated with an RASI and/or a CCB being more severely ill than others. However, despite this residual bias, the hazard ratios tended to be lower in each of the drug-treated groups compared to the untreated control group

(Fig. 1a, b, c). The above-mentioned bias inherent to the observational study may have obviated the difference between the RASI monotherapy and combination treatment groups, because complete matching regarding risk factors, exercise [13], drug usage [14] and severity of diseases between the two groups is difficult due to the limitation of the propensity score matching (Fig. 1d). Second, in this study cohort, the prevalence of patients with hypertension was approximately 50–70%; therefore, it may be limited to extrapolating these results to patients with hypertension. Finally, randomization of patients to each treatment arm was not conducted, because the JCAD study was an observational, non-randomized trial. Thus, to clarify the usefulness of combination treatment beyond the blood pressure lowering effects, a prospective, randomized trial consisting of an RASI or a CCB monotherapy and combination treatment groups is needed, although the exact matching of blood pressure levels between the monotherapy and the combination treatment groups may be difficult. In conclusion, our findings suggest that there may be no additional prognostic benefit beyond blood pressure lowering effects in combination of an RASI and a CCB in patients with CAD.

Acknowledgments This work was supported by a grant from the Japanese Circulation Foundation.

Conflict of interest None for all authors.

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Nutrition Research
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Smart-card-based automatic meal record system intervention tool for analysis using data mining approach

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Received 1 February 2010; revised 20 March 2010; accepted 7 April 2010

Abstract

The Smart-card-based Automatic Meal Record system for company cafeterias (AutoMealRecord system) was recently developed and used to monitor employee eating habits. The system could be a unique nutrition assessment tool for automatically monitoring the meal purchases of all employees, although it only focuses on company cafeterias and has never been validated. Before starting an interventional study, we tested the reliability of the data collected by the system using the data mining approach. The AutoMealRecord data were examined to determine if it could predict current obesity. All data used in this study (n = 899) were collected by a major electric company based in Tokyo, which has been operating the AutoMealRecord system for several years. We analyzed dietary patterns by principal component analysis using data from the system and extracted 5 major dietary patterns: healthy, traditional Japanese, Chinese, Japanese noodles, and pasta. The ability to predict current body mass index (BMI) with dietary preference was assessed with multiple linear regression analyses, and in the current study, BMI was positively correlated with male gender, preference for "Japanese noodles," mean energy intake, protein content, and frequency of body measurement at a body measurement booth in the cafeteria. There was a negative correlation with age, dietary fiber, and lunchtime cafeteria use (R^2 = 0.22). This regression model predicted "would-be obese" participants (BMI ≥ 23) with 68.8% accuracy by leave-one-out cross validation. This shows that there was sufficient predictability of BMI based on data from the AutoMealRecord System. We conclude that the AutoMealRecord system is valuable for further consideration as a health care intervention tool.

Keywords: Feeding behavior; Overweight; Nutrition assessment; BMI; Data mining
Abbreviations: AIC, Akaike information criterion; BIC, Bayesian information criterion; BMI, body mass index; GI, glycemic index; GL, glycemic load.

1. Introduction

Obesity is a significant issue in Western countries [1]. Similarly in Japan, the prevalence of obesity in males has been increasing for the past 20 years and is now more than 30% for males in their 40s to 60s [2]. Moreover, a longitudinal analysis at the individual level demonstrated that the prevalence of obesity increased among middle-aged Japanese participants [3]. To prevent lifestyle-related diseases, especially visceral fat obesity, the Ministry of Health, Labor and Welfare, Tokyo, Japan, has issued an act that regulates health insurance unions. Under the act, these unions are to recommend an annual medical checkup for insured individuals between the ages of 40 and 75 and to conduct health guidance for those who are diagnosed with or at risk for metabolic syndrome [4].

Because most people at risk for metabolic syndrome are of working age, some companies have started to create environments that aid employees in improving their lifestyles [5-7]. The company cafeteria plays an important role in the diet of employees and has come under the spotlight. Although

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doi:10.1016/j.nutres.2010.04.003

there are several methods for assessing intake of foods/nutrients, including weighed diet records, 24-hour recall, and food frequency questionnaires, few companies have attempted to monitor eating habits of all employees because available methods require tremendous amounts of time, effort, and money.

Recently, smart cards (pocket-sized cards with embedded integrated circuits that can process data) have become common as employee ID cards. An innovative system for company cafeterias has been developed to monitor employees' eating records using a smart card with an electronic wallet function. The smart-card-based Automatic Meal Record (AutoMealRecord system) relates point-of-sale purchase data to nutritional information per serving. For employees who registered, it also provides their nutritional records through email and its corresponding Web site [8]. The system also interfaces with body composition scales that have smart card readers. Employees can use their own dietary history and body composition records to improve their health.

The AutoMealRecord system was originally developed by an electric company as a commercially available health care service to make the smart-card-based system pervasive. Because of their withdrawal from the health care business, the AutoMealRecord system has only been operated in-house and received less attention, even within the company, for several years. Although the AutoMealRecord system only targets meals from company cafeterias, it is a unique nutrition assessment tool for automatically monitoring the meal purchases and body composition of all employees. One of the authors (SZ) had a chance encounter with the implementer of the AutoMealRecord system and saw massive potential in the system to be a powerful tool for health promotion and lifestyle disease prevention. So far however, the system has not received any validation as a nutrition assessment tool as it has only been used for providing a weekly nutrition summary to registered employees. We decided to assess the potential of the AutoMealRecord system as a preventive measure against lifestyle diseases. Before starting an interventional study though, it must be tested whether the data accumulated by the AutoMealRecord system is reliable as a diet record. We applied the data mining approach, which is commonly used in a wide range of profiling practices such as marketing and surveillance, to extract important patterns from large amounts of data [9]. We hypothesized that the AutoMealRecord system could explain current obesity status if the data were reliable as a diet record, and so, we explored whether data previously collected by the AutoMealRecord system could predict current obesity in this study.

2. Methods and materials

2.1. Participants and data sources

All data used in this study were collected through the head office of a major electric company based in Tokyo that has been operating the AutoMealRecord system for several years. We accessed the AutoMealRecord system database provided by Relieur-Interieur LLP, Tokyo, Japan, which recently administered the AutoMealRecord system outside the electric company with the nondisclosure agreement. There are 2 food service companies providing cafeteria-style dining at lunchtime and dinnertime. In September 2008, the administrator of the system sent an email to all permanent employees working at the office inviting them to register with the AutoMealRecord system. About 23% of them (n = 933) started using the system. Written informed consent was obtained from all participants at the time of registration.

All data used in this study were extracted from the AutoMealRecord system database on December 1, 2008. We were only able to access meal purchases and body composition records obtained from consenting participants and did not handle personal data such as names or contact information. Because all data used in our study were completely anonymous and secondary data, this study was started without an ethical review in compliance with the Ethical Guidelines for Epidemiological Studies [10]. However, the protocol of our project on the AutoMealRecord system (including this study) was approved by the ethics review board of the University of Tokyo (Japan).

The AutoMealRecord system (described in detail by Murakami [8]) has diners pay for their meals at a cafeteria terminal using an employee ID card with an electronic money function. All purchase data (electronic money ID, purchase date/time, code/quantity for each dish, and price) are stored on a central server. Nutritional information per serving (total energy, carbohydrate, protein, fat, salt, and fiber) and classification codes (food group, main ingredient, and cooking method) are delivered on a weekly basis to the database by national registered dietitians working for the cafeterias, under the supervision of Dr Ishida, Professor of Administrative Dietetics at Kagawa Nutrition University (Saitama, Japan). Each dish is also classified under 3 codes: food group, main ingredient, and cooking method (Table 1). Because of the complexity of laws regarding the details of the purchasing data such as the name of dish, we used these classification codes to track what was eaten.

The AutoMealRecord system database relates purchase data to nutritional information that it automatically saves. Employees who have registered with the AutoMealRecord system can check their daily diet record and nutritional balance by browsing the corresponding Web site (http://www.cooca.jp/fdk/index.php) that is protected by their unique IDs and passwords.

2.2. Meal purchasing-related data

To eliminate the effect of self-awareness, we analyzed the meal purchasing information that was stored in the

Table 1
Dish classification codes of the AutoMealRecord system used in dietary pattern analysis

	Classification code	Foods in the group[a]
Food group	Japanese main dish	Boiled/roasted fish, cooked vegetables
	Western main dish	Fry, cutlet, stew, croquette
	Chinese main dish	Stir-fried/braised meat and vegetables
	Japanese noodles	Buckwheat noodle (*soba*), Japanese wheat noodle (*udon*)
	Pasta	Pasta, spaghetti, gratin
	Chinese noodles	Chinese noodle
	Japanese rice	Rice, sushi, rice bowl with toppings (*donburi*), rice porridge
	Western rice	Curry and rice, risotto, doria
	Chinese rice	Fried rice, Chinese-taste rice bowl, Korean rice mixed with seasoned vegetables (bibimbob)
	Japanese combo meal	Meal includes Japanese main dish, side dish, and rice/rice bowl
	Western combo meal	Meal includes Western main dish, side dish, and rice
	Chinese combo meal	Meal includes Chinese main dish, side dish, and rice
	Sandwich	Sandwiches to go
	Garnishing	Boiled/sauted vegetables served with main dish
	Side dish	Boiled egg, *tofu* (soybean curd), *natto*, salad
	Miso soup	Miso (fermented soybean paste) soup, other kinds of soup
	Dessert	Fruit cup, jelly, pudding, cake, yoghurt
	Bento	Takeout lunch box with rice, fish/meat, vegetables
	Sauce	Sauce/dressing on the side
Main ingredient	Beef	Beef except minced/processed meat, such as *sukiyaki*, beef-over-rice-bowl (*gyu-don*), etc
	Pork	Pork except minced/processed meat, such as ginger pork (*shougayaki*), miso soup with pork and vesi (*tonjiru*)
	Chicken	Chicken except minced/processed meat, such as fried chicken, Japanese chicken stew (*chikuzen-ni*)
	Minced/processed meat	Hamburger steak, ham, sausage
	Seafood	Roasted/cooked fish, soup with shellfish or seaweed, vongole bianco/rosso
	Vegetables	Sauted vegetables, boiled spinach, deep-fried eggplant
	Eggs	Boiled egg, omelet
	Soy products	*Tofu*, *natto*
	Grains	White/brown rice, Japanese/Chinese noodles, pasta, breads
	Fruits	Fruit cup, fruit and yogurt
Cooking method[b]	Simmer (*niru*)	Cooked meat/fish/vegetables, curry, miso soup
	Stir-fry (*itameru*)	Stir-fried meat/vegetables, fried rice, spaghetti
	Grill/roast (*yaku*)	Roasted fish, gratin, hamburg steak
	Deep-fry (*ageru*)	*Tempura*, fried fish, cutlet, croquette
	Steam (*musu*)	Cup-steamed egg custard (*chawan musi*), steamed chicken, Dim Sum
	Dress (*aeru*)	Boiled and dressed vegetables, such as pumpkin salad, boiled spinach dressed with soy sauce and sesame (*goma-ae*)
	Chill (*hiyasu*)	Chilled tofu, *natto*, fresh green salad, fruit
	Boil (*yuderu*)	Japanese/Chinese noodles, boiled egg
	Cook (*taku* especially rice)	White/brown rice, rice mixed with vegetables and/or meat
	Marinade (*hitasu*)	Marinated fish, marinated deep-fried eggplant

Three types of classification codes (Food group, main ingredient and cooking method) are added to each dish in the AutoMealRecord system.
[a] The names of dish in Japanese are indicated in italics.
[b] Cooking methods in Japanese verbs are indicated in italics.

year before the registration of the AutoMealRecord system (October 1, 2007, to September 30, 2008). As dietary assessment data, we used annual mean of dietary intake (total energy [Kj], energy-adjusted fat content [percentage of total energy], energy-adjusted protein content [percentage of total energy], dietary fiber [gram], and salt [gram]). We also calculated use of the company cafeteria throughout the year (monthly use of cafeteria [times], lunchtime use [percentage], preference of food service companies [percentage], and purchase amount [Yen]) to estimate eating and living habits.

2.3. Other variables

At the cafeteria, there was a body measurement booth with a body composition scale and an electronic manometer, both of which have smart card readers and on-screen instructions. The body composition records were stored automatically in the database. The 3-month average weight as calculated by the latest body composition records (September 1, 2008, to November 14, 2008) was used to reflect recent body size. If there was no measurement history during the period, we used the self-reported anthropometric measurements that were entered upon registration. Body mass index (BMI) was calculated as mean body weight (automatically collected data, kilogram) divided by the square of self-reported body height (square meter). We also used self-reported demographic data (age and sex) and use of the body composition scale (times) as covariates.

2.4. Statistical analyses

Dietary patterns were identified using the principal component analysis (proc princomp in SAS [SAS Institute,

Cary, NC]) [11]. We analyzed the dietary patterns based on 39 classification codes (Table 1) using 156 345 items purchased (corresponding to 899 participants) at the headquarters' cafeteria from October 2007 to September 2008 and not including beverages. Principal component analysis was conducted to obtain synthetic variables uncorrelated with each other. Beverages were excluded because most cafeteria users do not buy beverages with meals because cafeterias in Japan ordinarily serve free water and/or tea and do not have sweetened beverages.

We used principal components (eigenvalue $\geq$ 1.0) as dietary patterns and assigned them to each purchase when the score of a principal component was the highest. Frequency of dietary patterns per purchase was counted by personal ID. Annual proportion of each dietary pattern was called *preference* and calculated as follows:

$$\text{(Preference of dietary pattern X)} = \frac{\text{(annual frequency assigned to the dietary pattern X)}}{\text{(annual total frequency of cafeteria use)}}.$$

We examined the correlation between dietary patterns and demographic variables (age, sex, and BMI). To determine the association between cafeteria use (including dietary patterns) and BMI, we developed a multiple linear regression model [11]. Among 899 participants who had purchased during the past year, 634 participants weighed themselves at least once from September 2008 to November 2008 or reported their weight at registration. Data from those 634 participants were assessed to develop a BMI prediction model based on multiple linear regression analysis. We used stepwise selection and set $P < .15$ as the level of significance as the commonly accepted threshold. To predict the current obesity status of all 634 participants, 11 variables were initially introduced (age, sex, total energy [Kj], fat content [percentage of energy], protein content [percentage of energy], dietary fiber [gram], salt [gram], monthly use of cafeteria [times], lunchtime use [percentage], preference of food service companies [percentage], and frequency of body measurement [times]). Nine variables, excluding age and sex, were used for subgroup analysis.

The Akaike information criterion (AIC) and the Bayesian information criterion (BIC; also called as Schwarz Bayesian Criterion [SBC]) were calculated to compare fitness (in SAS: proc reg/option AIC and SBC) [12-15]. The AIC is grounded in the concept of entropy or the balance of precision and complexity of the model. The BIC is very closely related to the AIC. In BIC, maximum likelihood estimation is used for model selection. Competing models are ranked according to their AIC and BIC, with the one having the lowest score being the best.

Furthermore, we conducted leave-one-out cross validation that is used to determine how accurately a model will be able to predict data that it was not trained on [9,16]. Data are divided into 2 subsets, the first one is the data of kth participant, and the second set contains the rest of the data. A BMI prediction model is constructed using the second set of data based on multiple linear regression analysis. Predicted BMI for the omitted participant is computed by putting his/her data into the acquired model. Predicted and measured BMIs are then dichotomized by more/less than 23 $kg \cdot m^{-2}$, and the accuracy of the model is checked. This set of calculations is repeated for N (numbers of participants) times, and the predictive capability of the models was evaluated by calculating the prediction accuracy rate. A BMI of more than 25 $kg \cdot m^{-2}$ is defined as obese in Japan by the Japan Society for the Study of Obesity [17]. However, in this study, we defined *obese* and *would-be obese* as BMI of 23 $kg \cdot m^{-2}$ or greater as based on a previous study that showed that AutoMealRecord registrants whose BMI was between 23 and 25 $kg \cdot m^{-2}$ tended to become obese. Yet, they significantly improved their eating behavior when using a nutritional education program [18]. We use BMI of 23 or greater as the cutoff point for the practical purpose of testing the potential of the AutoMealRecord system as a preventative measure against obesity.

3. Results

Participants were predominantly men in their 30s and 40s (Table 2). Mean BMI (±SD) was 22.2 ± 3.0 $kg \cdot m^{-2}$. Among

Table 2
Characteristics of the AutoMealRecord system registrants who were applied to BMI prediction analysis

Characteristics	n (%) of subjects[a]
Sex	
Male	467 (73.7)
Female	167 (26.3)
Age-group	
20s (20-29)	79 (12.5)
30s (30-39)	239 (37.7)
40s (40-49)	240 (37.8)
50s (50-59)	72 (11.4)
≥60	4 (0.6)
Characteristics	**Mean ± SD[b]**
Age	39.5 ± 8.3
Height (cm)	168.2 ± 7.9
Weight (kg)[c]	63.2 ± 11.2
BMI ($kg \cdot m^{-2}$)[c]	22.2 ± 3.0
Frequency of body measurement[d]	1.4 ± 3.9
Monthly use of cafeteria[e]	16.8 ± 7.2
Energy intake (Kj)[f]	3046.2 ± 470.1

[a] Values are number (percentage) of subjects (n = 634).
[b] Values are represented as mean ± SD.
[c] Three-month average weight during September 1, 2008, to November 14, 2008, was calculated for each participants using body composition data of the AutoMealRecord system.
[d] Three-month frequency of body measurement at the body measurement booth of the company cafeterias.
[e] Average frequency of monthly cafeteria use (lunchtime and dinner time) during October 1, 2007, to September 9, 2008.
[f] Mean energy intake from each meal.