the glycaemic control on HbA1c values, we only enrolled patients who had stable HbA1c values (82% within ±0.4% of the patient mean for the previous 3 months) and similar postprandial glucose concentrations. None of the patients had clinical evidence of pulmonary disease, heart failure or dehydration. Correlations were evaluated between HbA1c or glycated albumin (GA) and estimated glomerular filtration rate (eGFR) (determined by serum creatinine concentration, sex and age).[10] Furthermore, the patients were divided into four groups based on their stage of CKD evaluated by eGFR: Group 1 ($n = 30$, stages 1 and 2 together, eGFR $\geq$ 60 mL/min/1.73 m^2), Group 2 ($n = 30$, stage 3, eGFR < 60 mL/min/1.73 m^2 but $\geq$30 mL/min/1.73 m^2), Group 3 ($n = 13$, stage 4, eGFR < 30 mL/min/1.73 m^2 but $\geq$15 mL/min/1.73 m^2) and Group 4 ($n = 13$, stage 5, eGFR < 15 mL/min/1.73 m^2 without haemodialysis). The mean values of HbA1c and of RBC lifespan in Groups 2, 3 and 4 were compared with those in Group 1. To evaluate the influence of treatment with an erythropoietin-stimulating agent (ESA) on HbA1c, the patients in Groups 3 and 4 were divided into groups with or without ESA treatment (mean weekly dose of ESA: 4000 ± 2057 U) and HbA1c values were compared between them. Clinical characteristics of the patients are shown in Table 1.

Measurements

Postprandial plasma glucose value was obtained around two hours after a meal and shown as a mean of the values measured on three separate occasions approximately one month apart. HbA1c was measured by high-performance liquid chromatography using a Tosoh G7 Analyzer (Tosoh, Tokyo, Japan). The HbA1c values thus obtained (Japan Diabetes Society; JDS) were converted to National Glycohemoglobin Standardization Program (NGSP) values by adding 0.4% to JDS.[11] Serum GA was determined with a Siemens Dimension Xpand Plus (Siemens, Deerfield, IL, USA) by an enzymatic method using albumin-specific proteinase, ketoamine oxidase and albumin assay reagent (Lucica GA-L; Asahi Kasei Pharma Co, Tokyo, Japan).[12] RBC lifespan was calculated with the following formula proposed by Stocchi *et al*:[13]

$$\text{RBC lifespan} = \frac{\text{Hb}*K}{\text{endogenous CO (ppm)}}$$

$$\text{where } K = 1380 \text{ mL d/g}.$$

Endogenous CO was estimated by measuring exhaled carbon monoxide concentration determined with a Carbolyzer mBA-2000 (Taiyo, Osaka, Japan).

RBC lifespan in 18 healthy non-smoking volunteers was 128 ± 28 d.

Other laboratory measurements were performed on a standard autoanalyser (Biomajesty JCA-BM2250; Japan Electron Optics Laboratory, Tokyo, Japan).

Statistical analyses

Background characteristics were summarized and compared among groups defined by the stage of CKD. A Kruskal-Wallis test was used to compare the groups for continuous variables, and Fisher's exact test was used for categorical variables. Univariate linear regression analysis was performed to evaluate the relationship between HbA1c values and eGFR or RBC lifespan. HbA1c and RBC lifespan were compared among groups by analysis of variance followed by Dunnet's multiple comparison method with Group 1 serving as the reference group. Simple linear regression analyses were performed with HbA1c serving as the dependent variable and 21 different independent variables shown in Table 2. Then, multiple regression analysis was performed with only those independent variables that were significantly associated with

Table 1 Clinical characteristics of the study groups

Group	1	2	3	4	*P*
N	30	30	13	13	
Sex (F/M)	16/14	10/20	4/9	4/9	
Age (years)	63.4 ± 9.8	69.9 ± 10.9	69.8 ± 7.0	59.7 ± 10.3	0.04*
Diabetes duration (years)	9.7 ± 8.0	14.5 ± 9.4	13.6 ± 8.3	14.9 ± 7.7	
Body weight (kg)	63.2 ± 10.2	62.0 ± 12.4	64.7 ± 8.0	65.7 ± 11.4	
BMI (kg/m^2)	24.5 ± 2.7	24.4 ± 3.3	24.6 ± 2.9	24.8 ± 2.9	
Treatment					0.017†
Diet alone (%)	6.7	13.3	7.7	0.0	
OHA (%)	73.3	56.7	38.5	38.5	
Insulin (%)	20.0	30.0	53.8	61.5	
PPG (mmol/L)	9.3 ± 2.7	8.9 ± 2.2	8.9 ± 2.6	9.1 ± 2.9	
GA (%)	23.1 ± 4.4	23.4 ± 3.8	22.5 ± 5.6	22.4 ± 3.9	
eGFR (mL/min/1.73 m^2)	85.4 ± 15.8	46.4 ± 8.9	22.8 ± 5.3	10.5 ± 3.5	<0.001*
Hb (g/dL)	13.5 ± 0.9	12.3 ± 1.6	10.4 ± 1.1	9.4 ± 1.5	<0.001*
Total protein (g/dL)	7.2 ± 0.4	7.0 ± 0.5	6.7 ± 0.7	6.4 ± 0.8	<0.001*
Albumin (g/dL)	4.2 ± 0.4	4.0 ± 0.3	3.8 ± 0.5	3.5 ± 0.6	<0.001*
Urinary protein (g/g creatinine)	0.008 ± 0.02	0.8 ± 2.2	1.7 ± 3.4	2.8 ± 3.5	<0.004*
Cholinesterase (IU/L)	353.7 ± 56.6	310.7 ± 62.6	242.8 ± 69.4	230.6 ± 66.5	<0.001*

Hb, haemoglobin; BMI, body mass index; OHA, oral hypoglycaemic agent; GA, glycated albumin; PPG, postprandial glucose; eGFR, glomerular filtration rate estimated by serum creatinine concentration, sex and age[10]

*Kruskal-Wallis test

†Fisher's exact test

Table 2 Multiple regression analysis of HbA1c value

Variable	Type/category	Simple linear regression			Initial model of multiple regression ($P < 0.05$ in simple regression)			Final model of multiple regression (Backward selection with $P < 0.05$)		
		Coefficient	95% CI	P value	Coefficient	95% CI	P value	Coefficient	95% CI	P value
Sex	Female/male	−0.002	(−0.006, 0.001)	$P = 0.226$						
Age	Continuous	0.006	(−0.012, 0.023)	$P = 0.521$						
Body weight	Continuous	0.003	(−0.013, 0.020)	$P = 0.699$						
Serum creatinine	Continuous	−0.200	(−0294, −0.107)	$P < 0.001$	−0.085	(−0.180, 0.010)	$P = 0.080$			
eGFR	Continuous	0.010	(0.005, 0.016)	$P < 0.001$	−0.012	(−0.024, −0.000)	$P = 0.043$	−0.013	(−0.025, −0.002)	$P = 0.024$
CKD stage	Continuous	−0.292	(−0.426, −0.159)	$P < 0.001$	−0.398	(−0.712, 0.085)	$P = 0.014$	−0.530	(−0.813, −0.247)	$P < 0.001$
COAv	Continuous	−0.174	(−0.492, 0.144)	$P = 0.279$						
GA	Continuous	0.113	(0.078, 0.148)	$P < 0.001$	0.086	(0.057, 0.115)	$P < 0.001$	0.087	(0.060, 0.115)	$P < 0.001$
PPG	Continuous	0.007	(0.003, 0.011)	$P < 0.001$	0.003	(0.000, 0.005)	$P = 0.039$	0.003	(0.000, 0.005)	$P = 0.036$
Hb	Continuous	0.163	(0.078, 0.249)	$P < 0.001$	0.039	(−0.043, 0.121)	$P = 0.348$			
RBC lifespan	Continuous	0.007	(0.002, 0.012)	$P = 0.007$	0.005	(0.001, 0.008)	$P = 0.008$	0.005	(0.002, 0.008)	$P = 0.002$
GA/HbA1c	Continuous	−0.098	(−0.454, 0.259)	$P = 0.587$						
UP	0	Reference	–	$P = 0.040$	Reference	–	$P = 0.042$	Reference	–	$P = 0.047$
	<1.3	−0.596	(−1.072, −0.120)		−0.298	(−0.604, 0.008)		−0.288	(−0.572, −0.004)	
	≥1.3	−0.295	(−0.802, 0.212)		0.152	(−02.73. 0.578)		0.165	(−0.190, 0.519)	
Diabetes duration	Continuous	0.029	(0.010, 0.049)	$P = 0.004$	0.011	(−0.004, 0.027)	$P = 0.140$	0.015	(0.000, 0.030)	$P = 0.043$
Treatment	Diet	Reference	–	$P = 0.031$	Reference	–	$P < 0.001$	Reference	–	$P = 0.002$
	OHA	0.382	(−0.270, 1.034)		0.425	(0.025, 0.824)		0.383	(−0.018, 0.784)	
	Insulin	0.778	(0.101, 1.455)		0.794	(0.359, 1.229)		0.717	(0.281, 1.152)	
BMI	Continuous	0.023	(−0.038, 0.085)	$P = 0.457$						
Diabetic type	1/2	−0.012	(−0.019, −0.005)	$P = 0.002$	−0.001	(−0.007, 0.005)	$P = 0.758$			
Total protein	Continuous	0.339	(0.045, 0.632)	$P = 0.024$	−0.164	(−0.403, 0.075)	$P = 0.176$			
Albumin	Continuous	0.326	(−0.039, 0.691)	$P = 0.080$						
Cholinesterase	Continuous	0.004	(0.002, 0.007)	$P < 0.001$	0.003	(−0.001, 0.004)	$P = 0.004$	0.003	(0.001, 0.004)	$P = 0.003$
ESA	With/without	0.005	(−0.000, 0.011)	$P = 0.053$						

COAv, average CO concentration in exhaled breath (ppm); UP, urinary protein (g/g creatinine); ESA, erythropoietin-stimulating agents; eGFR, glomerular filtration rate estimated by serum creatinine concentration, sex and age; CKD, chronic kidney disease; GA, glycated albumin; HbA1c, glycated haemoglobin; Hb, haemoglobin; BMI, body mass index; OHA, oral hypoglycaemic agent; PPG, postprandial glucose

Variable significantly ($P < 0.05$) associated with HbA1c in the simple linear regression analysis are included in the initial model of multiple regression analysis

Variable selected from the initial model of multiple regression analysis by backward elimination procedure with elimination criteria of $P > 0.05$ are included in the final model

HbA1c in the simple regression analyses. From the model, variables were selected by a backwards elimination procedure with elimination criteria of $P \geqslant 0.05$. The final model of HbA1c included only those independent variables that were significant ($P < 0.05$).

Values are expressed as mean ± SD unless otherwise indicated. All the statistical analyses were performed with the use of SAS Version 9.1.3 (SAS Institute, Inc., Cary, NC, USA), and a P value < 0.05 was considered statistically significant.

Results

A significant correlation ($r = 0.37$, $P = 0.0004$) between HbA1c and eGFR was found, as shown in Figure 1. No significant differences in the mean postprandial plasma glucose concentrations or GA concentrations were found among the four groups as shown in Table 1. However, HbA1c values in Group 3 (6.8 ± 0.6%) and Group 4 (6.3 ± 0.5%) were significantly lower than that in Group 1 (7.4 ± 0.8%), but there was no difference between Group 2 (7.2 ± 0.7%) and Group 1, as shown in Figure 2a. Net differences in HbA1c concentrations between Group 1 and Group 3, and between Group 1 and Group 4 were 0.6% and 1.1%, respectively, and these corresponded to percent differences of 8.4% and 15.5%. There was no significant difference in HbA1c values between the patients treated with ESA ($n = 10$, 6.6 ± 0.6%), and without ESA ($n = 16$, 6.5 ± 0.5%). Furthermore, there was no significant difference in RBC lifespan between the patients treated with ESA (83.2 ± 22.2 d) and without ESA (102.6 ± 36.6 d); however, there was a significant difference ($P < 0.01$) in haemoglobin (Hb) concentration between the patients treated with ESA (8.8 ± 1.2 g/dL) and without ESA (10.7 ± 0.9 g/dL). Figure 3 depicts the HbA1c values plotted against the erythrocyte lifespan (a), and the erythrocyte lifespan plotted against eGFR (b) in the 86 subjects. As shown in this figure, a significant correlation existed between HbA1c and RBC lifespan ($r = 0.29$, $P < 0.0068$). There was also a significant correlation between RBC lifespan and eGFR

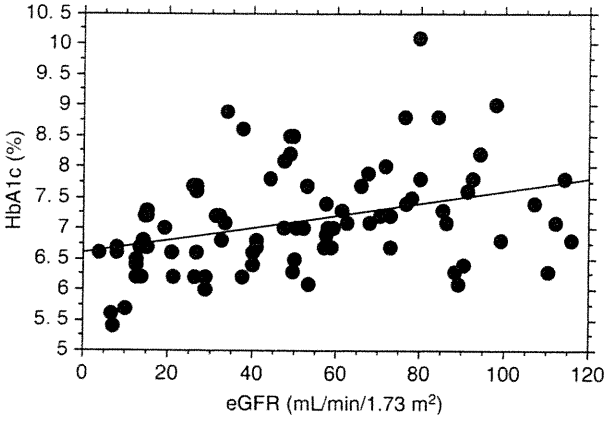

Figure 1 Scatterplot showing the association between HbA1c and eGFR in 86 diabetic patients with various levels of renal dysfunction. HbA1c, glycated haemoglobin; eGFR, glomerular filtration rate estimated with serum creatinine concentration, sex and age.[9] $r = 0.37$, $P = 0.0004$

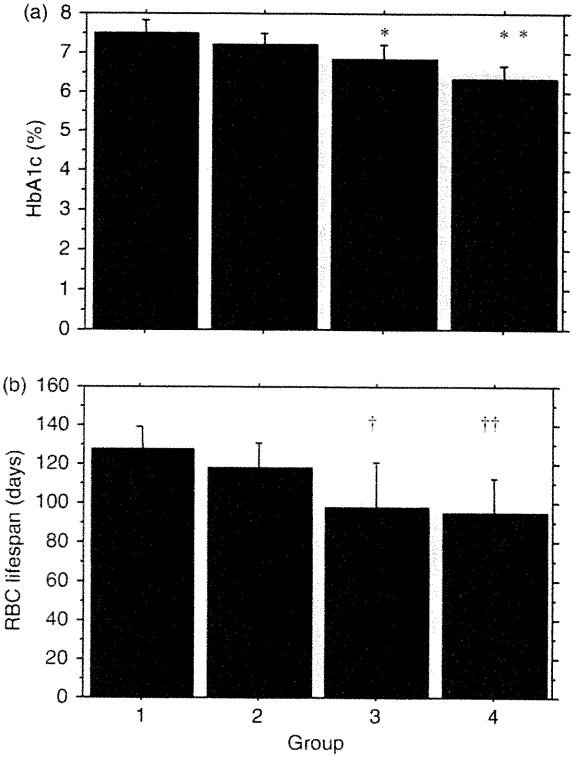

Figure 2 Mean values of HbA1c (a) and of erythrocyte lifespan (b) in the study groups. The subjects were divided into four groups according to their eGFR: Group 1 ($n = 30$, eGFR ≥ 60 mL/min/1.73 m²), Group 2 ($n = 30$, eGFR < 60 mL/min/1.73 m² but ≥30 mL/min/1.73 m²), Group 3 ($n = 13$, eGFR < 30 mL/min/1.73 m² but ≥ 15 mL/min/1.73 m²) and Group 4 ($n = 13$, eGFR < 15 mL/min/1.73 m² without haemodialysis). Data are presented as the mean ± SD. Different from Group 1; $^{*}P = 0.035$, $^{**}P < 0.001$, $^{\dagger}P = 0.016$, $^{\dagger\dagger}P = 0.009$. HbA1c, glycated haemoglobin; eGFR, glomerular filtration rate estimated with serum creatinine concentration, sex and age; RBC, red blood cell

($r = 0.36$, $P = 0.0005$). Furthermore, mean RBC lifespan in Group 3 (96 ± 31 d) and Group 4 (94 ± 30 d) were significantly shorter than that in Group 1 (127 ± 30 d), as shown in Figure 2b.

The final multiple regression model contained nine independent variables (eGFR, CKD stage, GA, postprandial glucose, RBC lifespan, urinary protein, diabetes duration, type of treatment for diabetes and cholinesterase) that were significantly associated with HbA1c, but Hb concentration or ESA treatment were not included, as shown in Table 2.

Discussion

This study showed that HbA1c values were significantly reduced relative to glycaemic control in diabetic patients with stage 4 or 5 CKD compared with diabetic patients without renal dysfunction. However, patients with stage 3 CKD did not show reduced HbA1c values relative to glycaemic control. Glycaemic control was assessed in all four patient groups by the mean postprandial glucose and GA values. Furthermore, to eliminate the influence of differences in glycaemic control among the four groups on HbA1c values, we selected patients with similar

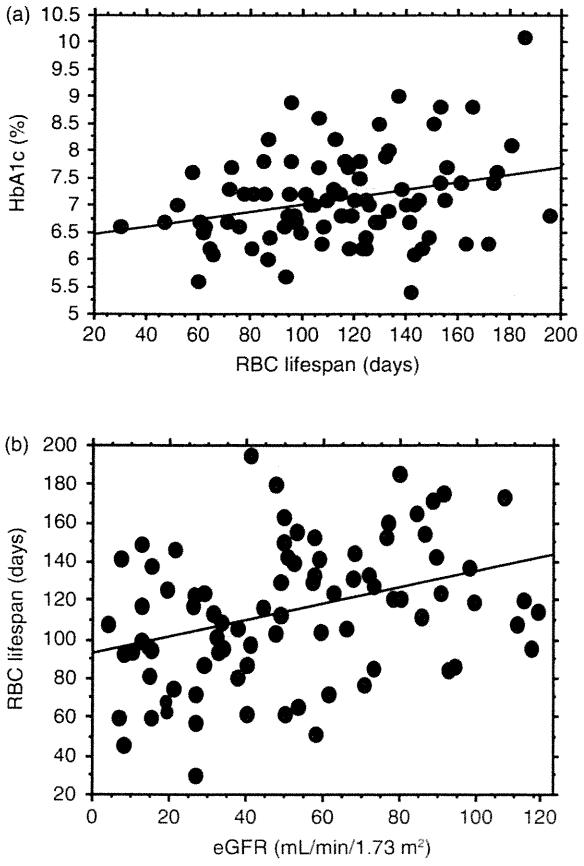

Figure 3 Scatterplot showing the association between HbA1c and erythrocyte lifespan (a), and erythrocyte lifespan and eGFR (b) in 86 diabetic patients with various levels of renal dysfunction. (a) $r = 0.29$, $P < 0.0068$ and (b) $r = 0.36$, $P = 0.0005$. HbA1c, glycated haemoglobin; RBC, red blood cell; eGFR, glomerular filtration rate estimated with serum creatinine concentration, sex and age

postprandial glucose and GA values so that the four groups were matched for glycaemic control. GA values in our Groups 3 and 4 (CKD stage 4 and 5, respectively) were apparently lower than those in Group 1, although the difference was not statistically significant. Okada *et al.*[14] reported that nephrotic-range proteinuria (≥3.5 g/d) decreased GA values probably due to rapid albumin turnover; however, non-nephrotic range proteinuria (< 3.5 g/d) did not significantly influence GA values. As shown in Table 1, urinary protein outputs were higher in Groups 3 and 4 compared with that in Group 1, and serum albumin concentrations in Groups 3 and 4 were lower than that in Group 1. This may be responsible for the apparent lower concentrations of GA in Groups 3 and 4, although no significant correlation between GA and serum albumin concentrations in these groups was observed (data not shown). Based on these results, it is reasonable to assume that the slightly but not significantly lower values of GA in Groups 3 and 4 might have been affected by factors associated with albumin turnover independent of glycaemic control.

Since glycaemic control was matched, the lower HbA1c values in diabetic patients with stage 4 or 5 CKD were not due to differences in the severity of diabetes, but rather due to other factors such as renal dysfunction unrelated to glycaemic control. These findings indicate that diabetic patients with ESRD have spuriously low concentrations of HbA1c, which might lead to the underestimation or misdiagnosis of their diabetic condition.

Recently, Koga *et al.*[9] reported GA/HbA1c ratios in diabetic patients with various nephropathic stages. However, we cannot directly compare our HbA1c values in patients with various CKD stages with theirs, because their classification of nephropathy was different from ours. In addition, our patients were divided according to their eGFR, whereas their patients were divided according to their urinary protein outputs and serum creatinine concentrations. Furthermore, our CKD stage 5 patients were not on haemodialysis, whereas their diabetic nephropathy stage 5 patients all underwent haemodialysis. Finally, there was a difference in the index of glycaemic control between the two studies: we employed HbA1c values but they used the GA/HbA1c ratio without showing any individual HbA1c values.

Nakao *et al.*[15] reported that ESA treatment decreased HbA1c concentrations without significant changes in blood glucose in patients undergoing maintenance haemodialysis. In contrast to their findings, we could not find any difference in HbA1c values between the patients treated with and without ESA. The mean weekly dose of ESA was 4000 ± 2057 U in our subjects, whereas 8400 ± 1265 U was given to their patients who showed significant changes in HbA1c values. Some of their patients who received a smaller dose of ESA (5100 ± 823 U) showed a negligible change in HbA1c concentrations after the study period. These findings suggest that the dose of ESA in our subjects was not sufficient to cause an increase in haematocrit and thereby changes in HbA1c.

In contrast to Koga *et al.*'s[9] findings that showed lower HbA1c concentrations in anaemic patients, no difference in HbA1c values was observed between the patients with and without ESA treatment, although Hb concentrations were lower in the ESA-treated group. As shown in Table 2, we could not find any association of HbA1c values with Hb concentration in our subjects. In patients with renal failure treated with an inadequate dose of ESA, a low concentration of Hb might not stimulate haemogenesis sufficiently to increase young erythrocytes, resulting in a decrease in HbA1c concentrations.

HbA1c is the product of the chemical condensation of haemoglobin and glucose. Biosynthetic studies *in vivo* indicate that HbA1c is formed slowly, continuously and irreversibly throughout the lifespan of the RBC. Thus, the concentration of HbA1c reflects the glucose concentrations in blood due to glycation of both newly formed and older RBCs. The glycation rate of newly formed RBCs has been shown to be lower than that of older RBCs.[16,17] If the RBC lifespan is shortened, HbA1c values will be decreased due to an increased ratio of new to old erythrocytes and to a shortened exposure of erythrocytes to glucose in peripheral blood. This suggests that the lifespan of erythrocytes in peripheral blood could be an important determinant of HbA1c concentrations in addition to blood glucose concentration.[18]

It is reasonable to assume, therefore, that a significantly shorter lifespan of erythrocytes occurred in Groups 3 and 4, which accounted for their lower HbA1c

concentrations compared with Group 1. The mean RBC lifespan was shorter in patients treated with than without ESA, although the difference in mean RBC lifespan between the two groups was not statistically significant. The mean HbA1c value should have been lower in the ESA group, but this was not observed. At the present time, we do not have an adequate explanation for these results. A further study is needed to address this issue.

A decrease in the lifespan of erythrocytes has been shown to be one of the contributory factors to anaemia in patients with chronic renal failure, probably caused by the toxic uremic milieu.[19] Other factors that are associated with anaemia in uremic patients include inflammation,[20] parathyroid hormone[21] and erythropoietin.[22] A 30–70% reduction in RBC lifespan in renal failure has been reported using radioactive tracers to measure RBC lifespan.[23–25] In contrast, a simple and rapid technique based on the concentration of CO in expired air was used to quantify erythrocyte survival in this study. This method produces results that are comparable to the results obtained with more complicated methods.[26,27] When applied to patients with type 2 diabetes, the CO method has shown a mean erythrocyte survival of 112 ± 25 d.[28]

We recognize that our study has several limitations. This was a cross-sectional study, and the sample size was relatively small, particularly in Groups 3 and 4. However, even with this small sample size, a significant difference in HbA1c and RBC lifespan was observed between diabetic patients with and without ESRD. To our knowledge, there is no previous information on RBC survival in patients with chronic renal failure using this simple method. Thus, further research will be necessary to confirm these initial results.

In summary, this study demonstrated that diabetic patients with stage 4 or 5 CKD who were not on haemodialysis showed significantly lower values of HbA1c and shorter RBC lifespan compared with diabetic patients without renal dysfunction. These results suggest that the spuriously lower concentration of HbA1c observed in the patients with ESRD was caused by the shorter RBC lifespan. Based on these results, the HbA1c concentrations should not be used alone to diagnose the presence or severity of diabetes in patients with ESRD.

DECLARATIONS

Competing interests: None declared.
Funding: No funding was required in this study.
Ethical approval: All study protocols were approved by the ethics committee at Kawashima Hospital, and written informed consent was obtained from each patient.
Guarantor: KS.
Contributorship: KS wrote and edited the manuscript and contributed to the discussions. KC researched data and contributed to the discussion. MY researched data and contributed to the discussion. MK, YN and TM contributed to the discussion, and reviewed and edited the manuscript.
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ORIGINAL ARTICLE

Outcomes of 6 years of activities by the Tokushima Medical Association's Steering Committee for Diabetes Prevention to prevent type 2 diabetes in the general population of Tokushima Prefecture

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Abstract
Objective The effectiveness of diabetes prevention programs for the general population of Tokushima Prefecture was investigated. The programs were designed by Tokushima Medical Association's (TMA's) Steering Committee for Diabetes Prevention.
Research design and methods The committee promoted diabetes prevention by disseminating educational messages on diabetes to the general public and medical care providers, and by establishing a referral system among public health centers and medical institutes throughout Tokushima Prefecture during the period from 2004 to 2009. The outcomes of these activities were evaluated by analyzing data from Prefectural Health and Nutrition Surveys conducted in Tokushima in 1997 (n = 998), 2003 (n = 1,008) and 2010 (n = 1,130).
Results The percentage of subjects with glucose intolerance at the time of initiation of the prevention program in Tokushima tended to increase from 1997 to 2003, but had slightly decreased by 2010, although these differences were not statistically significant. Obesity parameters, mean total energy intake and physical activity as evaluated by the daily step count changed favorably in parallel with changes in the prevalence of diabetes during the study period.
Conclusion The diabetes prevention programs initiated by the TMA committee may be useful in ameliorating the situation of diabetes in Tokushima Prefecture.

For the Tokushima Medical Association's Steering Committee for Diabetes Prevention

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Keywords Health education · General population · Diabetes prevention · Glucose intolerance · Obesity

Introduction

Diabetes and its complications represent major health problems in many parts of the world, including Japan, and the prevalence of diabetes appears to be increasing. To reduce the prevalence of diabetes in Japan, programs have been initiated by central and local governments and by various medical societies. These programs have included "Healthy Japan 21," "Special Health Checkup," "Special Health Promotion Program" and "Promotion of Diabetes Prevention." Despite these nationwide efforts, the prevalences of diabetes and prediabetes have been increasing rather than decreasing in Japan [1, 2].

Except for 2007, Tokushima Prefecture has shown the worst annual mortality rate from diabetes in the country since 1993. To address this issue, the Tokushima Medical Association (TMA) established a steering committee in 2004 for diabetes prevention consisting of medical professionals and administrative officials. This committee has promoted diabetes prevention by disseminating health education information on diabetes, diet and physical activity to the general population at various sites throughout the prefecture. Furthermore, the committee has tried to increase diabetes awareness in the population via newspapers and television, and has established a referral system among public health centers and medical institutes.

Three large-scale clinical trials, the Da Qing IGT and Diabetes Study [3], the Finnish Diabetes Prevention Study [4] and the Diabetes Prevention Program [5], have provided unequivocal evidence that type 2 diabetes in high-risk individuals can be prevented through lifestyle modifications, such as increased physical activity, weight loss and dietary changes. Efforts to translate such lifestyle modifications in high-risk individuals from health-care settings to community settings have achieved some degree of success [6–10]. However, as these interventions were open to selected individuals and there was relatively little systematic data collection and analysis of the implementation or outcomes of these programs, assessment of the success of lifestyle modification programs provided to the general population rather than only high-risk individuals has not been possible [11].

Surveys of health and dietary habits of residents selected at random in Tokushima Prefecture were performed in 1997, 2003 and 2010. The first survey was conducted 7 years before the start of our prevention initiative in 2004, and the last survey was conducted 7 years after starting the initiative. The comparison of data from these three time points should provide valuable information for assessing the effectiveness of our diabetes prevention programs in the general population.

Here, we describe the implementation and outcomes of our program together with the activities of several other organizations in Tokushima attempting to translate the results of clinical diabetes prevention trials into the community setting.

Methods and subjects

Programs of the TMA's Steering Committee for Diabetes Prevention from 2004 to 2009

Activities were divided into those conducted during the first half period from 2004 to 2006 and those during the latter half period from 2007 to 2009.

Activities during the first half of the study were mainly devoted to spreading diabetes knowledge among the gen-

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eral population, medical professionals and employers in the prefecture.

1. Lectures: Twenty-four lectures were provided to groups of ≥100 participants in the general population at various sites throughout the prefecture. Major topics of the lectures included diabetes prevention, awareness of diabetes-related risk factors, health-enhancing physical activity, healthful diet, diabetes medication and empowering participants to communicate effectively with their physicians.
2. Publicity: Fourteen mass media campaigns via newspaper and television were conducted. The governor of Tokushima Prefecture and the president of the TMA jointly issued a "Declaration of a State of Emergency on Diabetes" through newspaper and television media in November 2005. Two kinds of posters illustrating the actual conditions of the disease in Tokushima Prefecture were produced and circulated throughout the prefecture.
3. Education of medical professionals: To improve the common knowledge of diabetes prevention, educational activities were conducted for medical professionals including public health nurses, dietitians and primary care providers. A booklet entitled "A manual for early stage intervention in people at high-risk of diabetes" was prepared by the committee. These educational sessions were held on up to 31 occasions at local chapters of the TMA throughout the prefecture.
4. Training for employers on worksite health improvement: Nine lectures were given to employers and/or health-care providers at companies. In addition, articles on diabetes and lifestyle interventions were added to public relations brochures published by various industries.

Activities during the latter half period from 2007 to 2009 were focused on establishing efficient links among various health organizations, while the same educational initiatives that were started in the first half period were continued in the second half period.

1. Establishment of efficient links among health-care providers. We attempted to establish efficient links between primary, secondary and tertiary health-care providers involved in the treatment and management of diabetes and diabetic complications. We also attempted to establish links between primary health-care providers and public health centers. These linkage trees were published on the homepages of the TMA and prefectural offices.
2. Certifications of physicians with sufficient knowledge of diabetes: In 2008, 4-week training sessions (1.5 h/session) were held at four sites around the prefecture. These training sessions were continued in 2009. In total, 396 physicians who fulfilled the course requirements were certified as diabetes physicians by the committee. The curriculum focused on current status, pathophysiology, diagnosis of diabetes based on laboratory tests, treatment and complications, metabolic syndrome and prevention. Public health agencies were recommended to refer diabetic patients identified by public health checkups to these certified diabetes physicians.
3. Certification of diabetic educators: A 9-week training session (1.5 h/session) for medical support staff such as nurses, public health agents, dietitians, pharmacists and clinical laboratory technicians was initiated in 2008 and continued in 2009 (only 4-week sessions). In total, 108 support staff were certified as diabetes educators by the committee.
4. Preparation of a new walking diary [12]: Since activities such as swimming, farming or bicycling cannot be registered accurately on a pedometer, we developed a new walking diary to record the step equivalents of all physical activities. To increase physical activities, a brisk walk was recommended to the general population of the prefecture using the new walking diary, since the mean number of daily steps in Tokushima in 2003 was reported to be less than the national average by about 1,000 steps. Twenty thousand copies of the new walking diary were prepared and distributed without charge in 2008 and 2009.
5. Preparation of healthy menus and provision on the TMA homepage: Some 50 varieties of healthy menus were prepared under the supervision of dietitians and diabetologists of the committee and provided on the TMA homepage. About 1,000 visitors to the website have been recorded monthly.
6. Organized exercise events: AWA-ODORI Exercise was invented by T.T., a member of the committee, and was widely performed at various types of events to promote physical exercise. Some 5,000 DVDs of the AWA-ODORI Exercise routine were prepared and distributed without charge. Twenty-nine individuals were trained to lead these exercise activities as instructors. In addition, 2,529 and 3,072 residents of Tokushima participated in the Tokushima marathon in 2008 and 2009, respectively. Furthermore, walking rallies were initiated in 2008 by the Tokushima Walking Association.

Prefectural health and nutrition surveys in Tokushima [13]

Subjects for the survey were randomly selected at the age of 1 or older from 15 of 24 municipalities in Tokushima

Prefecture. Data on the items relevant to diabetes were collected from respondents ≥20 years old. Data were obtained from 998 subjects in 1997, 1,008 in 2003 and 1,130 in 2010 and used for the final analysis, except for data on glucose tolerance. Glucose tolerance data were obtained from subjects ≥40 years old to match with the age bracket in the nationwide survey. Data on various items were not necessarily obtained from all subjects, and the number of participants differed by item. Table 1 shows sex ratios, and Table 2 shows age-frequency distributions and mean ages in the group of subjects who responded to various survey items on the three occasions. All participants provided oral consent prior to the collection of any data.

Clinical assessment of participants

Demographic details, medical history, medication details, smoking and alcohol history, dietary habits (based on an interview with a registered dietitian and a 24-h dietary recall record) and exercise history (based on an interview with a public health nurse and 1-day pedometer record using ARNES 200 s®) were obtained. Measurements included weight, height, body mass index (BMI, kg/m^2), blood pressure and a blood test for hemoglobin (Hb)A1c. HbA1c was measured by the latex aggregation method using a standard autoanalyzer (JCA-BM9030; Japan Electron Optics Laboratory, Tokyo, Japan) at SRL Inc. (Tokyo, Japan). HbA1c values were converted to values based on the National Glycohemoglobin Standardization Program (NGSP) using the following equation: NGSP (%) = 1.02 × Japan Diabetes Society (JDS) (%) + 0.25 (%) [14].

Statistical analyses

Differences in the sex ratios (Table 1) and in frequency distributions of age range and mean ages (Table 2) of the participants in the three survey occasions were statistically analyzed using Fisher's exact test and the Kruskal–Wallis H test and Mann–Whitney U test with Bonferroni

Table 1 Sex ratio in the group of subjects who responded to various survey items in 1997, 2003 and 2010

Group responded to	Sex	Survey year			Comparison over 3 groups[a] P value
		1997	2003	2010	
Age (≥20 years old)	*N*	998 (100.0 %)	1,008 (100.0 %)	1,130 (100.0 %)	0.809
	Men	450 (45.1 %)	465 (46.1 %)	525 (46.5 %)	
	Women	548 (54.9 %)	543 (53.9 %)	605 (53.5 %)	
Height (≥20 years old)	*N*	859 (100.0 %)	743 (100.0 %)	1,025 (100.0 %)	0.359
	Men	369 (43.0 %)	331 (44.5 %)	474 (46.2 %)	
	Women	490 (57.0 %)	412 (55.5 %)	551 (53.8 %)	
Weight (≥20 years old)	*N*	858 (100.0 %)	743 (100.0 %)	1,021 (100.0 %)	0.351
	Men	369 (43.0 %)	331 (44.5 %)	473 (46.3 %)	
	Women	489 (57.0 %)	412 (55.5 %)	548 (53.7 %)	
BMI (≥20 years old)	*N*	858 (100.0 %)	743 (100.0 %)	1,021 (100.0 %)	0.351
	Men	369 (43.0 %)	331 (44.5 %)	473 (46.3 %)	
	Women	489 (57.0 %)	412 (55.5 %)	548 (53.7 %)	
HbA1c (≥40 years old)	*N*	421 (100.0 %)	426 (100.0 %)	466 (100.0 %)	0.676
	Men	156 (37.1 %)	162 (38.0 %)	186 (39.9 %)	
	Women	265 (62.9 %)	264 (62.0 %)	280 (60.1 %)	
Total energy intake (≥20 years old)	*N*	986 (100.0 %)	955 (100.0 %)	1,057 (100.0 %)	0.779
	Men	444 (45.0 %)	441 (46.2 %)	492 (46.5 %)	
	Women	542 (55.0 %)	514 (53.8 %)	565 (53.5 %)	
Daily steps (≥20 years old)	*N*	830 (100.0 %)	848 (100.0 %)	992 (100.0 %)	0.421
	Men	354 (42.7 %)	384 (45.3 %)	451 (45.5 %)	
	Women	476 (57.3 %)	464 (54.7 %)	541 (54.5 %)	
Annual health checkup (≥20 years old)	*N*	960 (100.0 %)	976 (100.0 %)	1,095 (100.0 %)	0.949
	Men	433 (45.1 %)	441 (45.2 %)	501 (45.8 %)	
	Women	527 (54.9 %)	535 (54.8 %)	594 (54.2 %)	

BMI body mass index

[a] Statistically analyzed using Fisher's exact test

Table 2 Frequency distribution of age and mean age in the group of subjects who responded to various survey items in 1997, 2003 and 2010

Group responded to	Age category	Survey year			Comparison over 3 groups	Post hoc test	
		1997	2003	2010		Survey year	
Age (≥20 years old)	*N*	998 (100.0 %)	1,008 (100.0 %)	1,130 (100.0 %)		1997 vs. 2003	$P = 0.897$**
	20–29	99 (9.9 %)	110 (10.9 %)	81 (7.2 %)	$P < 0.001$*	1997 vs. 2010	$P < 0.001$**
	30–39	102 (10.2 %)	115 (11.4 %)	117 (10.4 %)		2003 vs. 2010	$P = 0.003$**
	40–49	205 (20.5 %)	137 (13.6 %)	166 (14.7 %)			
	50–59	167 (16.7 %)	216 (21.4 %)	214 (18.9 %)			
	60–69	241 (24.1 %)	204 (20.2 %)	239 (21.2 %)			
	≥70	184 (18.4 %)	226 (22.4 %)	313 (27.7 %)			
	Mean	54.3	54.7	57.4	$P < 0.001$*	1997 vs. 2003	$P = 1.000$**
	SD	16.7	17.3	17.2		1997 vs. 2010	$P < 0.001$**
	Median	55.5	55	59		2003 vs. 2010	$P = 0.001$**
Height (≥20 years old)	*N*	859 (100.0 %)	743 (100.0 %)	1,025 (100.0 %)		1997 vs. 2003	$P = 0.008$**
	20–29	84 (9.8 %)	68 (9.2 %)	70 (6.8 %)	$P < 0.001$*	1997 vs. 2010	$P < 0.001$ **
	30–39	90 (10.5 %)	78 (10.5 %)	100 (9.8 %)		2003 vs. 2010	$P = 0.288$ **
	40–49	185 (21.5 %)	98 (13.2 %)	150 (14.6 %)			
	50–59	141 (16.4 %)	157 (21.1 %)	194 (18.9 %)			
	60–69	207 (24.1 %)	156 (21.0 %)	228 (22.2 %)			
	≥70	152 (17.7 %)	186 (25.0 %)	283 (27.6 %)			
	Mean	54	56	57.7	$P < 0.001$*	1997 vs. 2003	$P = 0.018$**
	SD	16.5	17	16.9		1997 vs. 2010	$P < 0.001$**
	Median	55	57	59		2003 vs. 2010	$P = 0.155$**
Weight (≥20 years old)	*N*	858 (100.0 %)	743 (100.0 %)	1,021 (100.0 %)		1997 vs. 2003	$P = 0.009$**
	20–29	84 (9.8 %)	68 (9.2 %)	70 (6.9 %)	$P < 0.001$*	1997 vs. 2010	$P < 0.001$**
	30–39	89 (10.4 %)	78 (10.5 %)	96 (9.4 %)		2003 vs. 2010	$P = 0.229$**
	40–49	185 (21.6 %)	98 (13.2 %)	150 (14.7 %)			
	50–59	141 (16.4 %)	157 (21.1 %)	194 (19.0 %)			
	60–69	207 (24.1 %)	156 (21.0 %)	228 (22.3 %)			
	≥70	152 (17.7 %)	186 (25.0 %)	283 (27.7 %)			
	Mean	54	56	57.8	$P < 0.001$*	1997 vs. 2003	$P = 0.020$**
	SD	16.5	17	16.8		1997 vs. 2010	$P < 0.001$**
	Median	55	57	60		2003 vs. 2010	$P = 0.120$**
BMI (≥20 years old)	*N*	858 (100.0 %)	743 (100.0 %)	1,021 (100.0 %)		1997 vs. 2003	$P = 0.009$**
	20–29	84 (9.8 %)	68 (9.2 %)	70 (6.9 %)	$P < 0.001$*	1997 vs. 2010	$P < 0.001$**
	30–39	89 (10.4 %)	78 (10.5 %)	96 (9.4 %)		2003 vs. 2010	$P = 0.229$**
	40–49	185 (21.6 %)	98 (13.2 %)	150 (14.7 %)			
	50–59	141 (16.4 %)	157 (21.1 %)	194 (19.0 %)			
	60–69	207 (24.1 %)	156 (21.0 %)	228 (22.3 %)			
	≥70	152 (17.7 %)	186 (25.0 %)	283 (27.7 %)			
	Mean	54	56	57.8	$P < 0.001$*	1997 vs. 2003	$P = 0.020$**
	SD	16.5	17	16.8		1997 vs. 2010	$P < 0.001$**
	Median	55	57	60		2003 vs. 2010	$P = 0.120$**
HbA1c (≥40 years old)	*N*	421 (100.0 %)	426 (100.0 %)	466 (100.0 %)		1997 vs. 2003	$P = 0.004$**
	20–29	0 (0.0 %)	0 (0.0 %)	0 (0.0 %)	$P < 0.001$*	1997 vs. 2010	$P < 0.001$**
	30–39	0 (0.0 %)	0 (0.0 %)	0 (0.0 %)		2003 vs. 2010	$P = 0.009$**
	40–49	99 (23.5 %)	69 (16.2 %)	55 (11.8 %)			
	50–59	93 (22.1 %)	108 (25.4 %)	97 (20.8 %)			
	60–69	155 (36.8 %)	123 (28.9 %)	141 (30.3 %)			
	≥70	74 (17.6 %)	126 (29.6 %)	173 (37.1 %)			
	Mean	59.7	62.2	64.8	$P < 0.001$*	1997 vs. 2003	$P = 0.003$**
	SD	10.9	11.6	11.8		1997 vs. 2010	$P < 0.001$**
	Median	61	63	66		2003 vs. 2010	$P = 0.003$**

Table 2 continued

Group responded to	Age category	Survey year			Comparison over 3 groups	Post hoc test	
		1997	2003	2010		Survey year	
Total energy intake (≥20 years old)	*N*	986 (100.0 %)	955 (100.0 %)	1,057 (100.0 %)		1997 vs. 2003	$P = 0.719$**
	20–29	98 (9.9 %)	99 (10.4 %)	70 (6.6 %)	$P < 0.001$*	1997 vs. 2010	$P < 0.001$**
	30–39	102 (10.3 %)	107 (11.2 %)	108 (10.2 %)		2003 vs. 2010	$P = 0.002$**
	40–49	201 (20.4 %)	131 (13.7 %)	157 (14.9 %)			
	50–59	164 (16.6 %)	211 (22.1 %)	200 (18.9 %)			
	60–69	239 (24.2 %)	196 (20.5 %)	230 (21.8 %)			
	≥70	182 (18.5 %)	211 (22.1 %)	292 (27.6 %)			
	Mean	54.3	54.8	57.6	$P < 0.001$*	1997 vs. 2003	$P = 1.000$**
	SD	16.7	17.1	16.9		1997 vs. 2010	$P < 0.001$**
	Median	55.5	55	59		2003 vs. 2010	$P < 0.001$**
Daily steps (≥20 years old)	*N*	830 (100.0 %)	848 (100.0 %)	992 (100.0 %)		1997 vs. 2003	$P = 0.153$**
	20–29	75 (9.0 %)	84 (9.9 %)	66 (6.7 %)	$P < 0.001$*	1997 vs. 2010	$P < 0.001$**
	30–39	86 (10.4 %)	87 (10.3 %)	102 (10.3 %)		2003 vs. 2010	$P= 0.034$**
	40–49	184 (22.2 %)	122 (14.4 %)	151 (15.2 %)			
	50–59	141 (17.0 %)	189 (22.3 %)	192 (19.4 %)			
	60–69	211 (25.4 %)	182 (21.5 %)	219 (22.1 %)			
	≥70	133 (16.0 %)	184 (21.7 %)	262 (26.4 %)			
	Mean	53.9	55	57.2	$P < 0.001$*	1997 vs. 2003	$P = 0.233$**
	SD	15.9	16.7	16.6		1997 vs. 2010	$P < 0.001$**
	Median	55	55	59		2003 vs. 2010	$P = 0.023$**
Annual health checkup (≥20 years old)	*N*	960 (100.0 %)	976 (100.0 %)	1,095 (100.0 %)		1997 vs. 2003	$P = 0.655$**
	20–29	92 (9.6 %)	105 (10.8 %)	76 (6.9 %)	$P < 0.001$*	1997 vs. 2010	$P < 0.001$**
	30–39	99 (10.3 %)	111 (11.4 %)	113 (10.3 %)		2003 vs. 2010	$P = 0.002$**
	40–49	201 (20.9 %)	134 (13.7 %)	161 (14.7 %)			
	50–59	164 (17.1 %)	211 (21.6 %)	210 (19.2 %)			
	60–69	236 (24.6 %)	197 (20.2 %)	232 (21.2 %)			
	≥70	168 (17.5 %)	218 (22.3 %)	303 (27.7 %)			
	Mean	54.1	54.6	57.5	$P < 0.001$*	1997 vs. 2003	$P = 1.000$**
	SD	16.4	17.2	17.1		1997 vs. 2010	$P < 0.001$**
	Median	55	55	59		2003 vs. 2010	$P < 0.001$**

* Statistically analyzed using the Kruskal–Wallis *H* test

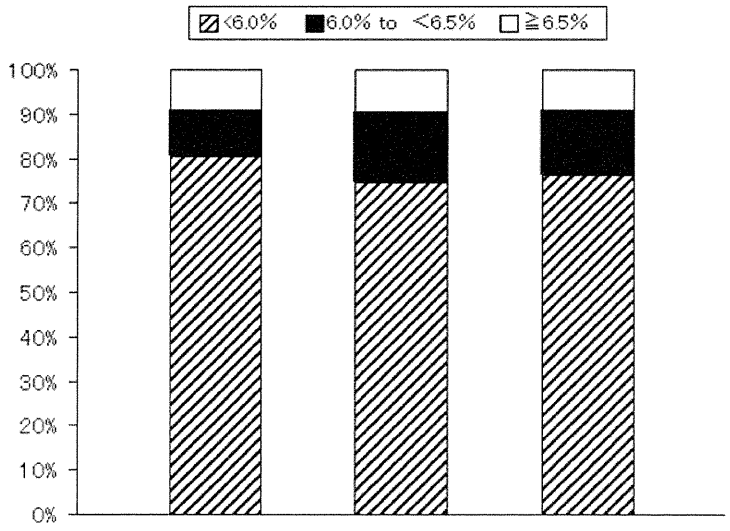
** Statistically analyzed using the Mann–Whitney *U* test with Bonferroni correction

correction, respectively. Data on other items in 1997 and 2010 were compared with those in 2003 as the reference using the Wilcoxon rank-sum test or Fisher's exact test. Values are expressed as the mean ± standard deviation (SD) unless otherwise indicated. All statistical analyses were performed using SAS version 9.1.3 (SAS Institute, Cary, NC, USA). Values of $P < 0.05$ were considered statistically significant.

Results

As shown in Table 1, the sex ratios of participants responding to the various survey items were almost identical on the three different occasions. Age frequency distributions and mean ages of participants in every survey item described in Table 2 were significantly different from each other among the three different occasions. Post hoc testing indicated that the relative distributions of subjects with advanced age had increased from 1997 and 2003 to 2010, so mean age was significantly higher for participants in 2010 for every survey item compared with those in 1997 and 2003 except for "height," "weight" and "BMI" in 2003. The difference in mean height between 2003 and 2010 was small but significant (158.0 ± 9.8 vs. 159.1 ± 9.5 cm, $P < 0.005$). Mean weight in 2003 (59.3 ± 11.3 kg) was significantly increased compared to that in 1997 (57.3 ± 10.3 kg, $P < 0.01$), but mean weight in 2010 (59.2 ± 11.9 kg) was not significantly different from that in 2003, although subjects in 2010 were significantly higher than those in 2003.

Figure 1 shows the temporal changes in the distribution of subjects with glucose intolerance from 1997 to 2010. Participants were classified into three categories according



Survey year		1997	2003	2010
HbA1c category				
<6.0%	(%)	80.5	74.6	76.4
6.0% to <6.5%	(%)	10.2	15.7	14.2
≥6.5%	(%)	9.3	9.6	9.4
N		421	426	466
Significance vs. 2003		P=0.062	Reference	P=0.577

Fig. 1 Temporal changes in the relative distribution of subjects ≥40 years old with glucose intolerance randomly recruited from the general population for the survey in Tokushima. Participants were divided into three categories according to HbA1c levels: <6.0 %, normal (*hatched bars*); 6.0 to <6.5 %, unable to exclude the possibility of diabetes (prediabetes) (*filled bars*); and ≥6.5 %, highly suspected as having diabetes (diabetes) (*open bars*). Data were statistically analyzed using the Wilcoxon rank-sum test

to HbA1c levels using the criteria proposed by the Ministry of Health, Labour and Welfare [1]: <6.0 %, normal; 6.0 to <6.5 %, unable to exclude the possibility of diabetes (prediabetes); ≥6.5 %, highly suspected as having diabetes (diabetes). The percentage of subjects with glucose intolerance in 2003 tended to be increased from that in 1997, but the difference was not statistically significant ($P = 0.062$). Compared with the percentage of subjects with glucose intolerance in 2003, a tendency toward a slight decrease was seen in 2010, although again the difference was not significant.

Figure 2 shows temporal changes in the percentage distribution of subjects based on BMI from 1997 to 2010. Participants were classified into three categories according to BMI: <18.5, thin; 18.5 to <25.0, normal weight; ≥25.0, obese. The relative distributions of thin, normal-weight and obese subjects in 2010 were significantly different ($P = 0.017$) from those in 2003; the percentages of thin and normal weight subjects were increased, whereas the percentage of obese subjects was decreased.

Table 3 shows temporal changes in total energy intake on the three different occasions. Total energy intake decreased gradually from 1997 and reached a significantly lower level in 2010 compared with that in 2003 ($P < 0.001$). Temporal change in mean total energy intake was greater in women than in men. Mean total energy intake in men in 2003 (2,133 ± 628 kcal) was significantly higher than that in 1997 (2,007 ± 580 kcal, $P < 0.001$), while that in 2010 (2,071 ± 602 kcal) was slightly but not significantly lower than that in 2003. Intakes of carbohydrates and protein were decreased, but fat intake remained stable from 1997 to 2010. Table 4 shows temporal changes in the number of daily steps. Mean number of daily steps decreased significantly during the period from 1997 to 2003, but remained stable thereafter. The reduction in number of daily steps was more marked in women than in men, and the mean number of steps actually increased in men from 2003 to 2010. Table 5 shows temporal changes in the percentage of subjects who underwent annual health checkups in 1997, 2003 and 2010. Changes in the percentage of subjects undergoing annual health checkups over the three occasions differed among the various age brackets. Percentages of subjects who underwent annual health checkups were significantly increased from 2003 to 2010 in total and among subjects in their 30s and upward, but were unchanged and decreased over these periods among subjects in their 30s and 20s, respectively.

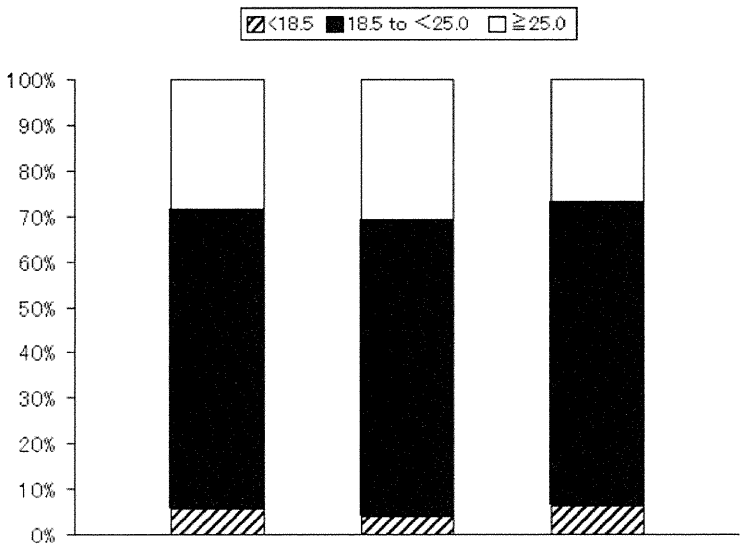


Fig. 2 Temporal changes in the relative distribution of subjects ≥20 years old with three categories of BMI who were randomly recruited from the general population for the survey in Tokushima. Participants were divided into three categories according to BMI: <18.5, thin (*hatched bars*); 18.5 to <25.0, normal weight (*filled bars*); ≥25, obese (*open bars*). Data were statistically analyzed using the Wilcoxon rank-sum test

Survey year		1997	2003	2010
BMI category				
<18.5	(%)	5.6	3.9	6.5
18.5 to <25.0	(%)	65.7	65.1	66.3
≥25.0	(%)	28.7	31	27.1
N		858	743	1021
Significance vs. 2003		P=0.163	Reference	P=0.017

Discussion

The results of this study suggest that our diabetes prevention programs along with those initiated by other organizations in Tokushima Prefecture affected the prevalence of diabetes from 2003 to 2010. The percentage of subjects with glucose intolerance tended to increase from 1997 to 2003 when no systematic programs for diabetes prevention were in place (Fig. 1). However, after the initiation of diabetes prevention programs in 2004, a slight decrease in the prevalence of diabetes was seen from 2003 to 2010, even though the participants in 2010 were older than those in 2003. If the programs had not been implemented during this period, the percentage of subjects with glucose intolerance would have increased in Tokushima in 2010, as it had increased during the period from 1997 to 2003. According to the National Health and Nutrition Surveys [1] conducted in 1997, 2002 and 2008, the percentage of subjects with glucose intolerance increased significantly from 20.2 % in 1997 to 23.8 % in 2002 and increased further to 27.0 % in 2008. Taking these facts together, it seems reasonable to infer that our prevention programs were effective in ameliorating the situation of diabetes in Tokushima Prefecture.

To the best of our knowledge, this is the first report assessing the effectiveness of diabetes prevention programs for the general public in a single prefecture. Tokushima prefecture was an ideal community in which to evaluate the effects of diabetes prevention programs since it has had one of the highest mortality rates from diabetes in Japan since 1993. Several recent clinical trials have demonstrated that lifestyle modifications with weight loss and moderate exercise can reduce the incidence of type 2 diabetes by up to 58 % among high-risk individuals [3–5, 15]. Translation of such results into community programs has been reported in many different settings and population groups [16, 17]. Successful programs have been implemented in rural areas of the USA [18, 19], Australia [20] and Japan [21] with an unsuccessful trial [22]. However, as the reported prevention measures have targeted selected individuals identified to be at increased risk, the benefits may not be applicable to the general population. Targeting of prevention measures to selected subjects is unsuitable for achieving health improvements among residents at the prefectural level. Although many trials on education and prevention have been conducted on municipal, prefectural or national scales in Japan, the outcomes of those trials have not been evaluated using objective measures. Based on an objective

Table 3 Temporal changes in total energy intake of subjects ≥20 years old who were randomly recruited for the survey in Tokushima

	Survey year		
	1997	2003	2010
Total			
Mean (kcal)	1,968	1,927	1,850
SD	568	591	555
N	986	955	1,057
P	0.17	Reference	<0.001
Men			
Mean (kcal)	2,007	2,133	2,071
SD	580	628	602
N	444	441	492
P	<0.001	Reference	0.063
Women			
Mean (kcal)	1,936	1,750	1,658
SD	557	495	427
N	542	514	565
P	<0.001	Reference	<0.001

Statistically analyzed using the Wilcoxon rank-sum test

Table 4 Temporal changes in the number of daily steps of subjects ≥20 years old who were randomly recruited for the survey in Tokushima

	Survey year		
	1997	2003	2010
Total			
Mean	6,838	6,228	6,210
SD	3,863	3,763	4,272
N	830	848	992
P	<0.001	Reference	0.42
Men			
Mean	6,736	6,508	6,719
SD	3,840	4,041	4,802
N	354	384	451
P	<0.001	Reference	0.907
Women			
Mean	6,913	6,228	5,785
SD	3,882	3,763	3,725
N	476	464	541
P	<0.001	Reference	0.218

Statistically analyzed using the Wilcoxon rank-sum test

analysis of prefectural health and nutrition surveys, we were able to show that our programs tended to reduce the prevalence of diabetes in the general population in Tokushima.

Weight loss has been linked to a reduction in the prevalence of diabetes in a community-based diabetes prevention study [23]. Evaluating temporal changes in the relative distribution of thin, normal weight and obese subjects in Tokushima was therefore important. Mean weight in 2010 (59.2 ± 11.9 kg) was not decreased from

Table 5 Temporal changes in the percentage of subjects who underwent an annual health checkup in 1997, 2003 and 2010

	Survey year		
	1997	2003	2010
Total			
Yes (%)	44.7	43.4	61.6
No (%)	55.3	56.6	38.4
N	960	976	1,095
P	0.533	Reference	<0.001
Men			
Yes (%)	39.7	43.3	63.5
No (%)	60.3	59.7	36.5
N	433	441	501
P	0.303	Reference	<0.001
Women			
Yes (%)	48.8	43.6	64.3
No (%)	51.2	56.4	35.7
N	527	535	594
P	0.097	Reference	<0.001
Age range (years)			
20–29			
Yes (%)	63.0	75.2	55.3
No (%)	37.0	24.8	44.7
N	92	105	76
P	0.087	Reference	<0.006
30–39			
Yes (%)	68.7	62.2	60.2
No (%)	31.3	37.8	39.8
N	99	111	113
P	0.384	Reference	0.785
40–49			
Yes (%)	40.8	47.0	67.1
No (%)	59.2	53.0	32.9
N	201	134	161
P	0.263	Reference	<0.001
50–59			
Yes (%)	35.4	34.6	74.3
No (%)	64.6	65.4	25.7
N	164	211	210
P	0.913	Reference	<0.001
60–69			
Yes (%)	33.5	34.5	59.1
No (%)	66.5	65.5	40.9
N	236	194	232
P	0.913	Reference	<0.001
≥70			
Yes (%)	47.2	33.0	53.8
No (%)	52.8	67.0	46.2
N	168	228	303
P	>0.001	Reference	>0.001

Statistically analyzed using the Wilcoxon rank-sum test

that in 2003 (59.3 ± 11.3 kg) under the conditions of higher mean height in 2010 comparing with 2003. The relative value of weight to height, BMI, would thus shed light on the relative prevalence of obesity. During the period from 1997 to 2003, the percentages of thin and normal-weight subjects as defined by BMI declined and the percentage of obese subjects increased in parallel with the increase in the percentage of subjects with glucose intolerance. In contrast to the change in obesity parameters during the period from 1997 to 2003, the percentages of thin and normal-weight subjects increased and that of obese subjects decreased from 2003 to 2010, accompanied by a tendency toward a decrease in the percentage of subjects with glucose intolerance. Despite a decrease in the percentage of obese subjects in Tokushima, at 27.1 % in 2010, the level remained higher than the 2008 national average of 24.2 %, suggesting that our programs should be continued to further reduce obesity parameters in Tokushima.

Mean total energy intake decreased gradually and reached a significantly lower level in 2010 (1,851 ± 556 kcal), similar to the 2008 national average (1,883 ± 562 kcal). It is reasonable to assume that a decrease in total energy intake contributed to the improvement of obesity parameters in 2010. However, mean total energy intake increased significantly from 1997 to 2003 in men but fell in women during the same period, resulting in a slight but non-significant decline in mean total energy intake in all subjects. The decrease in mean total energy intake from 2003 to 2010 might be partly attributable to an increase in subjects of advanced age in 2010 compared with 2003. Incidentally, the same trend was observed in the National Health and Nutrition Survey [1].

A lack of physical activity is one of the major risk factors for diabetes and may have contributed to the high prevalence of obesity and diabetes in Tokushima in 2003. We therefore evaluated the physical activity of residents according to daily steps registered on a pedometer that had been given to them beforehand and was installed on waking in the morning and taken off just before going to bed at night. Daily step counts were about 1,000 less in Tokushima in 1997 and 2003 compared to national averages at the corresponding times. Mean daily step counts fell significantly from 1997 to 2003, particularly among women (Table 4). However, mean daily step counts stopped declining in 2010. The National Health and Nutrition Surveys [1] revealed that mean daily step counts for the whole nation continued to decrease from 7,606 in 1997 to 7,103 in 2003 and decreased further to 6,428 in 2008. This suggests that our programs along with the Tokushima Marathon, the AWA-ODORI Exercise and the walk rallies might have contributed to halting the decline in mean step counts in Tokushima in 2010.

Individual health awareness is an important motivating factor for lifestyle modification. The percentage of subjects who underwent an annual health checkup was significantly increased in 2010. This is probably partly attributable to the increase in participants of advanced age in 2010, but appears mainly due to the commencement of the Special Health Checkup for metabolic syndrome in 2008 since the percentage of subjects who underwent an annual health checkup was significantly increased among subjects in their 40s and over who were recommended to have a checkup by local governments and the companies for which they worked. This appears to have had a beneficial impact on lifestyle modifications, such as increased physical activity, weight loss and dietary changes.

Despite these activities, Tokushima Prefecture still has the highest diabetes mortality rate in Japan. As several factors contribute to diabetes mortality, related problems must be overcome to reduce the number of deaths due to this disease. However, such problems are beyond the scope of the present research.

We recognize that this study suffers from several limitations. The numbers of participants at the lectures and seminars given to the general population and medical professionals were not counted and thus could not be quantified. Survey respondents were not the same on the three different occasions; participants were randomly recruited from among residents of various regions whenever the survey was planned using the same method applied in the national survey. No data on response rates were available. Since serial data were not collected on the same subjects, we could not prove that our programs had a significant effect on glucose tolerance or other parameters over time. Although we did not adjust our data for age, the effects of our programs were evaluated in respondents within the same age bracket so there was no need for age adjustment. Not all items in the surveys were obtained from all respondents, and missing information represents a serious limitation in a survey of this kind. As the prefectural health and nutrition surveys and the national surveys related to diabetes were not conducted in the same year, it was necessary to choose the values of the corresponding items in the national survey collected at the time closest to the prefectural survey.

In conclusion, this study demonstrated that diabetes prevention programs implemented by us along with other organizations in Tokushima Prefecture appear to have been beneficial in ameliorating the diabetes situation in Tokushima. These programs should be continued to help reduce the prevalence of diabetes in the prefecture and additional data should be accumulated to confirm the efficacy of the programs.

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Conflict of interest None declared.

Ethical approval All study protocols were approved by the ethics committee at the Tokushima Medical Association.

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魚沼地域における「プロジェクト８」

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はじめに

地域の糖尿病対策を進めるうえで，糖尿病地域医療連携の意義・重要性は現場では以前から認識されていた．2005年２月の日本糖尿病対策推進会議の設立以降さらに強く広く求められ，行政の医療計画にも盛り込まれ，全国でさまざまな形で取り組まれてきた．

その多くは病診・診診連携であり，地域の糖尿病診療レベルの向上や連携のレールに乗った患者の診療上の有益性は言うまでもない．だが，一方で必ずしも専門医の負担軽減になっていない形の連携があったり，クリニカルパスに乗れない患者も多く存在する．そして何より医療機関だけの連携では，糖尿病合併症のハイリスク者である未治療患者や治療中断者を救うことには限界があると考えられる．

そこでわれわれは医療機関のみならず，行政機関や歯科・薬局・健診機関・介護サービス事業所などの多職種連携（Inter professional work；IPW）と住民が学ぶシステムをつくり，地域の糖尿病対策を進めているので報告する．

魚沼地域糖尿病対策推進会議

新潟県は人口10万人対医師数が全国都道府県中42位（2010年）と少なく，なかでも魚沼地域は県内の７つの２次医療圏中最も少なく，医師数は全国平均の６割という医師不足の地域である．

神奈川県より広い地域に人口はわずか22万人，高齢化率30％の高齢過疎化の進んだ地域で，常勤の日本糖尿病学会専門医はひとりもいない地域である．だからこそ地域の医療者のネットワークは必須であり，必然的にでき，いくつかの糖尿病医療に関する研究会が開催されていた．

実は新潟県の糖尿病医療は「厚生労働省第２回医療計画の見直し等に関する検討会」（2011年２月18日）において，年齢調整受療率・新規透析導入など，９項目の評価の総合偏差値が全国で１位として評価された．これは県・市町村の保健行政と医療機関の連携の成果であると考えるが，特筆すべき取り組みとして，県医師会が中心となり平成８年に設立された「新潟県糖尿病検診研究会」の活動が挙げられる．そこでは従来，市町村によって糖尿病検診の判定基準が異なっていたり，せっかく検診で境界型や早期の糖尿病を見つけても医療機関では十分な指導・評価がされず，投薬が必要になってから，あるいは合併症が出てから介入されるという事態が多くみられていたことに対しての反省から，「糖尿病の診断手順フローチャート」作成，「検診におけるHbA1c全員実施」の推進，「境界型，軽症糖尿病指導・治療マニュアル」「境界型および糖尿病に対する早期からの指導・治療ガイドライン」の作成などが進められ，県内の糖尿病検診・診療の向上に寄与してきた．

そして，日本糖尿病対策推進会議設立の翌年度

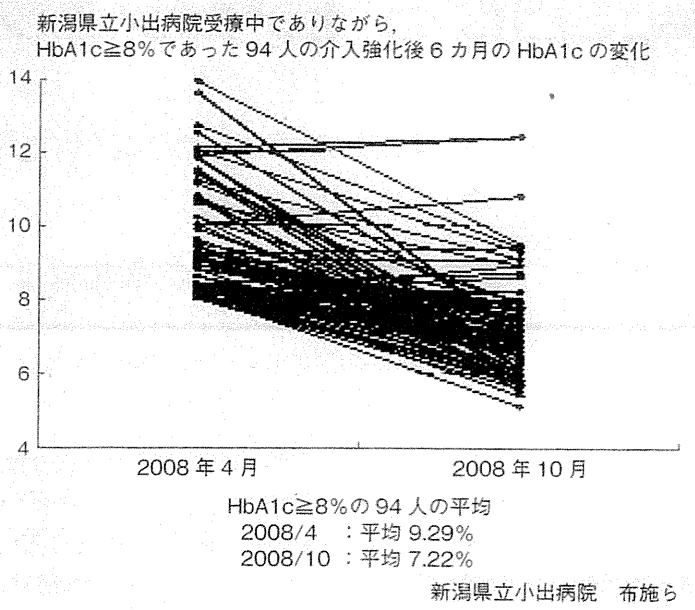

図1　医療者 Project 8

には，新潟県糖尿病対策推進会議および魚沼地域糖尿病対策推進会議が設立され，新潟県地域糖尿病療養指導士（LCDE新潟）の研修・認定制度も始まった．魚沼地域にも多くのCDEJ（日本糖尿病療養指導士），LCDEが育成され，さらに資格取得と関係なく，行政・歯科診療所・薬局・介護サービス事業所・健診機関などさまざまな施設の職員が，糖尿病の事例を中心に学ぶ「スタッフのための糖尿病教室」がIPE（Inter professional education）の場として定期開催されるようになった．

2008年4月から魚沼地域の中核病院である県立小出病院の院長に就任した布施は，糖尿病看護認定看護師らの協力を得て，糖尿病コントロール不可の者（HbA1c（JDS）≧8.0%）に対しての積極的治療介入を進め，その取り組みを「プロジェクト8」と命名し成果を上げていた（**図1**）．

また，2009年に新潟県糖尿病対策推進会議で実施した「新潟県糖尿病診療実態調査」の結果，県内糖尿病患者99,000人のうち11%（約1万人）がHbA1c（JDS）≧8.0%であり，魚沼地域でも糖尿病患者10,670人中9%（960人）がHbA1c（JDS）≧8.0%，すなわちコントロール不可であることがわかった．そこで，魚沼地域糖尿病対策推進会議として「プロジェクト8—すべての糖尿病患者のHbA1c（JDS）を8.0%未満に—」に取り組むこととした．

なぜ「プロジェクト8」か?

日本糖尿病学会による血糖コントロールの指標と評価でコントロール「不可」とされるHbA1c 8.4%以上（JDS値で8.0%以上）とは，細小血管症への進展の危険が大きい状態であり，治療の再検討を含めてなんらかのアクションをおこす必要がある場合を指すとされている．しかし実際の臨床現場では，コントロール「不可」症例でも数年間も処方の見直しもされずにいる例や，治療中断されたままでいる例が後を断たない．

これらの「不可」群は糖尿病腎症による透析導入や失明などのハイリスク群であり，将来の地域医療・保険財政への負担となることが危惧される

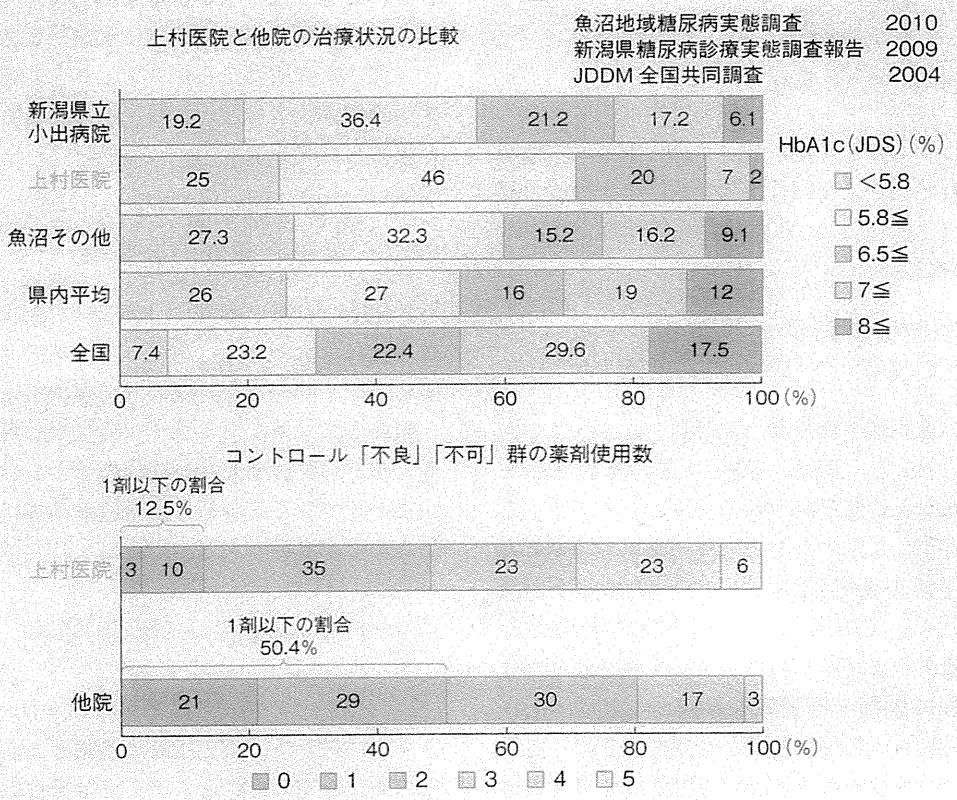

図2　糖尿病管理の実際（魚沼地域）

群である．医療資源が乏しく市町村の財政力も不足しているわれわれの地域で，これらのリスク群を看過・放置しておくことはできない．もちろんコントロール「優」「良」を目指すべきことは明らかだが，限られた医療資源のなかでまず介入すべきはコントロール「不可」群であることを，すべての医療者の共通認識とすべきであると考え「プロジェクト8」と名づけた．

魚沼地域糖尿病診療実態調査

地域の糖尿病対策事業としては①ポピュレーションアプローチ，②ハイリスクアプローチ，③診療機能の強化，④連携パスを利用した役割分担と医療連携推進に取り組んでいるが，事業の評価には糖尿病診療の実情を調査することが必要であると考え，2010年に実施した．

2010年の実態調査結果から当院とほかの医療機関での治療状況を比較すると，当院に通院する糖尿病患者のコントロールは他院に比べ良好であり，HbA1c（JDS）6.5%未満のコントロール「優」「良」が70%を超え，HbA1c（JDS）8%以上のコントロール「不可」群は全体の2%と他院の1/4～1/5であった（**図2**）．

その理由のひとつに薬剤選択の違いが挙げられると考えられた．すなわち，他院ではコントロール「不良」「不可」群においても使用薬剤が1剤以下の割合が50%もあり（当院では12.5%），治療強化が不十分な例が多いと考えられた．

さらに，事業所検診における調査でもHbA1c（JDS）≧8.0%でありながら無治療のまま2年間以上経過している例が働き盛りに多いことも明らかになり，健診機関による積極的介入が進められて