TABLE 2. Adjusted RH for Incidence of Stroke or TIA With a BP Increase of 10 mm Hg (Systolic) and 5 mm Hg (Diastolic)

		Stroke and TIA			Ischemic Stroke*			Hemorrhagic Stroke†		
Variable	Type	RH	95% CI	χ^2	RH	95% CI	χ^2	RH	95% CI	χ^2
Systolic										
Morning BP	All	1.31	1.18 to 1.46	24.4	1.32	1.16 to 1.50	17.4	1.34	1.09 to 1.64	7.7
	Treated	1.29	1.10 to 1.51	9.8	1.25	1.04 to 1.50	5.5	1.50	1.11 to 2.04	6.8
	Untreated	1.23	1.05 to 1.45	6.4	1.24	1.02 to 1.52	4.6	1.16	0.86 to 1.57	1.0
Evening BP	All	1.34	1.20 to 1.50	25.9	1.33	1.16 to 1.52	16.9	1.39	1.12 to 1.71	9.3
	Treated	1.30	1.09 to 1.54	8.7	1.20	0.98 to 1.46	3.1	1.72	1.23 to 2.41	10.1
	Untreated	1.28	1.09 to 1.50	9.2	1.32	1.08 to 1.61	7.4	1.17	0.87 to 1.56	1.1
Combined BP	All	1.36	1.21 to 1.52	27.0	1.35	1.18 to 1.55	18.4	1.40	1.13 to 1.73	9.1
	Treated	1.33	1.12 to 1.58	10.1	1.25	1.02 to 1.53	4.6	1.70	1.21 to 2.39	9.2
	Untreated	1.28	1.08 to 1.51	8.3	1.30	1.06 to 1.60	6.4	1.18	0.87 to 1.60	1.1
Diastolic										
Morning BP	All	1.21	1.12 to 1.32	20.6	1.21	1.10 to 1.34	15.0	1.25	1.07 to 1.47	7.7
	Treated	1.19	1.05 to 1.35	7.7	1.18	1.02 to 1.36	4.8	1.31	1.02 to 1.70	4.3
	Untreated	1.16	1.03 to 1.31	5.6	1.16	1.00 to 1.34	3.8	1.19	0.95 to 1.48	2.2
Evening BP	All	1.24	1.14 to 1.36	24.1	1.25	1.13 to 1.38	17.8	1.27	1.07 to 1.49	7.8
	Treated	1.23	1.08 to 1.41	9.5	1.17	1.00 to 1.37	4.0	1.52	1.14 to 2.02	8.2
	Untreated	1.18	1.04 to 1.33	6.8	1.21	1.05 to 1.41	6.5	1.12	0.89 to 1.41	1.0
Combined BP	All	1.25	1.14 to 1.36	23.9	1.25	1.13 to 1.39	17.5	1.28	1.08 to 1.52	8.3
	Treated	1.23	1.08 to 1.41	9.2	1.19	1.02 to 1.39	4.7	1.45	1.09 to 1.92	6.6
	Untreated	1.18	1.04 to 1.34	6.7	1.20	1.03 to 1.40	5.4	1.17	0.92 to 1.47	1.7

Adjusted factors: age, sex, body mass index, habitual smoking, diabetes mellitus, hypercholesterolemia, and past history of cardiovascular disease. χ^2 indicates Wald χ^2 tests.

*Cerebral infarction and TIA.

†Intracerebral hemorrhage and subarachnoid hemorrhage.

of antihypertensive medication and home BP for stroke risk was not statistically significant ($P=0.2$ among subjects with NT and those with morning HT). Although the risk in evening HT subjects tended to be higher than that in the NT subjects, there were no significant differences (all $P>0.05$). There were no significant differences among morning HT, evening HT, and sustained HT when these categories were compared directly in the Cox model (all $P>0.2$).

We also compared (1) morning HT group (morning HT and sustained HT) with the remaining 2 groups and (2) evening HT group (evening HT and sustained HT) with the remaining 2 groups, respectively. The stroke or TIA risk in the evening HT group was significantly higher than that in the remaining 2 (NT and morning HT) groups (Table 4). Furthermore, individuals in the morning HT group also had a significant stroke or TIA risk when compared with those in the remaining 2 (NT and evening HT) groups (Table 4). The risk in the morning HT group was more pronounced when subjects were taking antihypertensive medications at baseline (Table 4). There were no significant interactions between antihypertensive medication and risk classifications (all $P>0.1$).

The results of the ischemic type of stroke were essentially similar to those of total stroke; the risk of ischemic stroke in morning HT (RH: 3.00; 95% CI: 1.69 to 5.34) and the risk in sustained HT (RH: 2.55; 95% CI: 1.64 to 3.97) was significantly higher than the risk in NT, whereas the risk in evening HT (RH: 1.87; 95% CI: 0.78 to 4.48) was not significantly different from that in NT. The risk of hemorrhagic type of stroke was not assessed because of the insufficient number of events.

Discussion

This is the first study to demonstrate the difference in the predictive power of home BP measured at different periods of time, that is, morning and evening. Our findings were based on a comprehensive follow-up system in the Ohasama cohort and on accurate diagnoses of stroke and subtypes on the basis of computed tomography/MRI.[6] Our previous studies have shown high reproducibility, reliability, and predictive power of home BP in the morning.[5–7,11,14–17,22] In the Self-Measurement of Blood Pressure at Home in the Elderly: Assessment and Follow-Up (SHEAF) study, another prospective study to evaluate the prognostic significance of home BP, elderly hypertensive subjects with antihypertensive medication were asked to measure their BPs at home; the result indicated that the average of morning and evening BP values was a better predictor for cardiovascular disease than the average of casual-screening BP.[8] In the present study, we demonstrated that the predictive power of morning BP, as well as evening BP, was essentially similar to that of combined morning and evening BP; although adding diastolic combined BP values marginally improved the goodness of fit in the model based on diastolic morning BP values, further studies are required to clarify the clinical significance. However,

TABLE 3. Adjusted RH of Home BP and Casual-Screening BP Levels for Stroke or TIA Incidence With a BP Increase of 10 mm Hg (Systolic) and 5 mm Hg (Diastolic)

	Stroke and TIA			Ischemic Stroke*			Hemorrhagic Stroke†		
BP Variable	RH	95% CI	χ^2	RH	95% CI	χ^2	RH	95% CI	χ^2
Systolic									
Morning BP	1.34	1.18 to 1.51	21.1	1.33	1.15 to 1.53	14.4	1.46	1.14 to 1.86	9.0
Casual BP	1.00	0.91 to 1.10	0.0	1.02	0.91 to 1.14	0.1	0.90	0.74 to 1.08	1.3
Diastolic									
Morning BP	1.23	1.12 to 1.36	19.0	1.20	1.08 to 1.35	10.7	1.40	1.17 to 1.67	13.1
Casual BP	0.99	0.92 to 1.07	0.1	1.01	0.93 to 1.11	0.1	0.90	0.78 to 1.04	2.0
Systolic									
Evening BP	1.36	1.19 to 1.54	21.5	1.34	1.15 to 1.56	14.4	1.46	1.14 to 1.88	8.8
Casual BP	1.00	0.91 to 1.09	0.0	1.02	0.91 to 1.14	0.1	0.90	0.75 to 1.08	1.3
Diastolic									
Evening BP	1.27	1.14 to 1.40	21.2	1.26	1.12 to 1.41	14.2	1.36	1.12 to 1.65	9.4
Casual BP	0.98	0.91 to 1.06	0.3	1.00	0.91 to 1.09	0.0	0.91	0.78 to 1.06	1.6
Systolic									
Combined BP	1.39	1.22 to 1.59	23.2	1.37	1.17 to 1.61	15.6	1.52	1.17 to 1.99	9.8
Casual BP	0.99	0.90 to 1.09	0.1	1.01	0.90 to 1.13	0.0	0.89	0.73 to 1.07	1.6
Diastolic									
Combined BP	1.28	1.15 to 1.41	21.9	1.25	1.11 to 1.41	13.4	1.42	1.17 to 1.73	12.2
Casual BP	0.98	0.91 to 1.06	0.3	1.00	0.91 to 1.10	0.0	0.89	0.77 to 1.04	2.2

Subjects (1661), who measured casual BP in addition to home BPs, were included in the analysis. Casual BP and each home BP were simultaneously included into the Cox model. Adjusted factors: age, sex, body mass index, habitual smoking, diabetes mellitus, hypercholesterolemia, and past history of cardiovascular disease. χ^2 indicates Wald χ^2 tests.

*Cerebral infarction and TIA.

†Intracerebral hemorrhage and subarachnoid hemorrhage.

it is noteworthy that individuals with morning HT, whose BP values in the evening were relatively lower than those in the morning, had a high risk similar to sustained HT, in particular, among those taking antihypertensive medications.

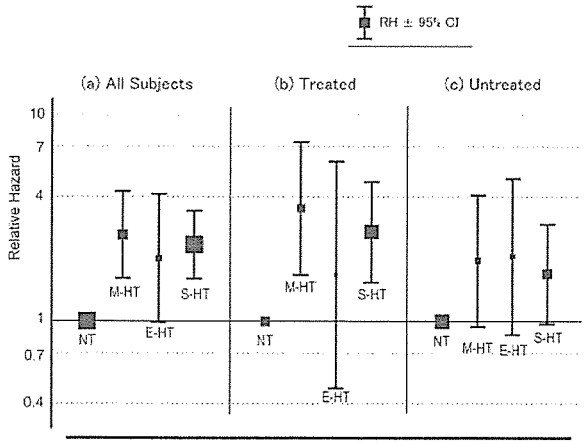

Figure 2. Risk of first stroke or TIA among groups. ■, sized in proportion to the number of events observed. The NT group is treated as the reference category for (a) all 1766 subjects, (b) 504 subjects with antihypertensive medications, and (c) 1262 subjects without antihypertensive medications. Adjusted factors were age, sex, body mass index, habitual smoking, diabetes mellitus, hypercholesterolemia, and past history of cardiovascular disease. M-HT indicates morning-HT; E-HT, evening-HT; S-HT, sustained-HT.

Casual BP values in this study were defined as the average of only 2 measurements; this might account for the weaker predictive power of casual BP for stroke or TIA risk when compared with both morning BP and evening BP. However, in our previous study, even 1 measurement value of morning BP on the first occasion was superior to the average of 2 casual BP values in terms of stroke or TIA prediction.[23] Such association was similarly observed in the present study for both morning BP and evening BP (data not shown). These results suggest that, in addition to the number of measurements, other factors, such as the lack of the white coat effect,

TABLE 4. Adjusted RH for Incidence of Stroke or TIA in Relation to 2 of 4 (NT, Morning HT, Evening HT, and Sustained HT) Categories

Category	Type	RH	95% CI	χ^2
Morning HT and Sustained HT	All	2.29	1.65 to 3.18	24.6
	Treated	2.71	1.61 to 4.57	14.0
	Untreated	1.67	1.04 to 2.68	4.5
Evening HT and Sustained HT	All	1.92	1.38 to 2.68	14.9
	Treated	1.78	1.10 to 2.87	5.5
	Untreated	1.63	0.998 to 2.67	3.80

Each RH was expressed relative to the other 2 categories combined. Definitions of categories were shown in Figure 1. Adjusted factors: age, sex, body mass index, habitual smoking, diabetes mellitus, hypercholesterolemia, and past history of cardiovascular disease. χ^2 indicates Wald χ^2 tests.

may be associated with the superior predictive power of home BP.

We reported previously that morning HT was observed more frequently in treated hypertensive subjects than in untreated hypertensive subjects.[11] In 1992, 70% of hypertensive subjects were treated with nifedipine sustained-release tablets, nicardipine sustained-release tablets, or by diltiazem sustained-release tablets in this Ohasama population.[13] At that time, β-blockers, diuretics, and angiotensin-converting enzyme inhibitors were prescribed for 30%, 25%, and 10% of hypertensive subjects, respectively.[13] Because the duration of action of most antihypertensive drugs used in 1992 was <12 hours for a twice-a-day prescription and <24 hours for a once-a-day prescription,[22] it is likely that morning HT was mediated at least in part by insufficient duration of action of the antihypertensive drugs. Moreover, the trough/peak ratios of most antihypertensive drugs are reported to be <50%, although they are long-acting drugs or long-acting formulae.[24] This may be one of the reasons why the predictive power of morning HT for stroke or TIA risk was stronger among treated subjects than that among all of the subjects. In the current study, however, we did not assess changes over time in antihypertensive treatment; it remains to be investigated whether changes in antihypertensive treatment during follow-up could modify the risk of stroke or TIA in subjects. It must be noted that, although new long-acting calcium channel blockers and new angiotensin II receptor blockers have been marketed, the control of morning BP is reported to be far from ideal even at the present time.[25]

Another possibility for the stronger prediction of morning HT in treated subjects compared with that in untreated ones is that treatment, per se, is a sort of marker of disease severity leading to a greater rate of events. Forty percent of the subjects under antihypertensive medication were included in the NT group, resulting in the low RH in the morning HT (Figure 2a). Most of the previous reports demonstrated a worse prognosis for treated hypertensive subjects than untreated hypertensive subjects.[26,27] We should be concerned about residual stroke or TIA risks in hypertensive patients.

Several Japanese studies, including ours, demonstrated that evening BP was lower than morning BP.[11,12,28] Conversely, 2 European studies reported that evening BP was higher than morning BP.[29,30] One explanation for the difference may be that most Japanese people bathe every night. Another reason for the difference might be the time of evening BP measurement. European studies measured evening BP in the early evening (before dinner[29] or 6:00 PM to 10:00 PM[30]), whereas in Japanese studies, measurements were taken in the late evening (before bedtime), based on the Japanese guidelines for home BP measurement.[3] Approximately one third of adults in Ohasama drink alcohol in the evening,[31] and this might also cause a transient fall in BP in the late evening. Home BP measured in the morning under well-controlled conditions may increase its predictive power, whereas it is likely that the uncontrolled measurement conditions in the evening may result in the insufficient predictive power of evening BP, especially of evening HT, for stroke and TIA incidence. Thus, the prognostic significance of evening home BP for people from other countries still remains to be investigated.

In addition, the first measurement of home BP is reported to be higher than the second or the third home BP values.[29] Therefore, both morning BP values and evening BP values might be lower in the present study if the second or the third home BP values were analyzed. However, regression to the mean occurs during long-term measurement of home BP even for the first measurement of home BP.[3] Moreover, the reference values for home BP have been derived from studies in the general population that used the average of the first measurement.[6,32,33] Further studies are needed to clarify the clinical significance and reference values of the second or the third home BP values compared with the first home BP values.

Perspectives

Morning BP, evening BP, and combined values of the 2, respectively, were a good index for stroke or TIA risk when these parameters were used as continuous variables. Morning HT, which indicates HT specifically observed in the morning, had a high predictive power for stroke or TIA risk, particularly among individuals using antihypertensive medication. We conclude that home BP measurements are applicable to the intervention strategy for primary prevention of cardiovascular disease in individuals whether they measure home BP in the morning or in the evening, whereas morning HT based on home BP might be a good indicator for uncontrolled management of HT.

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Disclosures

None.

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3)今後の研究計画

家庭血圧・24時間自由行動下血圧が、これまで健診等で用いられてきた随時血圧よりも予後予測能が高いことは本研究においてすでに報告されている通りである。また本年はこれに加え、血圧日内変動・朝晩の家庭血圧についての分析を行った。今後は、さらに詳細に、ambulatory arterial stiffness index (AASI)や血圧短期変動などの詳細な血圧成分をもとに、頭部MRI、Pulse Wave Velocity, Augmentation Index, 指尖容積脈波、24時間ホルター心電図、頸動脈エコー、ミニメンタルテスト、クレアチニンクリアランス、インスリン抵抗性、尿中微量アルブミン、BNP、高感度CRP、フィブリノーゲン、リポプロテイン(a)、マグネシウムなどの血清電解質等の、臓器障害・生化学パラメーターとの関連、および高血圧発症リスク・循環器疾患罹患・死亡リスクを評価していく。

また、本年は、家庭血圧の医療経済効果について、短期的なシュミレーションを行い、家庭血圧導入が医療費削減につながる可能性を明らかにした。今後はより長期的な効果について、マルコフモデルなどを用いた詳細な分析を実施していく予定である。

また、食事頻度摂取量に関する詳細な調査票データをもとに、栄養素や食品の組み合わせと高血圧等の脳心血管疾患危険因子発症・進展との関連、および、単一栄養素、食品と高血圧・動脈硬化の関連についての分析を行う。さらに、パーソナリティーの型等の個人的素因に関するデータに基き、生活習慣、個人的素因と食事摂取の関連についての分析も行う。

この他、冷凍保存してある大迫住民の白血球分画より抽出したDNAを遺伝解析し、高血圧、脂質、糖代謝に関する遺伝子を中心とした遺伝子型データとの相互作用を、具体的に検証する。

上記を通じ、生活習慣・遺伝情報の両面から循環器疾患発症のメカニズムを検討するとともに、日本人におけるきめ細かく無駄のない予防医学に貢献しうるエビデンス構築の一端を担いたいと考えている。

3. 滋賀県国保コホート研究

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研究成果

(1) 高血圧と糖尿病の合併と医療費の関連；滋賀県国保コホートにおける10年間の追跡による検討

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【 目的 】高血圧や糖尿病が医療費を上昇させることは知られている。しかし、これらの合併は稀ではない。この場合、循環器疾患などの発症リスクはそれぞれ単独よりも高いため、医療費もより上昇する可能性があり、これを追跡調査によって明らかにすることを試みた。

【 方法 】滋賀県内の7町1村における40-69歳の国民健康保険加入者4,535名（男性1,939名、女性2,596名）を約10年間追跡した。追跡開始時における高血圧（収縮期血圧140mmHg以上、拡張期血圧90mmHg以上、治療ありのいずれか）および糖尿病（既往あり）の状況によって、対象者を「非高血圧非糖尿病」、「高血圧のみ」、「糖尿病のみ」と「高血圧糖尿病合併」の４つのカテゴリーに分けて、各カテゴリーの一人あたりの医療費と総死亡のハザード比（非高血圧非糖尿病を基準）を評価した。

【 結果 】高血圧と糖尿病の合併の頻度は全対象者4,535名中1.3%であった。表に示すように、各カテゴリー一人あたりの医療費（算術平均）は16,699（円/月）（非高血圧非糖尿病）、24,704（円/月）（高血圧のみ）、38,547（円/月）（糖尿病のみ）、40,655（円/月）（高血圧糖尿病合併）であった。この４群の調整医療費（幾何平均）も同様な傾向を示し、統計学的有意差を認めた。また、高血圧糖尿病合併群では総死亡のハザード比（2.37）も上昇を示した。

【 結論 】高血圧と糖尿病の合併はそれぞれ単独よりもより医療費を増加させる。高血圧糖尿病合併群では死亡の危険が上昇しており、高血圧と糖尿病それ自体の治療だけではなく、重篤な合併症を介して医療費の上昇をもたらしたと推測される。これらを合併した患者に対してハイリスク・アプローチに基づいた治療をするとともに、どちらか一方だけを持った患者に対して生活習慣の是正による他方の新規発症を予防することが重要である。

表. 一人あたり医療費と総死亡のハザード比(滋賀県国保コホート)

高血圧糖尿病カテゴリー	対象者数	一人あたり医療費(円/月)		総死亡	
		算術平均	幾何平均 *	ケース数	ハザード比(95%CI) *
非高血圧非糖尿病	2,818	16,699	7,473	112	1.00
高血圧のみ	1,579	24,704	10,067	88	1.15 (0.86-1.55)
糖尿病のみ	77	38,547	14,545	6	1.16 (0.51-2.65)
高血圧糖尿病合併	61	40,655	19,111	9	2.37 (1.19-4.74)
			P<0.01		

* 年齢、性、BMI、喫煙、飲酒、総コレステロールを調整

【 研究成果の公表 】

Nakamura K, Okamura T, Kanda H, Hayakawa T, Okayama A, Ueshima H. Medical costs of patients with hypertension and/or diabetes: A 10-year follow-up study of National Health Insurance in Shiga, Japan.
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Medical costs of patients with hypertension and/or diabetes: a 10-year follow-up study of National Health Insurance in Shiga, Japan

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Background and methods A cohort study investigating medical costs associated with the combination of hypertension and diabetes was conducted. The participants included 4535 community-dwelling Japanese individuals, aged 40–69 years, who were classified into the following four categories: 'Neither hypertension nor diabetes', 'Hypertension alone', 'Diabetes alone' or 'Both hypertension and diabetes'. Medical costs per person per month were compared among the four categories.

Results and conclusion Of the study population, 1.3% had both hypertension and diabetes. During the 10-year follow-up period, participants with both hypertension and diabetes incurred higher medical costs, as compared with those without hypertension, diabetes or their combination, even after adjustment for other confounding factors. *J Hypertens* 24:2305–2309 © 2006 Lippincott Williams & Wilkins.

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Keywords: diabetes, hypertension, medical costs, Japan

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Introduction

It is well recognized that both hypertension [1,2] and diabetes [3,4] are major economic burdens on the health-care system. In addition, the combination of hypertension and diabetes is common [5,6], increasing the risk for macrovascular and microvascular complications [7–10], which may increase medical costs. Japan has a relatively higher incidence or mortality of stroke, especially hemorrhagic stroke [11–14], compared with western countries, mainly due to a higher prevalence of hypertension in Japan [13,15]. Furthermore, the mean level of blood pressure among the Japanese is higher than among western populations [15–18].

To our knowledge, only a few studies have measured medical costs of individuals with both hypertension and diabetes compared with individuals with only one of these conditions, and the follow-up was short ($\leq$ 2 years) [19,20]. A longer follow-up period, however, would be expected to provide a more accurate evaluation of medical costs, because many of the complications of hypertension and diabetes may require substantial time to develop [21,22].

We therefore attempted to measure medical costs over a 10-year period in Japanese community-based individuals with both hypertension and diabetes, and to compare these with the medical costs of individuals with just hypertension, diabetes or neither of these conditions.

Population and methods

Medical costs

In Japan, medical costs are based on the original medical insurance institution [23,24], which is under the control of the National Government. This official medical insurance institution consists of two insurance systems. Everyone living in Japan is required to enroll in either insurance system and there is no private medical insurance. The eligibility for each insurance system is the following: the first system is for employees and their dependants, while the other system is for self-employed individuals such as farmers and fishermen, as well as retirees and their dependants. The former insurance system covers 65.3% of the overall population, while the latter covers the remaining 34.7%. All eligible beneficiaries in either insurance system must pay an annual fee to help fund the system. In principle, both insurance systems guarantee that every beneficiary can have any medical services for any condition at any clinic or hospital throughout Japan. Medical costs depend upon the medical services a beneficiary receives at a clinic or hospital. No taxes are imposed on the medical costs. The clinic or hospital requests medical costs from both the insurance system and the beneficiary, with insurance paying 70% and the beneficiary paying 30%. In the

*Members of the committee are listed in the Appendix.

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present study, total medical costs were divided into outpatient and inpatient medical costs.

Study design and participants

The cohort in the present study comprised 4535 Japanese beneficiaries of the National Health Insurance (NHI), the insurance system for self-employed individuals. The details of the present cohort have been reported previously [2]. The participants, aged 40–69 years, lived in seven rural towns and a village in Shiga Prefecture, West Japan and had undergone a baseline survey in 1989–1991. In 1990, the study area had 82 155 residents, including 31 564 individuals aged 40–69 years old, of whom 11 900 were NHI beneficiaries [25]. The participants in the present study therefore represented approximately 38% of all NHI beneficiaries aged 40–69 years living in this area. Monthly NHI claim history files of the Shiga NHI Organizations were linked with the baseline survey data files at the Organizations. In order to protect the participants' privacy, their names were deleted from the linked data at the Organizations. The data were therefore analyzed without knowledge of the participants' identity. The present study was approved by the Institutional Review Board of Shiga University of Medical Science for ethical issues (No. 16–15).

Data collection

The baseline survey was performed during the period 1989–1991 using standardized methods in accordance with the Manual for Health Check-ups under the Medical Service Law for the Aged, issued by the Japan Public Health Association in 1987 [26]. Blood pressures were measured by well-trained public health nurses in the right arm in the sitting position using a standard mercury sphygmomanometer after the participants had rested for at least 5 min. The use of antihypertensive medications and a history of diabetes were obtained from interviews conducted by well-trained public health nurses and medical doctors. Hypertension was defined as a systolic blood pressure of at least 140 mmHg, a diastolic blood pressure of at least 90 mmHg or taking antihypertensive medication. Diabetes was defined as having a history of diabetes. The prevalence of type 1 diabetes in the Japanese population (< 0.01%) is considerably less than in western populations (0.1–0.3%), even among young individuals [27]. We therefore believe that the majority of diabetics in the cohort of 4535 participants had type 2 diabetes. On the basis of this information, all participants were classified into the following four categories: 'Neither hypertension nor diabetes', 'Hypertension alone', 'Diabetes alone' or 'Both hypertension and diabetes'. Smoking and drinking habits were also evaluated by the interviews. Body height and weight were measured and the body mass index was calculated as the body weight (kg) divided by the square of the height (m). Serum total cholesterol levels were measured by an enzymatic method.

We evaluated medical costs per person and the hazard ratio for all-cause mortality in each of the four categories after a 10-year follow-up period. Information on medical costs for each participant and information on participants who withdrew from the NHI or those who died were obtained from the monthly NHI claim history files, beginning from April in the year following their initial health check-up until March 2001. Costs were expressed in Euros, Japanese *Yen* and US dollars (100 Japanese *Yen* = €0.72 or US$0.85, at the foreign exchange rate on 1 January 2006). Data on medical costs for each participant differed depending upon the period of subscription to the NHI. The medical costs for each participant were therefore divided by the period of subscription, and expressed as costs per month of follow-up. If a beneficiary withdrew from the NHI or died, follow-up was stopped at that point. Follow-up was restarted for beneficiaries who withdrew and then re-enrolled in the NHI. Reasons for withdrawal from the NHI included moving to regions outside of Shiga Prefecture or transfer to the other insurance system.

Data analysis

Because the distribution of real medical costs was positively skewed, the data were logarithmically transformed to normalize the distribution and the results expressed as geometric means. For participants with costs of 0 Japanese *Yen* per month, the logarithmic transformations were performed by replacing 0 *Yen* with 1 *Yen*. There were 15 participants with total medical costs of 0 *Yen* and 16 participants with outpatient medical costs of 0 *Yen*. For comparison of total and outpatient medical costs per person in each category, we performed an analysis of covariance with the Bonferroni correction to adjust the *P* value for multiple post-hoc comparisons. The analysis of covariance incorporated the following variables as covariates: age (40–44, 45–49, 50–54, 55–59, 60–64 or 65–69 years old, using five dummy variables with 40–44 as a reference), sex, body mass index, smoking habit (nonsmoker or current smoker), drinking habit (nondrinker, current occasional or current daily drinker, using two dummy variables with nondrinkers as a reference) and serum total cholesterol. Because 2606 participants (57.5%) had inpatient medical costs of 0 *Yen*, logarithmic transformations were not performed, and the Wilcoxon's rank sum test was used to compare inpatient medical costs among the four categories.

A Cox proportional hazards model for all-cause mortality was used to calculate hazard ratios of each category, with the 'Neither hypertension nor diabetes' category as a reference. This model incorporated the same covariates listed above.

The analyses were repeated on data collected during the first and second halves of the follow-up period, because single assessment of hypertension and diabetes

conducted at baseline may show different associations between these diseases and medical costs or all-cause mortality after stratification of the follow-up period.

The statistical package SPSS 11.0J for Windows (SPSS Japan Inc., Tokyo, Japan) was used for the statistical analyses. All probability values were two-tailed and the significance level was set at P values less than 0.05.

Results

Table 1 summarizes the baseline risk characteristics of the 4535 participants, grouped according to their hypertension and diabetes status. Of all the participants, 1.3% (men, 1.7%; women, 1.1%) had both hypertension and diabetes, while 34.8% had hypertension alone and 1.7% had diabetes alone. The 'Both hypertension and diabetes' group had the highest mean age and body mass index in both sexes and the highest mean level of serum total cholesterol in men.

The total person-years were 41 536 and the mean follow-up time was 9.2 years. When we performed sex-specific analyses of the medical costs or all-cause mortality among the four categories, the results were similar for men and women. We therefore reported these relationships for both sexes combined. As shown in Table 2, during the 10-year follow-up period the total medical costs per person in the 'Both hypertension and diabetes' category [€293 (40 655 *Yen* or US$346) per month] were higher than in the 'Neither hypertension nor diabetes' category [€120 (16 699 *Yen* or US$142)], in the 'Hypertension alone' category [€178 (24 704 *Yen* or US$210)], and in the 'Diabetes alone' category [€278 (38 547 *Yen* or US$328)]. Even after adjusting for other confounding factors, similar differences in personal medical costs among the four categories were still observed. The adjusted hazard ratio of the 'Both hypertension and diabetes' category for all-cause mortality (2.21; 95% confidence interval, 1.11–4.42) was also higher compared with the 'Neither hypertension nor diabetes' category.

When the analyses were repeated on data collected during the first and second halves of the follow-up period, the results for each half were the following. For the first half, the personal medical costs in the 'Neither hypertension nor diabetes', 'Hypertension alone', 'Diabetes alone' and 'Both hypertension and diabetes' categories were €103 (14 315 *Yen* or US$122) per month, €140 (19 434 *Yen* or US$165), €243 (33 743 *Yen* or US$287) and €233 (32 315 *Yen* or US$275), respectively. Costs for the second half, however, were €138 (19 214 *Yen* or US$163), €230 (31 880 *Yen* or US$271), €252 (35 009 *Yen* or US$298) and €493 (68 521 *Yen* or US$582), respectively. The results of the multivariate-adjusted costs for each half also showed a pattern that was similar to the results for the entire 10-year period (Table 2).

Discussion

We carried out a 10-year follow-up study between 1990 and 2001 and demonstrated that Japanese participants with hypertension alone, those with diabetes alone and those with both hypertension and diabetes had increased personal medical costs by 1.5-fold, 2.3-fold and 2.4-fold, respectively, compared with those without hypertension and diabetes. The costs of the combined condition were

Table 1 Baseline risk characteristics in 1989–1991 of 4535 National Health Insurance beneficiaries in Shiga, Japan, grouped by sex and hypertension and diabetes status

	Hypertension and diabetes category				
	Neither	Hypertension alone	Diabetes alone	Both	*P* value
Men					
Number of participants	1157	696	53	33	
Distribution (%)	(59.7)	(35.9)	(2.7)	(1.7)	
Age (years)[a]	52.5 ± 8.3	55.7 ± 7.9	58.7 ± 6.3	59.8 ± 5.8	< 0.01
Body mass index (kg/m^2)[a]	22.2 ± 2.5	23.3 ± 2.9	21.9 ± 2.6	23.8 ± 2.8	< 0.01
Smoking habit[b]					0.67
Current smoker (%)	61.0	58.5	64.2	57.6	
Drinking habit[b]					0.01
Occasional drinker (%)	23.4	18.2	20.8	12.1	
Daily drinker (%)	54.8	63.6	54.7	60.6	
Serum total cholesterol (mmol/l)[a]	4.83 ± 0.88	4.91 ± 0.97	4.68 ± 0.80	5.12 ± 0.90	0.04
Women					
Number of participants	1661	883	24	28	
Distribution (%)	(64.0)	(34.0)	(0.9)	(1.1)	
Age (years)[a]	53.0 ± 8.0	57.1 ± 7.3	56.5 ± 7.9	60.3 ± 5.5	< 0.01
Body mass index (kg/m^2)[a]	22.5 ± 2.8	24.0 ± 3.1	23.2 ± 3.5	24.9 ± 3.3	< 0.01
Smoking habit[b]					0.16
Current smoker (%)	4.0	2.4	4.3	0.0	
Drinking habit[b]					0.50
Occasional drinker (%)	16.8	15.8	17.4	7.1	
Daily drinker (%)	3.7	4.2	8.7	0.0	
Serum total cholesterol (mmol/l)[a]	5.16 ± 0.89	5.43 ± 0.94	5.19 ± 0.77	5.41 ± 0.78	< 0.01

Data presented ± SD. [a]One-way analysis of variance. [b]Chi-squared test.

Table 2 Medical costs per person and all-cause mortality grouped by hypertension and diabetes, after 10-year follow-up from 1990 to 2001, in National Health Insurance in Shiga, Japan

		Medical costs per person per month						
		Total		Outpatient		Inpatient	All-cause mortality	
Hypertension and diabetes category	Number of participants	Arithmetic mean	Adjusted geometric mean[a]	Arithmetic mean	Adjusted geometric mean[a]	Arithmetic mean[d]	Number	Adjusted hazard ratio[e]
Neither	2818	€120 (16 699 *Yen*) (US$142)	7473 *Yen*	€64 (8946 *Yen*) (US$76)	5547 *Yen*	€56 (7770 *Yen*) (US$66)	112	1.00
Hypertension alone	1579	€178 (24 704 *Yen*) (US$210)	10 067 *Yen*[b]	€100 (13 940 *Yen*) (US$118)	7548 *Yen*[b]	€77 (10 762 *Yen*) (US$91)	88	1.15 (0.86–1.55)
Diabetes alone	77	€278 (38 547 *Yen*) (US$328)	14 545 *Yen*[b]	€130 (17 999 *Yen*) (US$153)	10 583 *Yen*[b]	€148 (20 548 *Yen*) (US$175)	6	1.16 (0.51–2.65)
Both	61	€293 (40 655 *Yen*) (US$346)	19 111 *Yen*[b,c]	€169 (23 511 *Yen*) (US$200)	12 531 *Yen*[b,c]	€123 (17 144 *Yen*) (US$146)	9	2.37 (1.19–4.74)
P value			< 0.01		< 0.01	< 0.01		

100 Japanese *Yen* = €0.72 or US$0.85, at the foreign exchange rate on 1 January 2006. [a]Analysis of covariance adjusted for age, sex, body mass index, smoking habit, drinking habit and serum total cholesterol. [b]Significance, versus neither, for multiple post-hoc comparisons with Bonferroni correction, $P < 0.05$. [c]Significance, versus hypertension alone, for multiple post-hoc comparisons with Bonferroni correction, $P < 0.05$. [d]Wilcoxon's rank sum test. [e]Analysis of a Cox proportional hazards regression model adjusted for age, sex, body mass index, smoking habit, drinking habit and serum total cholesterol. Values in parentheses indicate the 95% confidence interval of the hazard ratios.

higher than the medical costs of hypertension or diabetes alone by 1.6-fold and 1.1-fold, respectively.

French *et al.* [19] reported medical costs of Americans with hypertension and/or diabetes during 1 year between 2001 and 2002. Medical costs of the combined condition were higher than costs of hypertension or diabetes alone by 2.3-fold and 1.4-fold, respectively [19]. Amin *et al.* [20] also reported the costs of Americans with hypertension and/or diabetes during 2 years between 1995 and 1997. Medical costs of the combined condition were higher than costs of hypertension or diabetes alone by 1.6-fold [20]. Our results after 10 years of follow-up were similar to the previous results after short-term follow-up, although medical costs may differ between the United States and Japan.

Previous studies reveal that individuals with either hypertension or diabetes have an approximately two-fold increased risk of cardiovascular disease [7,8]. Furthermore, individuals with both hypertension and diabetes have approximately double the risk of those with just hypertension or diabetes [7,8]. In diabetic individuals, the risk of diabetic macrovascular complications is also associated with elevated blood pressure [9]. As a result, individuals with both hypertension and diabetes have more medical care utilization and lower health status than those without these conditions or with either condition alone [5]. In fact, higher all-cause mortality of the study participants with both conditions supports this suggestion. We therefore believe that the combined condition may increase medical costs due not only to medications for diabetes and hypertension, but also to medications for serious complications resulting from these conditions. Increased medical costs of the study participants with diabetes alone, compared with those with hypertension alone, are consistent with previous findings that diabetes is associated with more medical care utilization and lower health status than hypertension [5]. These previous findings tend to support the results of our study.

The present study has several limitations. First, the official medical insurance institution in Japan differs from that in other countries. Absolute values of medical costs for the participants with hypertension and/or diabetes in the present study may therefore not be directly comparable with other populations. Increased medical costs in individuals with hypertension and/or diabetes, however, are probably a general finding that applies to all populations. Second, we were not able to determine the prevalence or severity of other disease in the NHI beneficiaries at the baseline survey, and this may have influenced medical costs during follow-up. The NHI beneficiaries in the present study, however, consisted of healthy community-dwelling individuals who participated in the baseline survey without the need of assistance. We therefore believe that most of the participants were free of serious disease at baseline. Third, the costs of hypertension in the present study were estimated on the basis of a single measurement of blood pressure, whereas the costs of diabetes were estimated on the basis of an interview for diabetes. Classification of participants based on a single measurement of blood pressure is likely to overestimate the prevalence of hypertension. This overestimation leads to a regression dilution bias, which reduces the predictive power of hypertension. The differences in medical costs between the hypertensive and nonhypertensive categories may consequently have been underestimated in the present study. The difference in costs between the diabetic and nondiabetic categories may also have been underestimated, although self-recollection

of the diagnosis of diabetes is likely to underestimate the prevalence of diabetes. Fourth, we had no serial data on hypertension and diabetes after the baseline survey. Despite the lack of serial data, we believe that our results, based on a single baseline survey and 10-year follow-up, support our conclusions that the presence of hypertension and/or diabetes increases long-term medical costs. Finally, the details of the medical diagnoses, medical treatment status (e.g. prescriptions), clinical condition and cause of mortality were not available in the present study. Further studies are therefore needed to clarify the effect of these variables.

In conclusion, individuals with both hypertension and diabetes may be a greater burden on medical economics, as compared with those with just hypertension or diabetes. In order to relieve this economic burden, prevention of hypertension and diabetes is recommended for individuals at risk of developing either or both of these conditions. Appropriate treatment for hypertension and diabetes is also necessary for those with both or either of these conditions.

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Appendix: The Health Promotion Research Committee of the Shiga NHI Organizations

Chairman: Hirotsugu Ueshima (Department of Health Science, Shiga University of Medical Science).

Participating Researchers: Shigeo Yamashita (Kohoku General Hospital), Tomonori Okamura (Department of Health Science, Shiga University of Medical Science), Yoshinori Tominaga (Kohka Public Hospital), Kazuaki Katsuyama (Otsu Public Health Center), Fumihiko Kakuno (Nagahama Public Health Center), Machiko Kitanishi (Higashiomi City Yokaichi Public Health Center).

Associate Researchers: Koshi Nakamura (Department of Health Science, Shiga University of Medical Science), Hideyuki Kanda (Department of Hygiene and Preventive Medicine, Fukushima Medical University).

Secretary Members: Yukio Tobita, Kanehiro Okamura, Kiminobu Hatta, Takao Okada, Michiko Hatanaka (the Shiga NHI Organizations).

(2) 蛋白尿と医療費の関連；滋賀県国保コホートにおける10年間の追跡による検討

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【 目的 】蛋白尿は総死亡や循環器疾患死亡と関連があり、また長期のわたる人工透析を必要する慢性腎不全への進行の指標でもある。このため、蛋白尿が見られる者では医療費が上昇する可能性があり、これを追跡調査によって明らかにすることを試みた。

【 方法 】滋賀県内の7町1村における40-69歳の国民健康保険加入者4,490名（男性1,929名、女性2,561名）を約10年間追跡した。追跡開始時における蛋白尿の有無によって、対象者を「蛋白尿なし；(－) ～ (±)」と「蛋白尿あり；(＋) ～ (＋＋＋)」の２つのカテゴリーに分けて、各カテゴリーの一人あたりの医療費と累積入院のオッズ比、総死亡のハザード比（蛋白尿なしを基準）を評価した。

【 結果 】蛋白尿が見られる者の頻度は全対象者4,490名中1.0%であった。表に示すように、各カテゴリー一人あたりの医療費（算術平均）は20,029（円/月）（蛋白尿なし）、37,494（円/月）（蛋白尿あり）であった。この２群の調整医療費（幾何平均）も同様な傾向を示し、統計学的有意差を認めた。また、蛋白尿あり群においては累積入院のオッズ比（1.54）も総死亡のハザード比（1.60）も上昇を示した。

【 結論 】蛋白尿が見られる者では不良な予後を伴って医療費が上昇すると推測される。また、蛋白尿は将来の医療費上昇を予測する指標となると考えられる。

表. 一人あたり医療費、累積入院のオッズ比と総死亡のハザード比（滋賀県国保コホート）

蛋白尿カテゴリー	対象者数	一人あたり医療費(円/月)		累積入院		総死亡	
		算術平均	幾何平均 *	ケース数	オッズ比(95%CI) *	ケース数	ハザード比(95%CI) *
蛋白尿なし	4,443	20,029	8,451	1,883	1.00	209	1.00
蛋白尿あり	47	37,494	14,200	26	1.54 (0.84-2.84)	5	1.60 (0.64-4.03)
			P<0.01				

* 年齢、性、BMI、喫煙、飲酒、収縮期血圧、高血圧治療、総コレステロール、糖尿病を調整

【 研究成果の公表 】

Nakamura K, Okamura T, Kanda H, Hayakawa T, Okayama A, Ueshima H. Medical costs of individuals with proteinuria: A 10-year follow-up study of National Health Insurance in Shiga, Japan. Public Health 2007; 121: 174-176.

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Short Communication

Medical costs of individuals with proteinuria: A 10-year follow-up study of National Health Insurance in Shiga, Japan

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Proteinuria;
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Medical costs

Proteinuria is associated with all-cause and cardiovascular mortality,[1] in addition to being a marker of progression towards end-stage renal disease.[2] It is therefore likely that proteinuria may lead to an increase in medical costs. However, to our knowledge, the relationship between proteinuria and medical costs has never been measured. We therefore attempted to measure this relationship in a 10–year follow-up study.

The cohort in the present study comprised 4490 community-dwelling Japanese participants, aged 40–69 years (mean age, 54.3 years; 57% female), who were beneficiaries of the National Health Insurance System. The present study was approved by the Institutional Review Board of Shiga University of Medical Science for ethical issues (No.16-15). The baseline survey was carried out between 1989 and 1991, and included a spot urine test using a dipstick. The results of the test for proteinuria were recorded as (-), (±), (1+), (2+) or

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(3+). We defined proteinuria as readings of (1+), (2+) or (3+) and non-proteinuria as readings of (-) or (±). Information on the medical insurance costs for each participant and also information on withdrawal from the insurance system or death was obtained from monthly claim history files over the period from April in the year following the health check-ups until March 2001. The data obtained on medical costs for each participant differed depending upon the period of subscription to the insurance system. The medical costs for each participant were divided by the period of subscription, and expressed as costs per month of follow-up. If a beneficiary withdrew from the insurance or died, the follow-up was stopped at that point.

We then evaluated the medical costs per person for each urinary category over a 10-year follow-up period. For statistical analysis, we performed an analysis of covariance adjusted for potential confounding variables using logarithmically transformed data for costs. In addition, we evaluated the risk of cumulative hospitalization and all-cause mortality, by using a logistic regression model and a Cox proportional hazards model, respectively. The statistical analysis package SPSS 11.0J for Windows was used for these analyses. All probability values were two-tailed, and the significance level was set at $P<0.05$.

At baseline, the number of participants with (-), (±), (1+), (2+) and (3+) protein levels in their urine test were 4411 (98.2%), 32 (0.7%), 31 (0.7%), 15 (0.3%) and 1 (<0.1%), respectively. While proteinuria was present in only 1.0% of the population, as shown in Table 1, there was a positive relationship between proteinuria and total medical costs per person, expressed as arithmetic means. The difference in the costs was statistically significant, even after adjustment for hypertension, diabetes mellitus and other factors (Geometric means: 8,451 Japanese *Yen* (non-proteinuria) vs. 14,200 *Yen* (proteinuria); $P<0.01$). Proteinuria also tended to lead to an increased risk of hospitalization and all-cause mortality. The adjusted odds ratio of proteinuria for cumulative hospitalization was 1.54 (95% confidence interval, 0.84–2.84) and the adjusted hazard ratio of proteinuria for all-causes mortality was 1.60 (0.64–4.03).

Proteinuria is generally regarded as a sensitive predictor of end-stage renal disease.[2] End-stage renal disease is the most costly proteinuria-related disease, because individuals with this condition require either long-term dialysis, especially in Japan, or kidney transplantation, both of which are expensive treatments.[3–5] The number of individuals with end-stage renal disease has been increasing year by year in developed countries.[3–5] Proteinuria is also a predictor of cardiovascular disease,[1] because it is a marker of severe hypertension and diabetes mellitus,[6–8] both of which are major risk factors for cardiovascular disease.[9,10] Some participants with proteinuria in the present study may have had increased protein excretion as a result of either hypertensive organ damage or microangiopathy associated with diabetes mellitus. Such participants may incur high medical costs as a result of these cardiovascular events. In fact, at baseline 66% of the participants with proteinuria were hypertensive and 11% had diabetes. Moreover, proteinuria led to increased medical costs, even after adjustment for hypertension and diabetes mellitus. These results therefore provide support for our hypothesis.

The details of medical diagnoses, medical treatment status, clinical condition and cause of hospitalization and mortality were not available in the present study. It was therefore unclear what disease led directly to the increase in medical costs and events in the participants with proteinuria. Furthermore, in recent times proteinuria can be more accurately determined using the

Table 1 Medical costs per person, over a 10-year follow-up period (1990–2001), of National Health Insurance beneficiaries in Shiga, Japan, grouped according to proteinuric status.

Urine	Number of participants	Medical costs per person per month		
		Total	Outpatient	Inpatient
Non-proteinuria	4443	140 Euros (20,029*Yen*) (176 US Dollars)	76 Euros (10,901*Yen*) (96 US Dollars)	46 Euros (9,138 *Yen*) (80 US Dollars)
Proteinuria	47	262 Euros (37,494 *Yen*) (330 US Dollars)	187 Euros (26,768*Yen*) (236 US Dollars)	75 Euros (10,726*Yen*) (94 US Dollars)

100 Japanese *Yen* = 0.70 Euros or 0.88 US Dollars, at the foreign exchange rate on May 1st, 2006

microalbuminuria assay. Regardless of these issues, we consider further investigations on the relationship between proteinuria and medical costs or medical events are warranted.

This is the first study to assess the medical costs of individuals with proteinuria in a community-based population. Individuals with proteinuria may incur high medical costs in the future through mortality after hospitalization for events related to proteinuria.

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4. 都市部集団循環器疾患コホート研究

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Ⅰ. 吹田コホート研究の概要

1) 対象者の抽出:吹田コホート研究は、平成元年より吹田市の住民台帳より 12,200 名を無作為抽出し、その中で 6,485 名(誕生日:明治 43 年 4 月 1 日～昭和 35 年 3 月 31 日)がコホート集団として参加対象となった。また、平成 8 年にも同様に 3,000 名を無作為抽出し、その中で 1,329 名(誕生日:大正 7 年 4 月 1 日～昭和 43 年 3 月 31 日)が参加対象となった。抽出時に平成元年で抽出された対象者がいる場合には、その者をカウントしないこととした。また、コホート研究にボランティアで参加した 546 名(明治 39 年 1月 1 日～昭和 41 年 12 月 31 日)をあわせて 8,360 名が吹田コホート研究の全対象者である。

吹田コホート研究募集者	15,200 名
1次コホート(平成元年から平成4年)	12,200 名
2次コホート(平成8年から平成9年)	3,000 名
吹田コホート研究対象者数	8,360 名
1次コホート(平成元年から平成4年)	6,485 名
2次コホート(平成8年から平成9年)	1,329 名
ボランティア	546 名

2) ベースライン調査(初回健診):平成元年から 2 年ごとに基本健診を実施している。それに合わせて糖負荷検査、アンケート調査(身体活動問診・ストレス問診、判定量食物摂取頻度調査)、頚部超音波検査などを実施している。

3) 追跡方法:健康アンケートを年 1 回、受診希望票および脳卒中・心筋梗塞発症状況を健診案内時(2 年に 1 回)送付して、脳卒中・心筋梗塞の発症を把握する。健診受診時に脳卒中調査票・胸部症状についての問診票をとり、発症状況を把握する。発症状況に記載のある者に対して、診療情報提供に関するお願い、診療情報の提供に関する同意書を送付する。資料8の同意のあるものを対象に、吹田コホート脳卒中調査票・心筋梗塞調査票を用いてカルテ調査を行う。

4) エンドポイント(観察打ち切り):(a)脳卒中及び心筋梗塞の発症の追跡研究とした場合、

脳卒中及び心筋梗塞の発症、市外転出、または最後に追跡できた時点をもってエンドポイントとする。(b)脳卒中及び心筋梗塞の死亡の追跡研究とした場合、死亡または最後に追跡できた時点をもってエンドポイントとする。

5) 吹田市内外死亡者数(平成 18 年 9 月末現在)

生存	吹田市内	5,600 名
	吹田市外	1,495 名
死亡	吹田市内	1,152 名
	吹田市外	113 名

Ⅱ. 研究成果

1. 一般住民におけるメタボリックシンドロームの臨床像の解析:吹田研究

吹田市一般住民の中から、性年齢階層別に無作為抽出し, 空腹時採血を実施した 2,591 名(平均年齢 64.5 歳)を対象に断面研究を実施した。

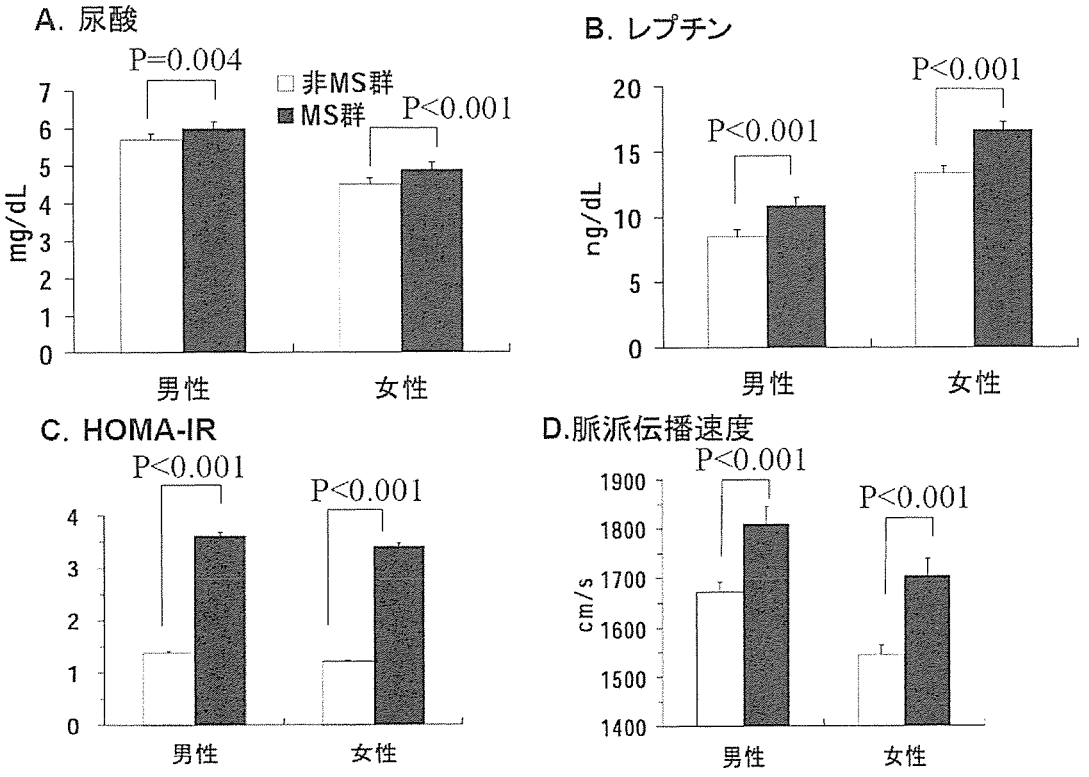

図1. メタボリック症候群と各種健診項目

尿酸、レプチン、HOMA-IR、脈派伝播速度(PWV)において、男女ともメタボリックシンドローム群で有意に高値であった(図1)。また、メタボリックシンドローム群の中で、喫煙、禁煙、非喫煙の順に、血漿フィブリノーゲン値が男女とも高値であった。メタボリックシンドローム群の中で、

運動する、時々運動、運動せず、の順に分けると、男性の体脂肪率で 23.9±0.6%、25.6±0.4%、26.7±0.4% (P=0.045)、女性の体脂肪率で 31.7±0.9%、32.7±0.6%、32.6±0.5 (P=0.081)であった(図2)。

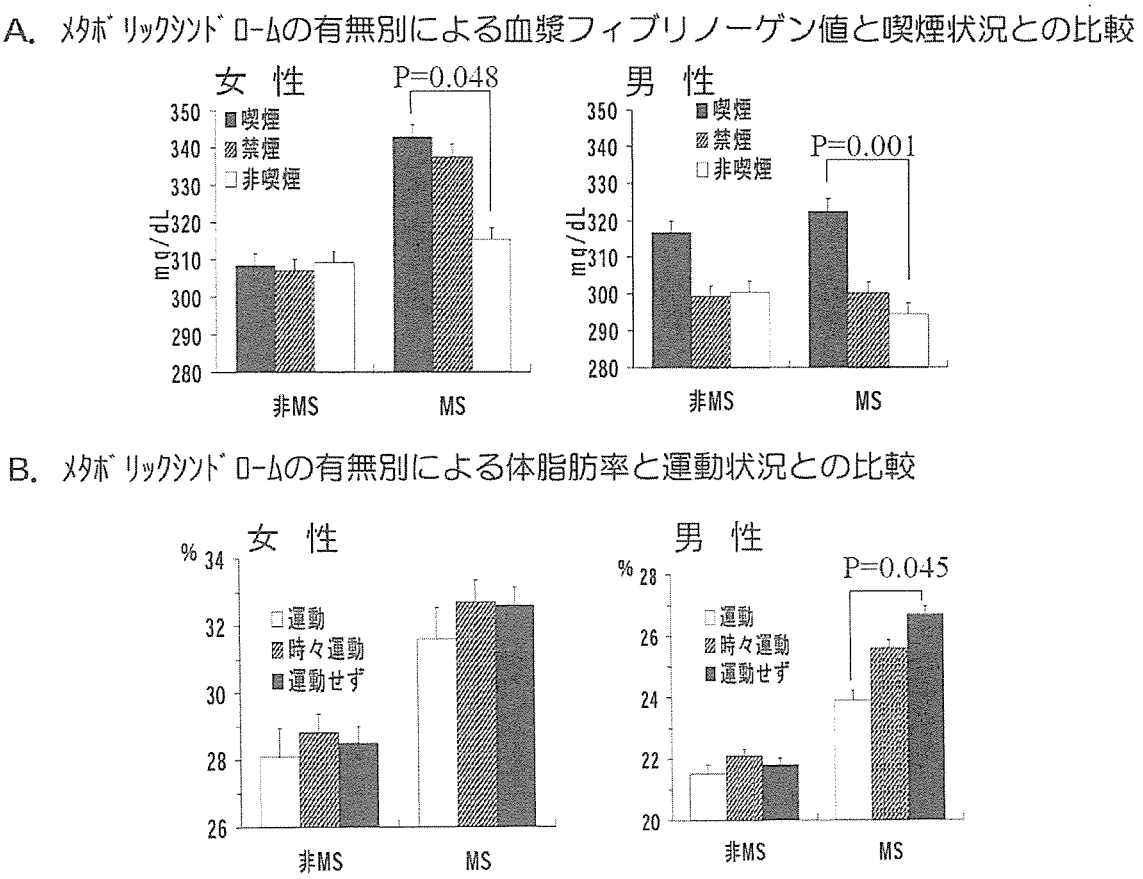

図2. メタボリック症候群と生活習慣とのの交互作用による健診項目

2. メタボリックシンドロームと頚動脈超音波検査との関係

吹田市一般住民の中から性年齢階層別に無作為抽出し、頚動脈超音波検査を受けた男性 2,148 名(平均年齢 58.7±12.3 歳)、女性 2,420 名(56.2±12.0 歳)を対象とした。頚動脈超音波検査所見から, 両側の総頚動脈の内膜中膜複合体(IMT)の平均値を平均 IMT、両側の総頚動脈、分岐部、内頚動脈の最大の IMT を最大 IMT と定義した。メタボリックシンドロームと頚動脈超音波検査との関連性は、性別に年齢、飲酒、喫煙にて調整された共分散分析とロジスティックモデルを用いて解析した。

図3は、メタボリックシンドローム有無別による頚動脈調整平均 IMT の比較を示した。総頚動脈の平均 IMT 値は、男女ともメタボリックシンドローム有所見群の方が有意に総頚動脈の平均 IMT 値が高く、メタボリックシンドローム有所見群の中で、高血圧有所見群がさらに高値であった。最大 IMT でも同様の結果が得られた。

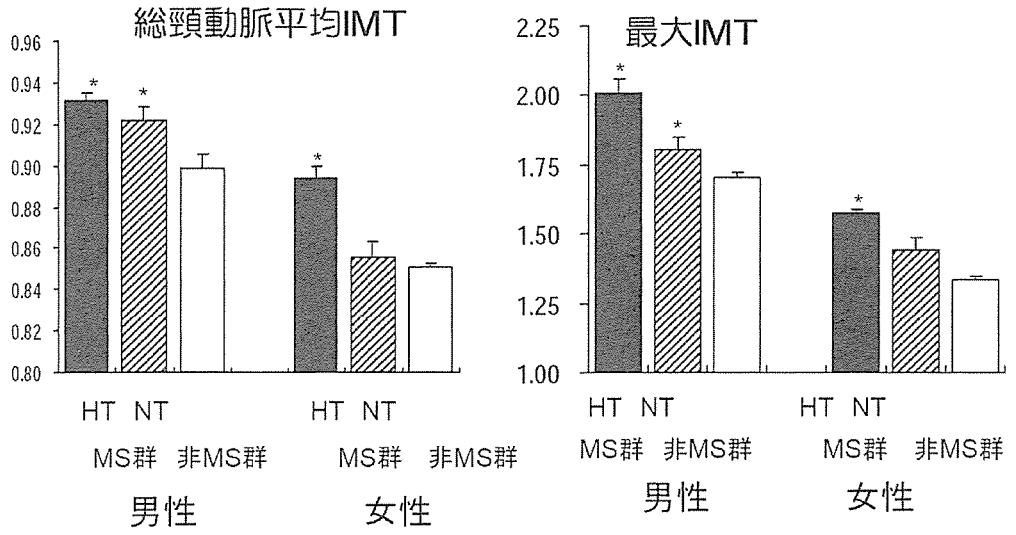

図3. メタボリック症候群有無別による頚動脈 IMT 値

3. メタボリック症候群と循環器疾患との追跡研究

目的: 近年、生活習慣の変化に伴い肥満が増加している。肥満により高血圧や耐糖能異常などの代謝性疾患が重積しやすく、メタボリックシンドロームとういう新しい概念がでてきた。しかし、メタボリックシンドロームと循環器疾患との追跡研究はほとんど報告されていない。そこで、都市部一般住民を対象にメタボリックシンドロームと循環器疾患との関係を追跡研究で検討することを目的とする。

方法: 平成元年に大阪府吹田市の住民台帳から性年齢別に無作為抽出した 12,200 人のうち、当センターで健診受診を希望し、初診時健診で脳卒中・心筋梗塞の既往のない追跡可能の男性 2,730 名(平均年齢 55.9 歳)、女性 3,117 名(平均年齢 54.5 歳)を今回の解析対象とした。平成元年～平成 4 年度の初診時健診後、2 年毎の健診、毎年の問診、発症登録制度、病院カルテ調査により、1997 年度末まで新規脳卒中・心筋梗塞の発症があるかについて追跡した。メタボリックシンドロームの定義は日本の診断基準を用い、メタボリックシンドロームと循環器疾患との関係は、性年齢調整、さらに喫煙・飲酒歴で調整された Cox 比例ハザードモデルを用いて解析した。内臓肥満、高中性脂肪血症または低 HDL コレステロール血症、血圧高値、耐糖能異常の各種コンポーネントの該当する数と脳卒中・心筋梗塞との関係も同様に解析した。

【結果】男性 15,550 人年、女性 18,203 人年の観察より(平均追跡期間 5.8 年間)、脳梗塞 55 人、脳出血 18 人、くも膜下出血 6 名、心筋梗塞 39 名の発症が確認された。ベースライン時調査のメタボリックシンドロームの割合は、30 歳代から 70 歳代まで、男性で 7.3%、8.0%、15.0%、23.5%、17.6%、女性で 0.2%、1.4%、3.4%、7.2%、9.7%であった(図 4)。メタボリックシンドロームの性年齢調整相対危険度は全脳卒中で 1.69 (95%信頼区間: 1.07-2.64)、心筋梗塞で 2.32 (1.10-4.90)であり、飲酒・喫煙を加えた調整相対危険度は全脳卒中で 1.74 (1.14-2.66)、心筋梗塞で 2.43 (1.60-3.70)であった。脳梗塞の性年齢、飲酒・喫煙を加えた調整相対危険度は、それぞれ 2.37