記録，目標の実行記録を毎日行うこととした。この記録は教室の受講時に回収し，受講者の目標の継続状況等の把握に使用した。身体活動による消費エネルギー量に関しては，スリム塾を実施した全期間にわたって加速度センサー付歩数計（ライフコーダ EX4 秒版（スズケン Co.））を装着し，日ごとの身体活動による消費エネルギー量を測定した。さらに1回目と9回目の問診時に，現在行っている運動の種類と実施頻度，1回あたりの運動時間を聞き取った。

3．統計分析

減量プログラムの介入前（1回目）と介入後（9回目）に実施した各検査値の変化について，全体と年代別で検討した。すなわち対象を30歳代以下，40歳代，50歳代，60歳代以上の4群にわけ，各年齢群での BMI，身体活動による消費エネルギー量，エネルギー及び栄養素摂取量，食品群別摂取量の介入前と介入後の平均値を比較した。検定にはウィルコクソン検定を用いた。次に，年代別，非肥満・肥満者別，単身者・非単身者，仕事有無別に，食行動7領域の改善効果を調べた。さらに，全年代において，介入前後の BMI の変化量と食行動7領域別のスコアの変化量，エネルギー及び栄養摂取量等，身体活動による消費エネルギー量との相関を調べた。さらに相関分析にて，BMI の変化量と有意な関連を認めた項目を独立変数に投入し，BMI の変化量を従属変数として，ステップワイズ法による重回帰分析を実施した。最後に，介入前後の BMI の変化量に最も有効であった食行動スコアとエネルギー及び栄養素摂取量等の変化量の相関を調べた。統計処理には，SPSS Ver.11. 5J for Windows を用いた。

受講者には，本プログラムから得られたデータを生活習慣病予防のための研究に使用する旨を口頭で説明し同意を得た。本研究は，「疫学研究に関する倫理指針」ならびに個人情報保護に関する国のガイドラインや指針等に則ってデータ解析を行ない，大阪府立健康科学センター倫理審査委員会の承認を得た（平成21年5月21日承認，受付番号1）。

結　　果

1．身体所見等の平均値の変化

身体所見の平均値の変化を表1に示す。介入後は介入前に比し，体重，BMI，腹囲，体脂肪率，体脂肪重量，トリグリセライド，空腹時血糖値，内臓脂肪量面積，皮下脂肪量面積の全ての平均値において有意な減少，収縮期血圧や拡張期血圧は有意な低下がみられ，逆に，身体活動による消費エネルギー量平均値の有意な増加を認めた。

2．主な栄養素摂取量，食品群別摂取量の平均値の変化

エネルギー及び主な栄養素摂取量は，介入後は介入前に比し，全年齢でみると，エネルギー，炭水化物，たんぱく質，脂質摂取量，脂肪エネルギー比率の全ての項目に有意な減少がみられた（表2）。年代別にみると，30歳代以下から60歳代以上のいずれの年代でも，30歳代以下の脂肪エネルギー比率を除く全ての項目に有意な減少が認められた。

食品群別摂取量は，介入後は介入前に比し，全年齢でみると，野菜類の摂取量の平均値が有意に増加し，逆に，肉類，卵類，果物，いも類，砂糖，油脂類，菓子エネルギー，ジュースエネルギー，アルコールエネルギー，食塩の摂取量は有意に減少した。年代別にみてもいずれの年齢階層でも，ほぼ同様の傾向が認められた。

3．各食行動スコアの平均値の変化

各食行動スコアの平均値の介入前後の変化を表3-1.2に示す。

表1　身体所見等の平均値の変化

	人数	介入前	介入後
体重（kg）	144	61.8 ± 9.5	60.0 ± 9.2***
BMI（kg/m^2）	144	25.7 ± 3.9	24.9 ± 3.7***
腹囲（cm）	144	88.5 ± 12.0	84.9 ± 12.0***
体脂肪率（%）	144	36.2 ± 5.2	34.7 ± 5.5***
体脂肪重量（kg）	144	22.6 ± 6.1	21.1 ± 6.0***
除脂肪重量（kg）	144	39.0 ± 4.7	38.8 ± 4.5
収縮期血圧（mmHg）	144	119.3 ± 17.3	112.8 ± 14.9***
拡張期血圧（mmHg）	144	75.4 ± 14.2	68.3 ± 10.3***
トリグリセライド（mg/dl）	144	118.5 ± 75.5	109.3 ± 63.6
HDL コレステロール（mg/dl）	144	61.9 ± 14.4	60.5 ± 14.0*
空腹時血糖値（mg/dl）	144	98.8 ± 20.3	96.0 ± 21.1**
内臓脂肪量面積（cm^2）	75	81.9 ± 37.8	72.9 ± 36.6***
皮下脂肪量面積（cm^2）	75	222.5 ± 80.6	211.5 ± 81.2***
身体活動による消費エネルギー量（kcal）	144	226.4 ± 99.8	309.7 ± 142.9***

平均値±標準偏差　*$p<0.05$　**$p<0.01$　***$p<0.001$（介入前との比較）

表2　主な栄養素摂取量，食品群別摂取量の平均値の変化（年代別）

	30歳代以下（n=18）		40歳代（n=27）		50歳代（n=51）		60歳代以上（n=48）		合計（n=144）	
	介入前	介入後	介入前	介入後	介入前	介入後	介入前	介入後	介入前	介入後
エネルギー（kcal）	2,033.2 ± 375.8	1,555.7 ± 269.6***	1,902.3 ± 557.6	1,474.0 ± 199.0***	1,793.5 ± 331.6	1,440.8 ± 199.5***	1,713.1 ± 300.1	1,499.4 ± 280.7***	1,817.1 ± 390.4	1,480.9 ± 238.9***
炭水化物（g）	245.8 ± 62.9	192.0 ± 31.6**	242.0 ± 85.7	190.1 ± 30.3**	227.1 ± 47.6	191.0 ± 32.0***	233.3 ± 48.8	205.4 ± 40.8***	234.3 ± 58.5	195.8 ± 35.2***
たんぱく質（g）	74.2 ± 12.6	64.3 ± 8.5**	71.1 ± 13.1	64.0 ± 11.2*	72.7 ± 13.2	63.8 ± 10.6***	71.4 ± 14.1	66.6 ± 11.8**	72.1 ± 13.3	64.8 ± 10.9***
脂質（g）	72.6 ± 17.2	52.0 ± 12.5**	68.4 ± 21.7	48.1 ± 10.0***	58.3 ± 14.7	42.9 ± 8.6***	51.8 ± 11.6	43.7 ± 10.1***	59.8 ± 17.2	45.3 ± 10.3***
脂肪エネルギー比率（%）	32.4 ± 3.9	30.2 ± 3.6	32.9 ± 4.6	29.6 ± 4.4**	29.8 ± 4.7	27.1 ± 3.7***	27.5 ± 4.1	26.4 ± 3.1*	29.9 ± 4.8	27.7 ± 3.9***
肉類（g）	88.6 ± 31.1	72.0 ± 29.2	82.5 ± 41.9	66.0 ± 33.5*	63.6 ± 27.4	49.4 ± 19.2**	52.8 ± 35.7	48.5 ± 32.6	66.7 ± 35.9	55.0 ± 29.5***
魚介類（g）	74.6 ± 27.6	82.5 ± 32.9	65.9 ± 34.1	81.4 ± 39.4**	94.9 ± 28.8	91.1 ± 30.3	97.2 ± 41.3	96.5 ± 35.0	87.7 ± 36.2	90.0 ± 34.2
卵類（g）	42.1 ± 24.6	32.4 ± 15.9	37.6 ± 20.8	31.3 ± 18.3	35.4 ± 20.3	30.6 ± 18.2	30.1 ± 19.7	27.0 ± 14.6	34.9 ± 20.9	29.8 ± 16.8**
大豆・大豆製品（g）	52.1 ± 41.4	48.6 ± 27.9	54.5 ± 32.4	57.1 ± 41.4	67.4 ± 40.2	64.4 ± 27.1	77.9 ± 44.1	68.2 ± 35.1*	66.6 ± 41.2	62.3 ± 33.3
乳・乳製品（g）	119.4 ± 105.3	121.9 ± 93.3	146.0 ± 113.2	118.0 ± 68.4	158.8 ± 107.1	138.9 ± 80.6	160.0 ± 107.7	164.4 ± 86.8	151.9 ± 107.9	141.4 ± 83.5
野菜類（g）	180.3 ± 85.4	238.4 ± 67.6**	213.7 ± 96.3	255.5 ± 89.8**	255.4 ± 64.2	303.2 ± 74.0***	267.3 ± 93.8	318.8 ± 97.1***	242.2 ± 88.3	291.3 ± 89.0***
果物（g）	79.4 ± 113.9	64.3 ± 68.2	83.6 ± 76.4	70.3 ± 48.2	158.1 ± 125.3	112.9 ± 74.5**	170.9 ± 127.2	152.8 ± 129.3	138.5 ± 122.1	112.1 ± 97.9**
穀物類（g）	390.3 ± 156.8	369.2 ± 103.8	402.9 ± 183.7	376.5 ± 75.8	350.9 ± 87.3	348.9 ± 83.9	377.9 ± 102.6	365.5 ± 95.9	374.6 ± 124.7	362.2 ± 89.0
いも類（g）	29.1 ± 21.7	26.6 ± 12.4	43.3 ± 72.1	20.1 ± 11.3*	43.4 ± 37.5	36.8 ± 27.8	39.1 ± 25.7	36.1 ± 20.5	40.2 ± 41.6	32.2 ± 22.2**
砂糖（g）	12.9 ± 7.0	9.6 ± 4.7*	10.7 ± 8.4	7.2 ± 3.0**	12.0 ± 9.5	9.0 ± 4.5**	10.5 ± 5.3	8.1 ± 3.4***	11.4 ± 7.7	8.4 ± 4.0***
油脂類（g）	26.8 ± 10.2	17.7 ± 9.1**	23.4 ± 14.2	15.2 ± 6.5***	17.3 ± 9.2	10.4 ± 5.7***	13.3 ± 7.9	9.4 ± 5.7**	18.3 ± 11.0	11.9 ± 7.0***
菓子エネルギー（kcal）	393.1 ± 259.1	121.4 ± 98.3***	332.7 ± 236.5	115.0 ± 85.8***	200.6 ± 159.1	66.2 ± 54.1***	171.7 ± 147.0	69.4 ± 74.8***	239.8 ± 202.0	83.3 ± 76.8***
ジュースエネルギー（kcal）	15.4 ± 25.4	10.7 ± 16.3	25.4 ± 63.2	7.3 ± 14.9	13.7 ± 24.8	6.0 ± 16.3**	13.7 ± 36.4	5.0 ± 16.9*	16.1 ± 38.4	6.5 ± 16.2***
アルコールエネルギー（kcal）	84.9 ± 193.1	58.3 ± 135.2	20.8 ± 42.3	10.7 ± 23.0*	82.6 ± 174.5	38.6 ± 107.8***	29.8 ± 65.2	20.2 ± 52.3	53.7 ± 132.7	29.7 ± 86.4***
食塩（g）	9.9 ± 2.3	9.0 ± 1.5	10.3 ± 2.4	9.3 ± 1.5*	11.0 ± 2.7	9.7 ± 2.0**	11.0 ± 2.5	10.0 ± 2.1**	10.7 ± 2.5	9.6 ± 1.9***

平均値±標準偏差　*$p<0.05$　**$p<0.01$　***$p<0.001$（介入前との比較）

表3-1　各食行動スコアの平均値の変化　—年代別検討—

	30歳代以下（n=18）		40歳代（n=27）		50歳代（n=51）		60歳代以上（n=48）		合計（n=144）	
	介入前	介入後	介入前	介入後	介入前	介入後	介入前	介入後	介入前	介入後
体質に関する認識	2.4 ± 0.8	2.6 ± 0.8	2.2 ± 0.8	2.6 ± 0.9*	2.5 ± 0.9	2.8 ± 0.8**	2.3 ± 0.9	2.8 ± 0.8***	2.4 ± 0.9	2.7 ± 0.8***
空腹感・食動機	2.5 ± 1.2	2.7 ± 1.1	2.9 ± 0.9	3.1 ± 0.9	2.7 ± 1.0	2.9 ± 0.8	2.6 ± 1.1	2.6 ± 1.1	2.7 ± 1.0	2.8 ± 0.9*
代理摂食	2.1 ± 0.7	2.5 ± 0.7*	2.1 ± 0.6	2.8 ± 0.8***	2.5 ± 0.8	3.0 ± 0.6***	2.6 ± 0.8	2.8 ± 0.9*	2.4 ± 0.8	2.9 ± 0.8***
満腹感覚	1.9 ± 0.7	2.4 ± 0.8*	2.2 ± 0.8	2.9 ± 0.8**	2.6 ± 0.8	3.1 ± 0.7***	2.5 ± 0.8	2.8 ± 0.9**	2.4 ± 0.8	2.9 ± 0.8***
食べ方	2.6 ± 0.6	2.9 ± 0.7	2.8 ± 0.8	3.1 ± 0.9*	2.9 ± 0.8	3.2 ± 0.7**	2.7 ± 1.0	3.1 ± 0.7**	2.8 ± 0.8	3.1 ± 0.7***
食事内容	2.6 ± 0.7	2.9 ± 0.8*	2.8 ± 0.8	3.1 ± 0.7**	3.1 ± 0.6	3.3 ± 0.5*	3.3 ± 0.4	3.4 ± 0.4*	3.0 ± 0.6	3.2 ± 0.6***
リズム異常	2.7 ± 0.5	3.0 ± 0.6*	2.9 ± 0.6	3.4 ± 0.6***	3.3 ± 0.4	3.5 ± 0.4**	3.4 ± 0.5	3.5 ± 0.5	3.2 ± 0.6	3.4 ± 0.5***

平均値±標準偏差　*$p<0.05$　**$p<0.01$　***$p<0.001$（介入前との比較）

表3-2 各食行動スコアの平均値の変化 —肥満，単身，仕事有無別の検討—

	肥満者（n=78）		非肥満者（n=66）	
	介入前	介入後	介入前	介入後
体質に関する認識	2.2 ± 0.8	2.5 ± 0.8**	2.7 ± 0.8	3.0 ± 0.7***
空腹感・食動機	2.6 ± 1.0	2.8 ± 0.9*	2.8 ± 1.0	2.9 ± 1.0
代理摂食	2.2 ± 0.7	2.8 ± 0.8***	2.6 ± 0.8	2.9 ± 0.8***
満腹感覚	2.1 ± 0.7	2.7 ± 0.8***	2.7 ± 0.8	3.0 ± 0.8***
食べ方	2.7 ± 0.8	3.0 ± 0.7***	2.9 ± 0.9	3.2 ± 0.8**
食事内容	3.1 ± 0.6	3.3 ± 0.5***	3.0 ± 0.7	3.2 ± 0.6***
リズム異常	3.2 ± 0.6	3.5 ± 0.5***	3.2 ± 0.6	3.4 ± 0.6*
	単身者（n=14）		非単身者（n=130）	
	介入前	介入後	介入前	介入後
体質に関する認識	2.2 ± 0.8	2.8 ± 0.8*	2.4 ± 0.9	2.7 ± 0.8***
空腹感・食動機	2.3 ± 1.2	2.3 ± 1.1	2.7 ± 1.0	2.9 ± 0.9*
代理摂食	2.3 ± 0.9	2.9 ± 0.9**	2.4 ± 0.8	2.9 ± 0.8***
満腹感覚	2.2 ± 0.9	2.6 ± 1.0	2.4 ± 0.8	2.9 ± 0.8***
食べ方	2.8 ± 1.1	3.3 ± 0.6*	2.8 ± 0.8	3.1 ± 0.7***
食事内容	3.0 ± 0.5	3.1 ± 0.4	3.0 ± 0.6	3.3 ± 0.6***
リズム異常	3.2 ± 0.4	3.4 ± 0.5*	3.2 ± 0.6	3.4 ± 0.5***
	仕事をもつ者（n=49）		仕事をもたない者（n=91）	
	介入前	介入後	介入前	介入後
体質に関する認識	2.4 ± 0.9	2.8 ± 0.8***	2.4 ± 0.9	2.7 ± 0.8***
空腹感・食動機	2.7 ± 1.0	2.9 ± 0.9	2.7 ± 1.0	2.8 ± 1.0
代理摂食	2.3 ± 0.7	2.9 ± 0.7***	2.5 ± 0.8	2.8 ± 0.9***
満腹感覚	2.3 ± 0.7	2.8 ± 0.8***	2.4 ± 0.8	2.9 ± 0.8***
食べ方	2.8 ± 0.8	3.2 ± 0.7**	2.8 ± 0.9	3.1 ± 1.0***
食事内容	2.9 ± 0.6	3.2 ± 0.6**	3.1 ± 0.6	3.3 ± 0.6**
リズム異常	3.0 ± 0.5	3.3 ± 0.5***	3.3 ± 0.6	3.5 ± 0.5***

平均値±標準偏差 *$p<0.05$ **$p<0.01$ ***$p<0.001$（介入前との比較）

全年齢でみると，介入後は介入前に比べ，食行動７領域の各スコアに有意な増加がみられた（表3-1）。年代別にみると，介入後は介入前に比べ，30歳代以下から60歳代以上のいずれの年代でも，代理摂食，満腹感覚，食事内容の各スコアに有意な増加がみられた。また，リズム異常のスコアは60歳代以上を除く年代で有意な増加がみられ，介入後のスコアは，７領域の各食行動の中で最も高くなった。体質に関する認識や食べ方のスコアは，40歳代以降で有意な増加がみられた。肥満の有無別では，肥満者は非肥満者に比べ，介入前は，体質に関する認識，空腹感・食動機，代理摂食，満腹感覚，食べ方の各スコアがいずれも低かったが，介入後のそれらの食行動のスコアは有意に増加し，特に代理摂食や満腹感覚のスコアの増加が大きくみられた。単身や仕事の有無別では，食行動のスコアの変化に有意な差はみられなかった（表3-2）。

４．BMI の変化量と食行動スコア，エネルギー及び栄養摂取量等の変化量との関連

介入前後における BMI の変化量と食行動のスコアの変化量（７領域別），エネルギー及び栄養素摂取量等の変化量との単相関係数を検討した結果，BMI の変化量と，空腹感・食動機，代理摂食，満腹感覚，食べ方，食事内容，リズム異常の各スコアの変化量には有意の負の相関を認めた（表４）。また，BMI の変化量とエネルギー，炭水化物，たんぱく質，脂質，穀物類，砂糖，油脂類，菓子エネルギーの各摂取変化量との間に有意な正の相関を認め，逆に，BMI の変化量と野菜類の変化量，消費エネルギー変化量との間に有意な負の相関が認められた。

相関分析にて BMI の変化量と有意差が認められた項目に年齢，性別を加えて，ステップワイズ法による重回帰分析を行った結果，BMI の減少には，代理摂食の改善及び身体活動による消費エネルギー量と野菜類摂取量の増加がそれぞれ独立した関連因子となった（表５）。さらに，BMI の減少との有意の関連を認めた代理摂食について，主な栄養摂取量の変化量との相関図を分析した結果，代理摂食のスコアの増加は，いずれも，エネルギー，炭水化物，たんぱく質，脂質，菓子エネルギー摂取量の減少，及び野菜類摂取量の増加と有意な相関を示した（図３）。

表4　BMIの変化量と食行動スコア，エネルギー及び栄養摂取量等の変化量との関連

		相関係数	p 値
全年齢	(n＝144)		
	体質に関する認識スコア	−0.066	n.s.
	空腹感・食動機スコア	−0.185	0.026
	代理摂食スコア	−0.462	<0.001
	満腹感覚スコア	−0.374	<0.001
	食べ方スコア	−0.191	0.022
	食事内容スコア	−0.259	0.002
	リズム異常スコア	−0.267	0.001
	エネルギー（kcal）	0.317	<0.001
	炭水化物（g）	0.246	0.003
	たんぱく質（g）	0.183	0.028
	脂質（g）	0.306	<0.001
	脂肪エネルギー比率（%）	0.130	n.s.
	肉類（g）	0.152	n.s.
	魚介類（g）	0.136	n.s.
	卵類（g）	−0.007	n.s.
	大豆・大豆製品（g）	−0.145	n.s.
	乳・乳製品（g）	−0.028	n.s.
	野菜類（g）	−0.413	<0.001
	果物（g）	0.060	n.s.
	穀物類（g）	0.197	0.018
	いも類（g）	0.119	n.s.
	砂糖（g）	0.218	0.009
	油脂類（g）	0.310	<0.001
	菓子エネルギー（kcal）	0.250	0.002
	ジュースエネルギー（kcal）	0.110	n.s.
	アルコールエネルギー（kcal）	0.013	n.s.
	食塩（g）	0.116	n.s.
	介入前 BMI	−0.271	0.001
	身体活動による消費エネルギー量（kcal）	−0.372	<0.001

スピアマンの相関係数
n.s.: not significant

表5　BMIの変化量と食行動スコア，エネルギー及び栄養摂取量等の変化量との関連　―重回帰分析による検討―

		β	p 値
全年齢	(n＝144)		
	代理摂食	−0.284	<0.001
	身体活動による消費エネルギー量	−0.272	<0.001
	野菜類	−0.202	0.007
	BMI（介入前）	−0.177	0.010
	$F=21.786$		<0.001
	$R^2=0.385$		
調整済み	$R^2=0.368$		

ステップワイズ法，β＝標準化偏回帰係数，R＝重相関係数

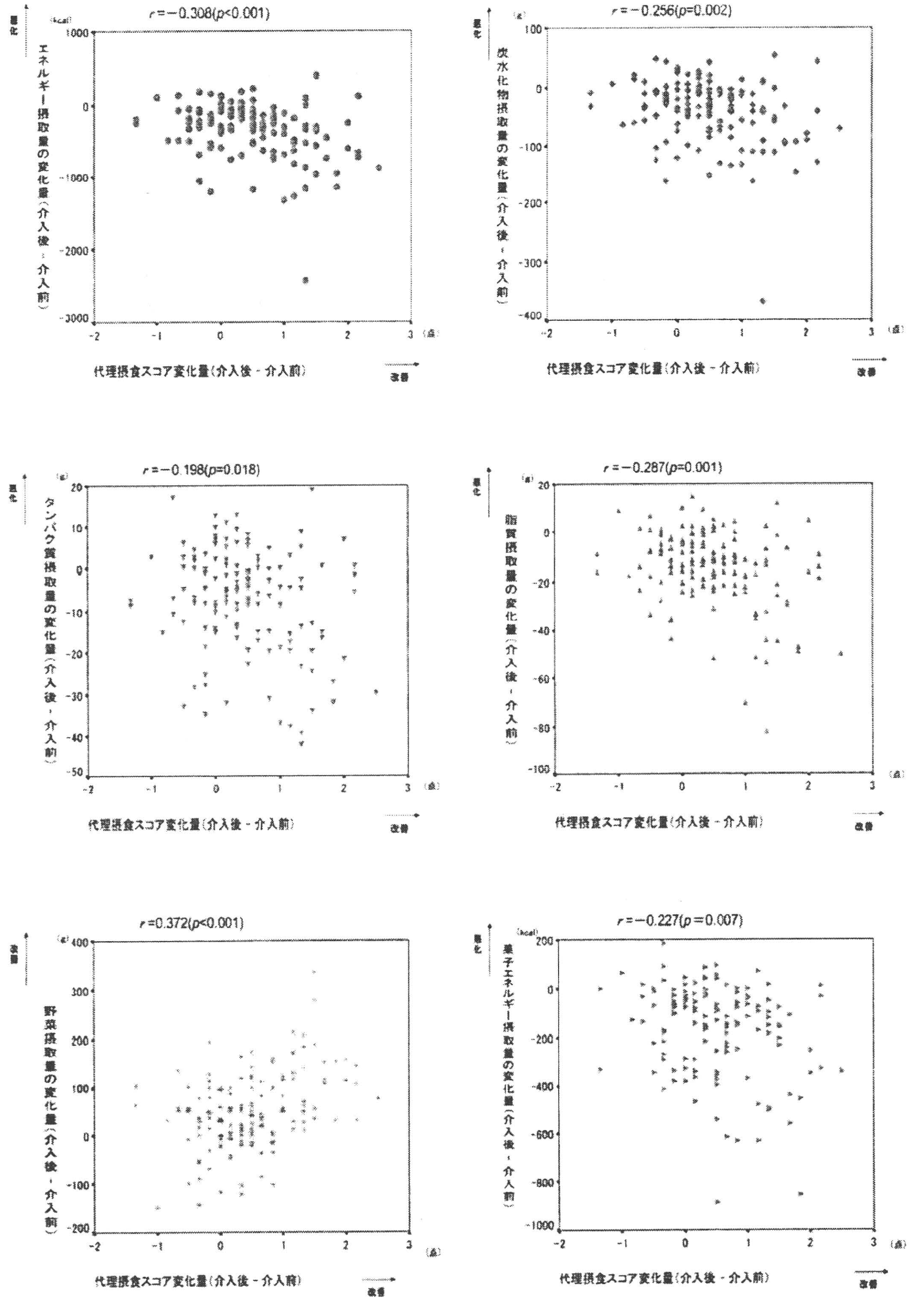

図3　代理摂食の変化量と主な栄養摂取量の変化量との相関（散布図）

考　　　　察

減量のための具体的な指導内容は，摂取エネルギー量の制限，ならびに身体活動による消費エネルギー量（運動量）の増加に力点がおかれることが多く，摂取エネルギー量の制限のためには，カロリーの多い食品の種類や摂取量に関する知識の伝授を目的とした指導が一般的である。しかしながら，実際の食品摂取には，知識のみでなく，食品の摂取行動に至るまでの意識や考え方，行動パターン，嗜好などの要因も影響することから，それらの要因を含む「食行動」に着目した現状分析とそれに基づく指導は減量に効果的であると考えられる。本研究では，われわれが実施してきた減量プログラムの受講者を対象に，介入前後の変化について，特に食行動に焦点をあてた分析を行った。今回の検討の結果，減量プログラ

ムの実施後は，体質に関する認識，代理摂食，満腹感覚，食べ方等，多くの食行動領域での改善が認められ，その改善度は特に肥満者において顕著であった。多変量解析の結果では，代理摂食の改善が，身体活動による消費エネルギー量や野菜摂取量の増加とともに減量に独立して関連していることが明らかとなった。代理摂食には，菓子類（間食）の摂取に関する行動内容が含まれており，実際，代理摂食のスコアの改善と菓子類の摂取量の減少量は有意に関連していた。したがって，「菓子類の買い置き」等の食行動に対する介入は，減量により効果的であると考えられた。

減量を目的とした食行動介入に関する先行研究としては，中高年女性を対象とした減量教室で介入前後の食行動異常の改善群は非改善群と比べ，体重の減少率が有意に高く，かつ1日の歩数による運動量や野菜類等摂取量も増加したことが報告されている[8,9]。同報告によると，肥満者は，介入前後の代理摂食，リズム異常，食行動全体の改善が腹囲の減少率に有意な相関があったという本研究とほぼ共通する結果が示されている。

本研究の一つ目の限界として，本プログラムは生活習慣全般の改善を促した総合的な指導を行ったもので，食行動の改善のみの指導を行ったわけではない。また，DXA 法による体脂肪重量の測定や腹部 CT 検査による内臓脂肪量面積の測定を含む各種検査の実施が，減量行動の動機付けの強化につながったことも考えられる。すなわち，本プログラムで得られた減量効果はあくまでも総合的な介入による結果であるため，食行動改善の単独の介入効果のみ取り出して示すことはできない。二つ目の限界として，今回の検討では，身体活動による消費エネルギー量の評価は加速度センサー付歩数計で行ったが，自転車や水泳，階段昇降などの身体活動量は評価されにくい。しかしながら，問診による身体活動量状況の聞き取りの結果では，自転車を外出の際に毎日利用する者は，受講者144名中で介入前79名，介入後70名とそれぞれ約5割を占めていたが，自転車の利用時間は，介入前後とも平均約31分と介入前後での差はなかった。また，運動としてエアロバイク等を利用している者は，介入前2名，介入後3名，水泳では介入前11名，介入後13名，階段昇降は介入前1名，介入後2名といずれも少なく，これらの運動による影響は大きくないと考えられた。三つ目の限界として，本研究は，比較対照群を設けず無作為割付をせずに，本プログラム受講者における介入前後の各指標の比較のみを行ったため，本プログラムによる食行動改善と減量効果を明確には評価できていない。そこで，本研究では，同じ介入という曝露を受けた中で生じた，個々人の食行動の変化と体重変化との関連を検討し，さらに多変量解析により体重変化に影響する主要な他の交絡要因を調整した検討において，有意な関連性を認めた。この結果は，厳密には食行動の変化と体重変化との間の因果関係を立証したとは言えないが，食行動の改善が減量に寄与するという本研究の仮説を支持する説得力のある証拠と考えられる。

以上をまとめると，当センターにおいて一般健常者の女性に対して実施した減量プログラム「スリム塾」により，参加者の有意な減量効果が認められ，血圧や血液所見も有意に改善した。栄養摂取状況にも改善がみられ，エネルギー，炭水化物，脂質，砂糖，油脂類，菓子等の摂取量が有意に減少するとともに野菜類の摂取量と身体活動による消費エネルギー量が有意に増加した。さらに，多くの食行動領域での改善が認められ，多変量解析の結果，代理摂食の改善は減量に独立して関連していることが明らかとなった。すなわち，代理摂食の改善の指導は，減量により効果的であることが窺われた。今後の課題として，メタボリックシンドロームの有所見率は男性に多く，また高校生を対象にした介入研究では，坂田らの食行動質問表[2]を参考に作成した尺度において，代理摂食，過食，リズム異常，食事内容の食行動で男女間の差が認められたという報告があり[13]，さらに最新の食行動質問表は男女別に改変されていることから[14]，男性の対象者を増やして検討していくことが必要である。

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Original Article

Use of Doubly Labeled Water to Validate a Physical Activity Questionnaire Developed for the Japanese Population

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ABSTRACT

Background: No study has attempted to use the doubly labeled water (DLW) method to validate a physical activity questionnaire administered to a Japanese population. The development and refinement of such questionnaires require that physical activity components related to physical activity level be examined.

Methods: Among 226 Japanese men and women 20 to 83 years of age, total energy expenditure (TEE) was assessed using the Japan Arteriosclerosis Longitudinal Study Physical Activity Questionnaire (JALSPAQ), and the results were compared with TEE measured by the DLW method as a gold standard. Resting metabolic rate (RMR) was measured using the Douglas Bag method.

Results: The median TEE by DLW and physical activity level (PAL: TEE/RMR) were 11.21 MJ/day and 1.88, respectively, for men, and 8.42 MJ/day and 1.83 for women. JALSPAQ slightly underestimated TEE: the differences in mean and standard error were −1.15 ± 1.92 MJ/day. JALSPAQ and DLW TEE values were moderately correlated (Spearman correlation = 0.742, $P < 0.001$; intraclass correlation coefficient = 0.648, $P < 0.001$), and the 95% limit of agreement was −4.99 to 2.69 MJ. Underestimation of TEE by JALSPAQ was greater in active subjects than in less active subjects. Moderate and vigorous physical activity and physical activity during work (ie, occupational tasks and housework) were strongly related to physical activity level. However, the physical activity components that differentiated sedentary from moderately active subjects were not clear.

Conclusions: Physical activity level values on JALSPAQ and DLW were weakly correlated. In addition, estimation of TEE in active subjects should be improved, and the use of a questionnaire to differentiate activity in sedentary and moderately active subjects must be reassessed.

Key words: physical activity questionnaire; doubly labeled water; physical activity; energy expenditure

INTRODUCTION

Accurate assessment of physical activity level is fundamental in epidemiological studies that examine the effect of physical activity on disease prevention and health promotion. Although there are several methods for estimating physical activity level, questionnaires are the most common assessment tool in such studies. Many types of physical activity questionnaires are used in epidemiological studies, but a validation study of such questionnaires suggested that the reliability and validity of measurements of habitual physical activity are quite low.[1–3] In addition, Neilson et al suggested that the ability of physical activity questionnaires to predict total energy expenditure (TEE) is limited. Westerterp et al suggested that questionnaires are satisfactory as an instrument for ranking physical activity level, but not as tools for assessing absolute TEE.[4] We previously examined the International Physical Activity Questionnaire (IPAQ) and reported that it was difficult to distinguish sedentary from moderately active individuals in the Japanese population.[5] Although the IPAQ was developed for international use, we maintain that questionnaires designed to suit each country or culture would increase the validity of assessments of physical activity level. The Japan Arteriosclerosis Longitudinal Study Physical Activity Questionnaire (JALSPAQ) was developed to assess physical activity in the Japan Arteriosclerosis Longitudinal Study.[6,7] This questionnaire was developed using data from physical activity records for the Japanese

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population and included detailed questions on occupational work, housework, and leisure-time physical activity.

The doubly labeled water (DLW) method is an excellent method for measuring TEE in free-living subjects over a period of 1 to 2 weeks[8] and is often used as a gold standard to validate field methods of assessing physical activity levels. However, to our knowledge, only our previous study[5] has used it to examine the validity of a questionnaire used for the Japanese population.

The primary objective of this study was to use the DLW method as the gold standard to validate a physical activity questionnaire developed for the Japanese population. To aid in the development of a valid physical activity questionnaire for Japanese, the secondary objective was to identify the physical activity component that had the greatest impact on physical activity level (PAL).

METHODS

Subjects

The study participants were 226 Japanese men and women age 20 to 83 years (mean ± standard deviation, 50.4 ± 17.1 years) who volunteered at community health care centers and workplaces or enrolled via the internet homepage of our institute. The inclusion criteria of the present study were as follows: absence of any condition affecting energy or water metabolism (eg, thyroid or kidney disease), not pregnant or breast-feeding, residence in home prefecture 2 weeks before and during the study, not on weight-loss or treatment diet, and not consuming more than 40 grams of alcohol per day. The occupations of the participants were homemaker ($n = 59$), office worker ($n = 57$), shipbuilder ($n = 17$), shop assistant ($n = 14$), no regular work ($n = 14$), nurse ($n = 13$), teacher ($n = 11$), salesperson ($n = 11$), factory worker ($n = 6$), clinical examination technician ($n = 5$), physiotherapist ($n = 4$), and other ($n = 12$, cleaner, gardener, dietitian, priest, sports instructor, carpenter, etc.). We were unable to randomly select subjects according to physical activity level. Over the entire assessment period, the participants were carefully instructed to maintain their normal daily activities and eating patterns and to make no conscious effort to lose or gain weight.

Study protocol

This study was approved by the Ethics Committee of the National Institute of Health and Nutrition in Japan. All subjects gave their informed consent in writing before the investigation was begun. TEE was estimated over 1 or 2 weeks, depending on the 2 half-lives of the isotopes used in the DLW method. Body mass and height were measured in the fasting state before administering the dose of DLW and on the last day of the study. On the first day of the study period, baseline urine was collected, and measurements of resting metabolic rate (RMR) and DLW dosing were obtained. The physical activity questionnaire and dietary assessment were completed between the 10th and 12th day of the study period and were checked by the researchers on the last day.

Measurement of resting metabolic rate

Subjects were instructed to refrain from moderate to vigorous physical activity for 24 hours, to fast at least 12 hours, and to get sufficient sleep before the measurements. They were instructed to arrive at the laboratory between 8AM and 9AM. After arrival, they rested quietly in the supine position for 30 minutes before the measurements. Using a mask connected to a Douglas bag, expired gas was collected twice for 10 minutes, with a 1-minute interval between collections. During all RMR measurements, the room temperature was maintained at approximately 24°C. Subjects were lying down and fully awake during the measurements. They were also free from emotional stress and were familiar with the apparatus used. The volume of expired air was measured with a certified gas meter (DC-5, Shinagawa, Tokyo, Japan), the accuracy and precision of which were maintained within 1% of the coefficient of variation (CV). Concentrations of oxygen and carbon dioxide were measured with a mass spectrometer (ARCO-1000, Arco Systems, Chiba, Japan). The precision of expired gas measurement was 0.02% for oxygen and 0.06% for carbon dioxide. RMR was calculated using Weir's equation.[9]

DLW energy measurement

After providing a baseline urine sample, a single dose of approximately 0.06 g/kg body weight of ^2H_2O (99.8 atom%, Cambridge Isotope Laboratories, MA, USA) and 1.4 g/kg body weight of $H_2{}^{18}O$ (10.0 atom%, Taiyo Nippon Sanso, Tokyo, Japan) was given orally to each subject. Then subjects were asked to collect urine samples at 8 predetermined times during the study period, at the same time of day. Except for the baseline collection, all urine samples were collected by the participant, and the time of sampling was recorded. All samples were stored by freezing at −30°C in airtight parafilm-wrapped containers and then analyzed in our laboratory.

Gas samples for the isotope ratio mass spectrometer (IRMS) were prepared by equilibration of the urine sample with a gas. CO_2 was used to equilibrate ^{18}O, and H_2 was used for ^2H. Pt catalyst was used for equilibration of ^2H. The gas sample of the CO_2 and H_2 was analyzed by IRMS (DELTA Plus; Thermo Electron Corporation, Bremen, Germany). Each sample and the corresponding reference were analyzed in duplicate. The average standard deviations for the analyses were 0.5‰ for ^2H and 0.03‰ for ^{18}O. TEE was expressed as mean TEE per day over the study period.

Calculations of isotopic abundance and TEE

The ^2H and ^{18}O zero-time intercepts and elimination rates (k_H and k_O) were calculated using a least-squares linear regression on the natural logarithm of isotope concentration as a function of the elapsed time from dose administration. Zero-time intercepts were used to determine the isotope pool sizes. Total body water (TBW) was calculated from the mean value of the isotope pool size of ^2H divided by 1.041 and that of ^{18}O divided by 1.007. The mean ko/kd of the present study was 1.28 ± 0.06 (range, 1.15–1.56). All ko/kd values were maintained within the recommended range (1.1 to 1.7) for quality control of the analysis, as recommended by the International Atomic Energy Agency.[10] rCO_2 was calculated as follows: $rCO_2 = 0.4554 \times TBW \times (1.007ko - 1.041k_H)$. Calculation of TEE (kcal/day) was performed using a modified Weir's formula based on the CO_2 production rate (rCO_2) and food quotient (FQ).[9] FQ was calculated from the dietary survey during the study period. The calculation assumed that under conditions of perfect nutrient balance, the FQ must equal the respiratory quotient (RQ).[11–13] The average FQ of each occupational group was used for each group (FQ = 0.85–0.95). However, FQ values stratified by occupational group, sex, and age were not significantly different. Physical activity level (PAL) was calculated as TEE/RMR.

Physical activity questionnaire

The physical activity questionnaire developed for the Japan Arteriosclerosis Longitudinal Study (JALSPAQ) was used in this study.[6,7] This questionnaire comprises 14 questions on occupation, locomotion, housework, sleep time, and leisure-time physical activities. In this questionnaire, occupational work was assessed as duration of sitting, standing, walking, and heavy work. Heavy work was defined as lifting more than 10 kg or manual labor of similar intensity. Leisure-time physical activity was assessed by type, duration, and frequency. Questionnaire data were converted to the intensity of each physical activity expressed in metabolic equivalents (METs), according to the Compendium by Ainsworth et al, and summarized as METs·h/day and energy expenditure.[14] In the present study, we used TEE per day, METs·h/day, and PAL as indices of physical activity level from JALSPAQ. Duration of light (<3 METs), moderate (3–5.9 METs), and vigorous (≥6 METs) physical activities was calculated for all physical activities (including occupational activity, housework, and leisure-time physical activity), as well as for leisure-time physical activity only. Working time, including occupational and housework time, was divided into the duration of sitting (<2 METs), standing (2 to <3 METs), walking (3 to <6 METs), and heavy work (≥6 METs), including housework. We calculated the durations of occupational activity and housework together because their frequencies and durations were quite complicated.

Dietary assessment

Dietary habits were assessed by using a brief self-administered diet history questionnaire (BDHQ)—a 4-page structured questionnaire that requested information on the consumption frequencies for a total of 56 food and beverage items, with specified serving sizes described in terms of the servings commonly consumed in the general Japanese population.[15] Energy and macronutrient intakes were calculated using a computer algorithm for the BDHQ, which was based on the Standard Tables of Food Composition in Japan. FQ was calculated by using the equation of Black et al.[11]

Statistical analysis

Statistical analyses were performed using SPSS for Windows (version 16.0J; SPSS Inc., IL, USA). Physical characteristics are classified using the sex and age groups outlined in the Dietary Reference Intake (DRI) of Japan. The estimated energy expenditure data were generally not normally distributed; therefore, medians and interquartile ranges are used to describe these results. Sex and age-group differences were compared using 2-way analysis of covariance. The Bonferroni procedure was used as the post-hoc test. The relation between TEE as estimated by DLW and JALSPAQ was expressed as Spearman correlations, intraclass correlation coefficient (ICC), and 95% limits of agreement (95% LOA: mean difference $\pm 2 \times$ SD of the mean difference). Bland-Altman plots were also created to evaluate the differences between the 2 methods. To examine the type of physical activities that affected physical activity level, we used 1-way analysis of covariance, Pearson's correlation coefficients, and partial correlation coefficients adjusted for sex and age group.

RESULTS

The physical characteristics of the subjects are shown in Table 1. Body weight did not change significantly during the study period ($P = 0.313$). Among all subjects, 2.8% of men and 6.8% of women were classified as lean (body mass index [BMI] <18.5 kg/m^2), and 31.5% of men and 17.8% of women were classified as obese (BMI >25 kg/m^2) according to the criteria for Japanese.[16] The average TBW was 37.3 ± 7.1 kg in men and 25.9 ± 2.8 kg in women. When 73.2% was defined as the proportion of water in fat-free mass, the percent of fat mass was 24.3 ± 6.1% in men and 33.4 ± 7.0% in women.[17] Three men aged 30 to 49 years had a body weight higher than 100 kg; however, they were fit and their percent of fat mass was less than 25%. In addition, in the assessment of TEE by DLW and JALSPAQ, they did not significantly differ from other subjects.

The medians plus interquartiles for RMR, TEE, and PAL by DLW, TEE by questionnaire, and the differences between the 2 methods are shown by sex and age group in Table 2. The respective medians of TEE and PAL were 11.21 MJ/day and 1.88 for men and 8.42 MJ/day and 1.83 for women. PAL significantly differed by age group, but not by sex. PAL in subjects older than 70 years was significantly higher than in those aged 30 to 49 years ($P = 0.016$) and 50 to 69 years

Table 1. Characteristics of study subjects

Age group, years	n	Age (years)	Height (cm)	Body weight pre (kg)	Body weight post (kg)	Body weight change (kg)	BMI (kg/m²)	TBW (kg)
Male								
20–29	18	25.0 ± 2.5	171.5 ± 6.0	62.1 ± 7.9	62.3 ± 8.0	0.2 ± 0.7	21.1 ± 2.0	36.4 ± 3.7
30–49	42	36.7 ± 5.3	173.8 ± 6.6	74.8 ± 16.7	74.9 ± 16.6	0.0 ± 1.1	24.6 ± 4.7	41.8 ± 8.3
50–69	31	60.2 ± 6.5	163.8 ± 6.6	63.9 ± 8.1	64.0 ± 8.3	0.1 ± 0.9	23.8 ± 2.4	34.5 ± 4.1
≥70	17	75.1 ± 4.0	162.1 ± 5.0	60.7 ± 8.1	60.8 ± 8.2	0.2 ± 0.9	23.1 ± 2.7	32.0 ± 4.2
Female								
20–29	8	25.3 ± 2.4	157.0 ± 3.9	51.3 ± 2.5	51.2 ± 2.5	−0.1 ± 0.8	20.9 ± 1.6	25.5 ± 1.5
30–49	42	38.7 ± 4.4	158.0 ± 5.4	53.7 ± 8.3	53.7 ± 8.3	0.0 ± 0.7	21.5 ± 3.2	26.9 ± 3.1
50–69	49	62.0 ± 5.1	154.0 ± 4.6	54.6 ± 7.8	54.7 ± 7.9	0.1 ± 0.7	23.0 ± 3.2	25.8 ± 2.7
≥70	19	73.4 ± 3.9	148.0 ± 4.4	50.2 ± 6.1	50.1 ± 6.1	0.1 ± 0.6	22.9 ± 2.8	24.1 ± 2.0

All values are mean ± SD, unless otherwise indicated.
BMI: body mass index; TBW: total body water measured by doubly labeled water method.

Table 2. Resting metabolic rate (RMR) and total energy expenditure (TEE) measured by doubly labeled water (DLW) method and questionnaire

Age group, years		RMR (MJ/day)	TEE by DLW (MJ/day)	PAL	TEE by JALSPAQ (MJ/day)	Difference between DLW and JALSPAQ (MJ/day)	Difference between DLW and JALSPAQ (%)
Male							
	20–29	6.27 (0.92)	12.00 (0.19)	1.89 (0.35)	9.60 (2.12)	−1.69 (2.89)	−15.7 (23.0)
	30–49	6.72 (1.53)	12.88 (4.64)	1.87 (0.45)	11.14 (2.85)	−1.18 (3.30)	−9.5 (20.3)
	50–69	5.50 (1.30)	10.81 (2.11)	2.08 (0.55)	9.18 (1.61)	−2.02 (1.99)	−18.1 (17.5)
	≥70	5.76 (1.41)	11.76 (3.59)	2.11 (0.52)	8.03 (1.65)	−0.97 (2.34)	−12.2 (21.0)
Female							
	20–29	4.73 (0.27)	8.10 (1.18)	1.86 (0.22)	7.43 (1.01)	−1.09 (1.85)	−13.2 (22.3)
	30–49	4.83 (0.82)	8.82 (1.80)	1.84 (0.32)	7.33 (1.75)	−1.26 (1.73)	−14.9 (19.1)
	50–69	4.58 (0.95)	8.53 (1.42)	1.86 (0.37)	8.12 (1.28)	−0.43 (1.76)	−5.3 (20.4)
	≥70	4.62 (0.99)	8.56 (0.86)	1.86 (0.41)	7.08 (1.33)	−0.36 (1.68)	−5.2 (23.3)
P value	Sex	<0.001	<0.001	0.067	<0.001	0.003	0.071
	Age group	<0.001	<0.001	<0.001	<0.001	0.335	0.370
	Sex by age	0.010	0.004	0.481	<0.001	0.591	0.188

All values are median (interquartile), unless otherwise indicated.
PAL: physical activity level (TEE/RMR); JALSPAQ: Japan Arteriosclerosis Longitudinal Study Physical Activity Questionnaire.

($P < 0.001$). JALSPAQ slightly underestimated TEE, with differences in mean and standard error of the mean of −1.15 ± 1.92 MJ/day and −0.020 ± 0.030 MJ/kg/day. TEE values by JALSPAQ and DLW were moderately correlated (Spearman correlation = 0.742, $P < 0.001$; ICC = 0.648, $P < 0.001$). The 95% LOA was −4.99 to 2.69 MJ. The absolute difference between TEE values by DLW and JALSPAQ was significantly greater in men than in women, but the percent difference was not significantly different. The Spearman correlation coefficient and ICC for PAL were 0.423 ($P < 0.001$) and 0.332 ($P < 0.001$), respectively, and the 95% LOA for PAL was −0.86 to 0.46. Use of Bland-Altman plots to compare TEE and PAL by DLW and JALSPAQ suggested that TEE tended to be underestimated in subjects with higher TEE (Spearman correlation, −0.201; $P = 0.002$); however, most values were within the 2 SD of the difference in TEE as determined by the 2 methods (Figure). PAL was not underestimated even in subjects with higher PALs (Spearman correlation, −0.011; $P = 0.866$); however, individual differences were widely distributed.

Using PAL determined using TEE measured by DLW, the subjects were divided into 3 groups according to Dietary Reference Intake (Table 3).[18] The proportions of active (PAL >1.9), moderately active (PAL 1.6 to <1.9), and sedentary (PAL <1.6) individuals were 45.4%, 43.5%, and 11.1% in men, respectively, and 40.7%, 41.5%, and 17.8% in women. TEE by JALSPAQ in the sedentary group was significantly lower than in moderately active and active adults. Total METs assessed by JALSPAQ was lower in sedentary and moderately active individuals than in active individuals. The differences between the 2 methods in the TEE of sedentary and moderately active adults were significantly smaller than in active adults. The total duration of each intensity of physical activity, including occupational and housework activity and leisure-time physical activity, was compared among physical activity levels. The duration of moderate and vigorous

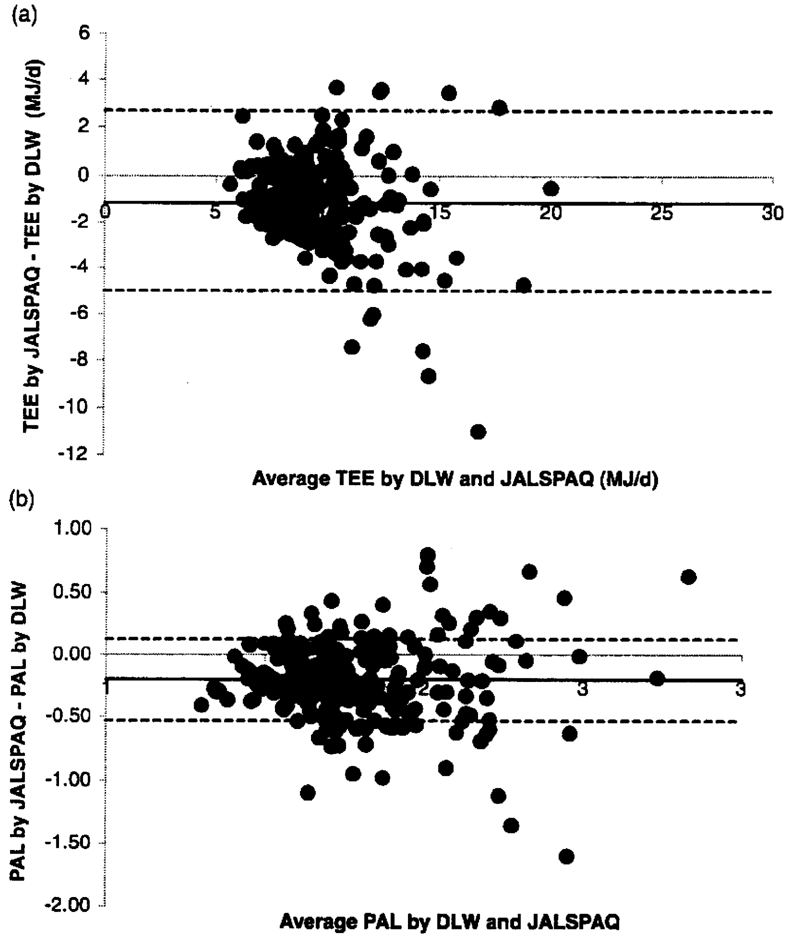

Figure. Bland-Altman plots of total energy expenditure (TEE) and physical activity level (PAL). (a) Comparison of mean TEE estimated by the doubly labeled water (DLW) method and the Japan Arteriosclerosis Longitudinal Study Physical Activity Questionnaire (JALSPAQ), and the difference in TEE as estimated by the 2 methods. (b) Comparison of mean PAL by DLW and JALSPAQ, and the difference in PAL as estimated by the 2 methods. Solid lines indicate the mean difference, and the broken lines indicate 2 SD limits.

physical activity in sedentary and moderately active adults was significantly shorter than in active adults. When we compared only leisure-time physical activity, there was no difference in duration of physical activity. Regarding physical activity during work, duration of walking was significantly shorter in sedentary individuals than in moderately active and active individuals. In addition, walking duration was significantly shorter in moderately active adults than in active adults. The proportion of heavy work differed significantly among groups; greater activity was associated with heavier work.

Regarding the types of physical activity that were correlated with PAL, correlation coefficients and partial correlation coefficients adjusted for sex and age group are shown in Table 4. Duration of total, moderate, and vigorous physical activity were weakly correlated with PAL. However, duration of leisure-time physical activity was not correlated with PAL. During working time, duration of standing, walking, and heavy work were weakly correlated with PAL.

DISCUSSION

This study used the DLW method as a gold standard to examine the validity of a physical activity questionnaire designed for the Japanese population in a large number of subjects with widely varying physical activity levels. With the DLW method as the gold standard, JALSPAQ estimated TEE relatively well, but underestimation was more frequent at higher physical activity levels.

The body height and weight of the present subjects were similar to the standard values for the Japanese population.[18] RMR was also similar to the standard RMR values for the Japanese population presented in Dietary Reference Intake.[18] Thus, we conclude that the present subjects had the general physical characteristics of the Japanese general population. However, the physical activity level of the present subjects was higher than that noted in our previous studies: 42.9% of the present subjects were classified as active, using the definition in the Dietary Reference Intake.[18] We recruited

Table 3. Total energy expenditure (TEE) and duration of each activity among groups by physical activity level

	Physical activity level			P
	I Sedentary	II Moderately active	III Active	
TEE by DLW (MJ/day)	8.11 (1.39)[a,b]	9.18 (2.29)[b]	10.76 (4.25)	<0.001
TEE by questionnaire (MJ/day)	7.78 (1.21)[b,c]	8.45 (2.87)	8.90 (3.06)	0.006
Total METs (METs·h/day)	33.5 (4.1)[b]	34.4 (4.8)[b]	35.8 (6.4)	<0.001
Difference in TEE between DLW and PAQ (MJ/day)	−0.07 (0.50)[b]	−0.80 (1.62)[b]	−2.02 (2.23)	<0.001
Difference in TEE between DLW and PAQ (%)	−0.9 (15.3)[b]	−8.4 (17.6)[b]	−19.1 (19.0)	<0.001
Total duration of physical activity (h/day)				
Light (<3 METs)	3.41 (3.58)	4.14 (3.50)	4.16 (3.72)	0.155
Moderate (3–5.9 METs)	1.65 (1.81)[b]	2.06 (2.07)[b]	2.53 (3.89)	<0.001
Vigorous (≥6 METs)	0.00 (0.09)[b]	0.00 (0.20)[a]	0.0 (0.54)	0.007
Duration of leisure-time physical activity (h/day)				
Light (<3 METs)	0.00 (0.26)	0.00 (0.07)	0.00 (0.09)	0.766
Moderate (3–5.9 METs)	0.01 (0.17)	0.02 (0.23)	0.03 (0.27)	0.965
Vigorous (≥6 METs)	0.00 (0.08)	0.00 (0.02)	0.00 (0.00)	0.556
Duration of work (h/day)				
Sitting	0.00 (2.86)	1.55 (4.61)	0.00 (4.29)	0.129
Standing	1.75 (2.20)	1.42 (2.14)	2.00 (2.85)	0.176
Walking	0.25 (0.86)[b,c]	0.54 (1.90)[b]	1.00 (3.07)	<0.001
Proportion of subjects participating in heavy work (%)	6.1	24	36.1	0.003

TEE: total energy expenditure; DLW: doubly labeled water; MET: metabolic equivalent; PAQ: physical activity questionnaire.
All values are median (interquartile), unless otherwise indicated.
[a]$P < 0.05$ as compared with physical activity level III.
[b]$P < 0.01$ as compared with physical activity level III.
[c]$P < 0.01$ as compared with physical activity level II.

Table 4. Correlation coefficients for physical activity level (as measured by doubly labeled water method) and duration of physical activities

	Correlation coefficient	P value	Partial correlation coefficient	P value
Total duration of physical activity (h/day)				
Light (<3 METs)	0.034	0.608	0.022	0.746
Moderate (3–5.9 METs)	0.257	<0.001	0.225	0.001
Vigorous (≥6 METs)	0.354	0.481	0.330	<0.001
Duration of leisure-time physical activity (h/day)				
Light (<3 METs)	−0.018	0.790	0.008	0.910
Moderate (3–5.9 METs)	0.002	0.978	0.000	0.996
Vigorous (≥6 METs)	−0.048	0.474	−0.072	0.286
Duration of work (h/day)				
Sitting	−0.064	0.337	−0.133	0.047
Standing	0.165	0.013	0.256	<0.001
Walking	0.271	<0.001	0.239	<0.001
Heavy	0.376	<0.001	0.354	<0.001

MET: metabolic equivalent; TEE: total energy expenditure.
Partial correlation coefficients are adjusted for sex and age group.

subjects at worksites requiring vigorous physical activity (ie, shipbuilding and hospitals). This may explain the higher physical activity level of the subjects.

Neilson et al reviewed a validation study of a physical activity questionnaire and suggested that, at the group level, the mean difference in TEE ranged from −800 to 1589 kcal/day (−3.35 to 6.65 MJ/day) and that the Spearman correlation coefficient for TEE ranged from 0.15 to 0.51.[2] As compared with these results, JALSPAQ showed a smaller negative mean difference of −1.15 MJ/day and a higher correlation (Spearman correlation, 0.742; $P < 0.001$). A comparison of individual-level agreement indicates that the width of the 95% LOA in our study (7.68 MJ/day) was smaller than that in most other questionnaires described in the review of Neilson and colleagues (1133 to 17 948 kcal/day; 4.74 to 75.09 MJ/day).[2] The relatively good agreement in this study partly resulted from the greater number of subjects ($n = 226$ in the present study vs $n = 13$ to $n = 65$ in previous studies) and the wide variation in TEE. Standard deviation was 2.77 MJ in the present study and 0.35 to 3.51 MJ in previous studies. A study by Racette showed the lowest 95% LOA (−2.42 to 0.16 MJ/day).[19] However, that study was part of an investigation of a 17-week outpatient weight loss treatment, so the subjects were thought to be highly motivated and to have answered the questionnaire carefully. One reason why TEE is assumed to have greater accuracy than the existing questionnaire is that it is believed to have more detailed questions regarding occupational activity, housework, and leisure-time physical activity.

JALSPAQ tended to greatly underestimate TEE in more active subjects, possibly because the algorithm for the calculation of TEE for JALSPAQ only includes duration of time spent sitting, standing, and walking. These activities were scored on a scale from 1.5 to 4.0 METs. Even when there was a question regarding carrying heavy objects or engaging in activity of similar intensity, such activity was not used to calculate TEE. Thus, underestimation would be greater in subjects who expended considerable energy at work. In the present study, 16 subjects were engaged in shipbuilding, and the differences between TEE by DLW and JALSPAQ ranged from −10.98 to 0.34 MJ/day; TEE was overestimated by JALSPAQ in only 2 subjects.

Although TEE estimated by JALSPAQ showed a relatively good correlation with TEE by DLW, RMR accounted for a large part of TEE. To lessen the contribution of RMR, PAL was compared between the two methods. The results for PAL were poor, and individual differences were widely distributed. Therefore, JALSPAQ must either be improved or another new questionnaire should be developed to assess individual PAL.

We also attempted to identify a physical activity that characterized physical activity level. Our results showed that total time spent in moderate physical activity was significantly greater in the active group. In addition, moderate and vigorous physical activity had a weak but significant correlation with PAL. Thus, moderate physical activity is an important component of physical activity level, as Westerterp has suggested.[20] However, the duration of moderate physical activity did not differ in the sedentary and moderate groups. Wareham et al used a very brief questionnaire that only included physical activity during work and recreational activities and found that physical activity ratio (daytime energy expenditure/resting metabolic rate), which was estimated using a heart rate monitor, did not differ between inactive and moderately inactive groups, even though VO_{2max} was different between these groups.[21] Another method of classifying physical activity in sedentary subjects should thus be considered.

The present results also suggest that intensity and duration of physical activity during work (including occupational activity and housework) strongly affect PAL, whereas leisure-time physical activity does not. Both work and leisure-time physical activity play fundamental roles in total physical activity, which explains why previous brief physical activity questionnaires assessed only physical activity during work and leisure time.[21,22] In the present study, because the mean duration of all leisure-time physical activity was 22 ± 21 minutes per day, the effect of leisure-time physical activity on TEE might be very small.

The most significant limitation of this study was that subjects were not selected randomly: they joined the study as volunteers. Hence, as compared with the general population, they might have remembered their physical activities better and completed the questionnaire more carefully. In addition, the variation in their physical activity level might differ from that of the general Japanese population. However, we were unable not determine the nature or extent of error that resulted from these subject characteristics. A second limitation is that the study periods for DLW and JALSPAQ were not identical. The DLW method determined the average TEE over 1 or 2 weeks. In contrast, JALSPAQ assessed typical physical activity over 1 month. This discrepancy could affect the validation of JALSPAQ. Finally, the relatively small proportion of sedentary subjects made it difficult to characterize the sedentary population. Although we tried to collect subjects with a broad range of physical activities, we could not collect comparable numbers of sedentary and active subjects.

In conclusion, PAL by JALSPAQ weakly correlated with PAL by DLW, although TEE by JALSPAQ was better correlated with TEE by DLW than with TEE assessed by the questionnaires used in previous studies. TEE underestimation was greater in active subjects than in sedentary and moderately active subjects. In addition, in this population, total moderate physical activity and physical activity during work were related to physical activity level, whereas leisure-time physical activity was not. To improve the physical activity questionnaire, an algorithm for heavy work should be added. In addition, to better differentiate sedentary subjects form moderate subjects, additional questionnaire items should be added or the algorithm should be reevaluated.

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Original Contributions

Impact of Glucose Tolerance Status on Development of Ischemic Stroke and Coronary Heart Disease in a General Japanese Population

The Hisayama Study

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Background and Purpose—Few studies have shown the association between glucose tolerance status defined by a 75-g oral glucose tolerance test and the development of different types of cardiovascular disease.

Methods—A total of 2421 community-dwelling Japanese subjects aged 40 to 79 years who underwent the oral glucose tolerance test were followed up for 14 years.

Results—In multivariable analysis, the risks of ischemic stroke in both sexes and coronary heart disease (CHD) in women were significantly higher in subjects with diabetes determined by the World Health Organization criteria than in those with normal glucose tolerance even after adjustment for other confounding factors, but such association was not seen for CHD in men (ischemic stroke: adjusted hazard ratio [HR]=2.54, $P=0.002$ in men; adjusted HR=2.02, $P=0.03$ in women; CHD: adjusted HR=1.26, $P=0.47$ in men; adjusted HR=3.46, $P=0.002$ in women). Similar associations were observed for fasting plasma glucose levels of ≥7.0 mmol/L (ischemic stroke: adjusted HR=2.15, $P=0.03$ in men; adjusted HR=2.10, $P=0.045$ in women; CHD: adjusted HR=1.29, $P=0.47$ in men; adjusted HR=3.83, $P=0.003$ in women) and for 2-hour postload glucose levels of ≥11.1 mmol/L (ischemic stroke: adjusted HR=2.71, $P=0.003$ in men; adjusted HR=2.19, $P=0.03$ in women; CHD: adjusted HR=1.58, $P=0.16$ in men; adjusted HR=4.44, $P<0.001$ in women). The age-adjusted incidences of ischemic stroke and CHD did not significantly increase in subjects with impaired fasting glycemia or impaired glucose tolerance in either sex.

Conclusions—Our findings suggest that diabetes is an independent risk factor for ischemic stroke in both sexes and CHD in women in the Japanese population. (***Stroke*. 2010;41:203-209.**)

Key Words: coronary heart disease ■ diabetes ■ ischemic stroke ■ oral glucose tolerance test ■ prospective study

Cardiovascular disease continues to be a major global public health concern. Investigations into glucose tolerance levels and cardiovascular disease have become increasingly important, because the impact of diabetes on cardiovascular disease is considered to be rising due to the rapid increase in the worldwide prevalence of diabetes mellitus in recent years. A number of epidemiological studies have demonstrated that Type 2 diabetic subjects have approximately 2.0 to 4.0 times higher risk of cardiovascular disease compared with nondiabetic subjects.[1–13] However, most of these studies had important limitations. In many cohort studies used to investigate this issue, the outcomes were evaluated using mortality data.[3–9,11,12] Because nonfatal events were not included in these studies, the results may not have represented the true association between glucose tolerance levels and cardiovascular disease. Thus, prospective studies using incidence data would provide further information for predicting cardiovascular disease. In addition, the methods used to define diabetes have varied among the epidemiological studies, ranging from administration of questionnaires to measurement of casual blood glucose levels or fasting plasma glucose (FPG) alone.[1,2,11,12] Furthermore, many investigators have evaluated cardiovascular generally, rather than by type, and did not separately evaluate sex, although it is well known that the effects of each risk factor are different for each type of cardiovascular disease and sex. Thus, there have been few cohort studies investigating the associations between glucose tolerance levels, defined by a 75-g glucose tolerance test (OGTT), and the risks of developing stroke and coronary heart disease (CHD) in each sex in Asian populations.

The purpose of the present study was to address the association between glucose tolerance levels and the devel-

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opment of ischemic stroke and CHD in a prospective study of a defined community-dwelling Japanese population, all members of which underwent the OGTT.

Materials and Methods

Study Population

In 1988, a screening survey for the present study was performed in the town of Hisayama, a suburb of the Fukuoka metropolitan area in southern Japan.[14] Of a total 3227 residents aged 40 to 79 years on the town registry, 2587 (participation rate, 80.2%) consented to participate in the examination and underwent a comprehensive assessment. After excluding 82 subjects who had already had breakfast, 10 who were on insulin therapy and 15 due to nausea or general fatigue during the ingestion of glucose, a total of 2480 subjects completed the OGTT. From a total of 2490 subjects including 10 on insulin therapy, 68 who had a history of stroke or CHD based on questionnaires and medical records, and one who died before follow-up was started, were excluded. The remaining 2421 (1037 men and 1384 women) were enrolled in this study.

Follow-Up Survey

The subjects were followed up prospectively for 14 years, from December 1988 to November 2002, by repeated health examinations. The health status was checked yearly by mail or telephone for subjects who did not undergo a regular examination or who had moved from town. We also established a daily monitoring system among the study team, local physicians, and members of the town's health and welfare office. Using this system, we gathered information on new events of cardiovascular disease, including suspected cases. When stroke or CHD occurred or was suspected, physicians in the study team examined the subject and evaluated his or her detailed clinical information. The clinical diagnosis of stroke or CHD was based on the patient's history, physical and neurological examinations, and ancillary laboratory examinations. Additionally, when a subject died, an autopsy was performed at the Departments of Pathology of Kyushu University. During the follow-up period, one subject was lost to follow-up and 418 subjects died, of whom 312 (74.6%) underwent autopsy.

Definition of Cardiovascular Events

In principle, stroke was defined as a sudden onset of nonconvulsive and focal neurological deficit persisting for ≥24 hours. The diagnosis and classification of stroke were determined on the basis of clinical information, including brain CT and MRI, cerebral angiography, echocardiography, carotid duplex imaging, or autopsy findings. Ischemic stroke was classified as either lacunar or nonlacunar infarction based on the Classification of Cerebrovascular Disease III criteria proposed by the National Institute of Neurological Disorders and Stroke.[15] In brief, lacunar infarction was diagnosed as the presence of a relevant brain stem, basal ganglia, or subcortical hemispheric lesion with a diameter <1.5 cm demonstrated on brain imaging and no evidence of cerebral cortical or cerebellar impairment. Patients who had typical clinical findings of lacunar infarction and a negative imaging were also categorized as cases of lacunar infarction. The other ischemic strokes were defined as cases of nonlacunar infarction.

CHD included acute myocardial infarction, silent myocardial infarction, sudden cardiac death within 1 hour after the onset of acute illness, and coronary artery disease treated by coronary artery bypass surgery or angioplasty. Acute myocardial infarction was diagnosed when a subject met at least 2 of the following criteria: (1) typical symptoms, including prolonged severe anterior chest pain; (2) evolving diagnostic electrocardiographic changes; (3) cardiac enzyme levels more than twice the upper limit of normal range; and (4) morphological changes, including local asynergy of cardiac wall motion on echocardiography, persistent perfusion defect on cardiac scintigraphy, or myocardial necrosis or scars ≥1 cm long accompanied by coronary atherosclerosis at autopsy. Silent myocardial infarction was defined as myocardial scarring without any historical indication of clinical symptoms or abnormal cardiac enzyme changes.

During the follow-up, we identified 132 cases of ischemic stroke (for men, 61 total, or 27 lacunar and 34 nonlacunar infarctions; for women, 71 total, or 42 lacunar and 29 nonlacunar infarctions) and 112 CHD events (75 men and 37 women). All of the ischemic stroke cases underwent brain imaging.

Risk Factors

At the baseline examination, we performed the OGTT after at least a 12-hour overnight fast. Plasma glucose levels were determined by the glucose-oxidase method. FPG and 2-hour postload glucose (PG) levels were divided into 4 categories: for FPG: <5.6, 5.6 to 6.0, 6.1 to 6.9, and ≥7.0 mmol/L; for 2-hour PG: <6.7, 6.7 to 7.7, 7.8 to 11.0, and ≥11.1 mmol/L. Glucose tolerance status was also defined by the 1998 World Health Organization criteria[16]; namely, for normal glucose tolerance (NGT), FPG <6.1 and 2-hour PG <7.8; for hyperglycemia, FPG ≥6.1 and/or 2-hour PG ≥7.8; for impaired fasting glycemia (IFG), FPG 6.1 to 6.9 and 2-hour PG <7.8; for impaired glucose tolerance (IGT), FPG <7.0 and 2-hour PG 7.8 to 11.0; and for diabetes mellitus, FPG ≥7.0 mmol/L and/or 2-hour PG ≥11.1 mmol/L. Total and high-density lipoprotein cholesterol levels were determined enzymatically.

Blood pressure was measured 3 times using a sphygmomanometer after at least 5 minutes of rest; the average of 3 measurements was used for the analysis. Hypertension was defined as blood pressure levels of ≥140/90 mm Hg or current treatment with antihypertensive agents. Body mass index (kg/m^2) was used as an indicator of obesity. Electrocardiographic abnormalities were defined as left ventricular hypertrophy (Minnesota Code 3 to 1) or ST depression (4 to 1, 4 to 2, or 4 to 3). Each participant completed a self-administered questionnaire covering medical history, antidiabetic and antihypertensive treatments, smoking habits, alcohol intake, and leisure time activity. Smoking habits and alcohol intake were classified as either current use or not. Those subjects engaging in sports or other forms of exertion ≥3 times a week during their leisure time made up a regular exercise group.

Statistical Analysis

The SAS software package Version 9.2 (SAS Institute Inc, Cary, NC) was used to perform all statistical analyses. Incidence was calculated by a person-year method and was adjusted for age by the direct method using 10-year age groupings. The age- and multivariable-adjusted hazard ratios (HRs) and their 95% CIs were estimated using the Cox proportional hazards model.

Ethical Considerations

This study was conducted with the approval of the Ethics Committee of Kyushu University, and written informed consent was obtained from the participants.

Results

The baseline characteristics of the subjects are summarized by sex in Table 1. Mean values of age and body mass index did not differ between the sexes. The means of FPG, 2-hour PG, and systolic and diastolic blood pressures and frequencies of diabetes, hypertension, electrocardiographic abnormalities, smoking habits, alcohol intake, and regular exercise were higher in men than in women, whereas women had higher concentrations of total and high-density lipoprotein cholesterol.

The age-adjusted incidences and age-adjusted and multivariable-adjusted HRs of ischemic stroke and CHD according to FPG levels are shown in Table 2. The age-adjusted incidences of ischemic stroke and CHD did not differ between subjects with FPG levels of <5.6 mmol/L and those with FPG levels of 5.6 to 6.0 mmol/L in either sex. In women, the age-

Table 1. Characteristics of Subjects by Sex, 1988

	Men (n=1037)	Women (n=1384)
Age, years	57 (10)	58 (10)
Fasting plasma glucose, mmol/L	5.9 (1.3)	5.7 (1.3)
2-hour PG, mmol/L	7.7 (4.0)	7.4 (3.3)
Diabetes, %	15.1	9.7
Systolic blood pressure, mm Hg	134 (20)	131 (20)
Diastolic blood pressure, mm Hg	81 (11)	76 (11)
Hypertension, %*	43.3	34.8
Electrocardiographic abnormalities, %†	19.6	12.6
Body mass index, kg/m^2	22.9 (2.9)	23.0 (3.2)
Total cholesterol, mmol/L	5.07 (1.07)	5.51 (1.05)
High density lipoprotein cholesterol, mmol/L	1.25 (0.31)	1.33 (0.29)
Current smoking, %	50.1	6.7
Current alcohol use, %	62.2	9.0
Regular exercise, %	11.2	9.0

All values are given as the mean (SD) or as a percent.
*Blood pressure ≥140/90 mm Hg or current use of antihypertensive agents.
†Minnesota Codes 3–1, 4–1, 4–2, or 4–3.

adjusted incidence and HR of ischemic stroke were significantly higher in subjects with FPG levels of 6.1 to 6.9 mmol/L than in those with the FPG levels of <5.6 mmol/L; however, this association was attenuated after adjustment for the following confounding factors: age, systolic blood pressure, electrocardiographic abnormalities, body mass index, total and high-density lipoprotein cholesterol, smoking habits, alcohol intake, and regular exercise. An FPG level of ≥7.0 mmol/L was a significant risk factor for ischemic stroke in both sexes and for CHD in women, even after adjustment for the previously mentioned confounding factors (ischemic stroke: multivariable-adjusted HR=2.15, 95% CI, 1.07 to 4.31, P=0.03 in men; multivariable-adjusted HR=2.10, 95% CI, 1.02 to 4.35, P=0.045 in women; CHD: multivariable-adjusted HR=3.83, 95% CI, 1.59 to 9.25, P=0.003 in women).

Table 3 presents data of the analyses for ischemic stroke and CHD according to 2-hour PG levels. Compared with subjects with 2-hour PG levels of <6.7 mmol/L, the age-adjusted incidences and multivariable-adjusted HRs of ischemic stroke in both sexes and CHD in women were significantly higher in those with glucose levels of ≥11.1 mmol/L (ischemic stroke: multivariable-adjusted HR=2.71, 95% CI, 1.41 to 5.20, P=0.003 in men; multivariable-adjusted HR=2.19, 95% CI, 1.07 to 4.48, P=0.03 in women; CHD: multivariable-adjusted HR=4.44, 95% CI, 1.85 to 10.6, P<0.001 in women). Subjects with a prediabetic range of 2-hour PG levels did not have an increased risk of either ischemic stroke or CHD.

Finally, the relationships between glucose tolerance levels defined by the World Health Organization criteria and the risks of ischemic stroke and CHD are displayed in Table 4. Compared with those in women with NGT, the age-adjusted incidences and HRs of ischemic stroke and CHD were significantly increased in women with hyperglycemia, but these associations disappeared after adjustment for other confounding factors. In regard to subtypes of hyperglycemia, the age-adjusted incidences and HRs of ischemic stroke and CHD did not significantly increase in those with IFG or IGT

Table 2. Age-Adjusted Incidence and Age- and Multivariable-Adjusted HRs and Their 95% CIs for the Development of Cardiovascular Diseases According to FPG Levels

	FPG Level, mmol/L	Person-Years	No. of Events	Age-Adjusted Incidence per 1000 Person-Years	Age-Adjusted HR (95% CI)	P	Multivariable-Adjusted HR (95% CI)	P
Ischemic stroke								
Men	<5.6	5391	26	5.4	1 (referent)		1 (referent)	
	5.6 to 6.0	3791	13	4.0	0.70 (0.36 to 1.36)	0.29	0.66 (0.33 to 1.29)	0.22
	6.1 to 6.9	1909	9	4.7	0.85 (0.40 to 1.82)	0.68	0.68 (0.30 to 1.54)	0.36
	≥7.0	1170	13	11.7	2.06 (1.06 to 4.00)	0.03	2.15 (1.07 to 4.31)	0.03
Women	<5.6	9707	28	3.4	1 (referent)		1 (referent)	
	5.6 to 6.0	4821	18	3.9	1.11 (0.61 to 2.00)	0.74	0.98 (0.54 to 1.79)	0.95
	6.1 to 6.9	1733	14	7.1	2.01 (1.05 to 3.84)	0.03	1.59 (0.80 to 3.13)	0.18
	≥7.0	1107	11	9.6	2.47 (1.22 to 4.97)	0.01	2.10 (1.02 to 4.35)	0.045
CHD								
Men	<5.6	5450	33	7.0	1 (referent)		1 (referent)	
	5.6 to 6.0	3808	16	4.7	0.68 (0.38 to 1.24)	0.21	0.67 (0.37 to 1.23)	0.20
	6.1 to 6.9	1942	14	7.3	1.01 (0.54 to 1.90)	0.97	0.80 (0.42 to 1.54)	0.50
	≥7.0	1195	12	9.9	1.50 (0.77 to 2.90)	0.23	1.29 (0.65 to 2.58)	0.47
Women	<5.6	9844	12	1.4	1 (referent)		1 (referent)	
	5.6 to 6.0	4893	9	1.8	1.31 (0.55 to 3.10)	0.55	1.13 (0.47 to 2.71)	0.78
	6.1 to 6.9	1815	6	2.5	1.99 (0.74 to 5.36)	0.17	1.36 (0.49 to 3.81)	0.56
	≥7.0	1138	10	7.0	5.30 (2.28 to 12.35)	<0.001	3.83 (1.59 to 9.25)	0.003

Multivariable adjustment was made for age, systolic blood pressure, electrocardiogram abnormalities, body mass index, total and high-density lipoprotein cholesterol, smoking habits, alcohol intake, and regular exercise.

Table 3. Age-Adjusted Incidence and Age- and Multivariable-Adjusted HRs and Their 95% CIs for the Development of Cardiovascular Diseases According to 2-Hour PG Levels

	Two-Hour PG Levels, mmol/L	Person-Years	No. of Events	Age-Adjusted Incidence per 1000 Person-Years	Age-Adjusted HR (95% CI)	P	Multivariable-Adjusted HR (95% CI)	P
Ischemic stroke								
Men	<6.7	6253	25	4.4	1 (referent)		1 (referent)	
	6.7 to 7.7	2246	7	3.5	0.81 (0.35 to 1.87)	0.61	0.84 (0.36 to 1.96)	0.68
	7.8 to 11.0	2363	13	5.5	1.22 (0.62 to 2.38)	0.57	1.05 (0.52 to 2.13)	0.89
	≥11.1	1399	16	10.9	2.66 (1.42 to 4.98)	0.002	2.71 (1.41 to 5.20)	0.003
Women	<6.7	8728	25	3.3	1 (referent)		1 (referent)	
	6.7 to 7.7	3982	17	5.3	1.51 (0.82 to 2.80)	0.19	1.29 (0.69 to 2.44)	0.43
	7.8 to 11.0	3374	15	3.8	1.18 (0.62 to 2.24)	0.62	0.99 (0.51 to 1.92)	0.96
	≥11.1	1284	14	10.3	2.80 (1.45 to 5.40)	0.002	2.19 (1.07 to 4.48)	0.03
CHD								
Men	<6.7	6239	33	6.0	1 (referent)		1 (referent)	
	6.7 to 7.7	2277	9	4.7	0.78 (0.37 to 1.63)	0.50	0.73 (0.34 to 1.55)	0.41
	7.8 to 11.0	2430	18	7.3	1.20 (0.67 to 2.13)	0.54	0.97 (0.53 to 1.77)	0.93
	≥11.1	1449	15	11.5	1.82 (0.99 to 3.34)	0.06	1.58 (0.83 to 3.00)	0.16
Women	<6.7	8858	11	1.4	1 (referent)		1 (referent)	
	6.7 to 7.7	4079	6	1.4	1.16 (0.43 to 3.15)	0.77	0.91 (0.33 to 2.52)	0.86
	7.8 to 11.0	3430	6	1.5	1.10 (0.40 to 2.97)	0.86	0.82 (0.29 to 2.29)	0.70
	≥11.1	1323	14	8.5	6.49 (2.93 to 14.36)	<0.001	4.44 (1.85 to 10.62)	<0.001

Multivariable adjustment was made for age, systolic blood pressure, electrocardiogram abnormalities, body mass index, total and high-density lipoprotein cholesterol, smoking habits, alcohol intake, and regular exercise.

in either sex. Diabetes was a significant risk factor for ischemic stroke in both sexes and for CHD in women. These significant associations also remained robust even after adjustment for the previously mentioned confounding factors (ischemic stroke: multivariable-adjusted HR=2.54, 95% CI, 1.40 to 4.63, P=0.002 in men; multivariable-adjusted HR=2.02, 95% CI, 1.07 to 3.81, P=0.03 in women; CHD: multivariable-adjusted HR=3.46, 95% CI, 1.59 to 7.54, P=0.002 in women). When ischemic stroke was classified as either lacunar or nonlacunar infarction, diabetes was an independent risk factor for lacunar infarction in women (multivariable-adjusted HR=2.65, 95% CI, 1.19 to 5.93, P=0.02) and nonlacunar infarction in men (HR=3.78, 95% CI, 1.74 to 8.19, P=0.001) after adjustment for other confounding factors (Table 5).

Discussion

Using data from a 14-year follow-up study of a defined general Japanese population, we demonstrated that diabetes defined by the OGTT is an independent risk factor for the development of ischemic stroke in both sexes and CHD in women after adjustment for other confounding factors. Furthermore, we found that diabetes significantly increased the risk of lacunar infarction in women and nonlacunar infarction in men. By contrast, an FPG level of 5.6 to 6.0 mmol/L, a newly extended range from the American Diabetes Association, was not associated with ischemic stroke or CHD in either sex. In women with the FPG levels of 6.1 to 6.9 mmol/L, the age-adjusted incidence of ischemic stroke increased significantly; however, this association was attenuated after multivariable adjustment.

Very few prospective studies have provided evidence of the associations between glucose tolerance levels defined by the OGTT and the incidence of stroke and CHD. Only investigators of the Strong Heart Study of American Indians have evaluated the association of glucose tolerance status defined by the 1998 World Health Organization criteria with the risk of developing stroke. The results showed that, compared with the subjects with NGT, subjects with diabetes had a 2-fold higher risk of stroke, but subjects with IFG or IGT did not have a higher risk.[13] In a follow-up examination of a Finnish population who was free of diabetes at baseline, diabetes that developed during the follow-up was a significant risk factor for CHD, but baseline IGT was not.[17] These findings are in accordance with those of the present study. In our study, diabetes was significantly associated with the development of ischemic stroke in both sexes as well as CHD in women, but such an association was not observed for CHD in men. Although the precise reasons for this sex difference in the CHD risk conferred by diabetes are unknown, the higher prevalence of smoking in men may be responsible for this phenomenon; a smoking habit, which is a major risk factor for CHD, is considered to increase the risk of CHD in subjects with normal glucose levels, which would weaken the association of diabetes with CHD in men. Several cohort studies indicated that elevated 2-hour PG levels of 7.8 to 11.0 mmol/L, a category of IGT, was associated with an increased mortality from cardiovascular disease.[6–8,18,19] However, there have been some epidemiological studies in which IGT was not a risk factor for cardiovascular death.[3,5,9] In the present study, IGT was not associated with the development of ischemic stroke or CHD. However, our previous study of

Table 4. Age-Adjusted Incidence and Age- and Multivariable-Adjusted HRs and Their 95% CIs for the Development of Cardiovascular Diseases According to Glucose Tolerance Levels Defined by the WHO Criteria

	WHO Criteria	Person-Years	No. of Events	Age-Adjusted Incidence per 1000 Person-Years	Age-Adjusted HR (95% CI)	P	Multivariable-Adjusted HR (95% CI)	P
Ischemic stroke								
Men	NGT	7397	29	4.6	1 (referent)		1 (referent)	
	Hyperglycemia	4863	32	6.6	1.47 (0.89 to 2.43)	0.14	1.32 (0.79 to 2.23)	0.29
	IFG	987	2	1.9	0.45 (0.11 to 1.89)	0.28	0.41 (0.10 to 1.74)	0.23
	IGT	2183	11	5.0	1.10 (0.55 to 2.21)	0.78	0.91 (0.44 to 1.89)	0.79
	Diabetes	1694	19	11.3	2.55 (1.43 to 4.55)	0.001	2.54 (1.40 to 4.63)	0.002
Women	NGT	11 769	35	3.6	1 (referent)		1 (referent)	
	Hyperglycemia	5600	36	5.7	1.60 (1.00 to 2.56)	0.049	1.34 (0.82 to 2.20)	0.25
	IFG	807	7	7.9	2.20 (0.98 to 4.97)	0.06	1.89 (0.82 to 4.34)	0.13
	IGT	3224	13	3.4	1.01 (0.53 to 1.92)	0.97	0.88 (0.46 to 1.70)	0.71
	Diabetes	1569	16	9.3	2.46 (1.36 to 4.46)	0.003	2.02 (1.07 to 3.81)	0.03
CHD								
Men	NGT	7415	37	5.9	1 (referent)		1 (referent)	
	Hyperglycemia	4979	38	7.8	1.31 (0.83 to 2.07)	0.24	1.10 (0.69 to 1.76)	0.69
	IFG	982	5	4.9	0.89 (0.35 to 2.27)	0.81	0.80 (0.31 to 2.05)	0.64
	IGT	2244	18	8.0	1.33 (0.76 to 2.35)	0.32	1.11 (0.62 to 2.00)	0.72
	Diabetes	1754	15	9.4	1.53 (0.84 to 2.78)	0.17	1.26 (0.67 to 2.35)	0.47
Women	NGT	11 932	16	1.5	1 (referent)		1 (referent)	
	Hyperglycemia	5759	21	3.1	2.07 (1.07 to 3.99)	0.03	1.52 (0.76 to 3.04)	0.23
	IFG	871	1	0.9	0.65 (0.09 to 4.88)	0.67	0.48 (0.06 to 3.76)	0.48
	IGT	3278	6	1.6	1.05 (0.41 to 2.70)	0.92	0.82 (0.31 to 2.15)	0.68
	Diabetes	1610	14	6.9	4.82 (2.34 to 9.94)	<0.001	3.46 (1.59 to 7.54)	0.002

Multivariable adjustment was made for age, systolic blood pressure, electrocardiogram abnormalities, body mass index, total and high-density lipoprotein cholesterol, smoking habits, alcohol intake, and regular exercise.

WHO indicates World Health Organization.

a 5-year follow-up of the same cohort showed that IGT was an independent risk factor for the occurrence of cardiovascular disease.[4] During a long follow-up period, a potential change in the glucose tolerance of participants may occur, which would induce some misclassification and weaken the relationship between 2-hour PG levels and cardiovascular disease. Thus, the association between the prediabetic range of 2-hour PG and cardiovascular events would attenuate over time.

The American Diabetes Association lowered the FPG cutoff point from 6.1 to 5.6 mmol/L in 2003.[20] This decision was prompted partly by population-based studies showing that the cutoff point of 5.6 mmol/L would increase the sensitivity of predicting future diabetes. In addition, this change was also intended to improve the selection of individuals at risk for cardiovascular diseases.[20] Two major organizations recently adopted the cutoff point of 5.6 mmol/L in the diagnostic criteria of metabolic syndrome.[21,22] Thus, it is very important to appropriately determine the FPG cutoff value for the prediction of cardiovascular disease. However, there is less evidence concerning the positive association between FPG levels of 5.6 to 6.0 mmol/L and the risk of cardiovascular disease. A recent study of a community-based medical center in the United States found that individuals with glucose of 5.6 to 6.0 mmol/L had lower prevalence of most CHD risk factors compared with individuals with glucose of 6.1 to 6.9 mg/dL.[23] Furthermore, some epidemiological studies have shown that the mortality and incidence of cardiovascular disease did not increase in those with FPG levels of 5.6 to 6.0 mmol/L.[11,12,19,24] These findings, together with those of the present study, suggest that FPG levels of 5.6 to 6.0 mmol/L are not associated with the risk of cardiovascular disease.

Conflicting data for FPG levels of 6.1 to 6.9 mmol/L as a risk factor for cardiovascular disease also exist. At least 4 studies have shown no significantly increased risk of cardiovascular disease in those with FPG levels of 6.1 to 6.9 mmol/L,[6,8,18,19] although others have found that this glucose range is a significant risk factor for cardiovascular disease.[7,11,12,24] In our study, the age-adjusted incidence of ischemic stroke was significantly higher in women with FPG levels of 6.1 to 6.9 mmol/L than in those with normal FPG levels, but after controlling for confounding risk factors, the risk was no longer statistically significant. Other known cardiovascular risk factors such as hypertension, obesity, and dyslipidemia tend to accumulate at this glucose level.[23] Thus, FPG levels of 6.1 to 6.9 mmol/L seem to have increased the risk of ischemic stroke through other coexisting risk factors in our population.

The strengths of our study include its longitudinal population-based design, long duration of follow-up, perfect follow-up of subjects, sufficient number of cardiovascular events, and accuracy of diagnosis of cardiovascular disease. One limitation of our study is that the diagnosis of glucose