厚生労働科学研究費補助金(循環器疾患等生活習慣病対策総合研究事業)
日本人2型糖尿病患者における生活習慣介入の長期予後効果
並びに死亡率とその危険因子に関する前向き研究
(Japan Diabetes Complications Study; JDCS)

平成２６年度　分担研究報告書

糖尿病腎症（腎症）

日本人2型糖尿病における腎機能低下に対する観察開始時のGFRの影響-JDCSサブ解析-

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はじめに

“糖尿病における血管合併症の発症予防と進展抑制に関する研究（JDCS）”[1]が腎症に関して明らかにしたものは，顕性アルブミン尿発症に対するrisk factor[2]と腎機能低下に対する糖尿病網膜症と微量アルブミン尿の影響[3]である．今回は，2014年度の検討結果を報告する．

腎症の臨床的特徴は，尿アルブミン（尿蛋白）の増加と腎機能(GFR)の低下である．2014年に腎症合同委員会が発表した病期分類[4]もその観点から作成されている．したがって，尿アルブミン（尿蛋白）の増加と腎機能(GFR)の低下を阻止することは極めて重要で，それらの因子を明らかにすることは大きな意義があることである．

【背景・目的】2014年度は腎機能(GFR)低下に着目し，検討を行った．腎機能低下は，糖尿病性腎症（腎症）患者の予後およびQOLに大きく影響するため，腎機能低下のリスク因子を明らかにする意義は大きい．欧米人1型糖尿病あるいは2型糖尿病で当初のGFR高値（糸球体過剰濾過-glomerular hyperfiltration (GHF)-を含む）が腎機能低下に関連すると報告されている．し

かしこの点に関しては，日本人2型糖尿病の多数例において観察開始時のGFRが，その後の腎機能低下に与える影響は不明である．さらに，上記欧米人の報告は，GHFがその後のGFR低下に関連する可能性は示されていても，観察終了時に正常範囲を割って低下することまでを示したものはない．そこで2014年度はJDCS登録患者の腎機能低下のリスクファクターを明らかにし，さらに開始時のGFRの影響を検証することを目的に検討を行った．

【対象・方法】対象例は過去に検討したものとoverlapする．JDCS総登録患者2033人のうち尿アルブミンクレアチニン比（ACR）が150以下の2型糖尿病患者1407人[男性52.6%，年齢59±7歳，糖尿病病悩期間11±7年，HbA1c 8.3±1.3%，血圧132±16/77±10 mmHg，eGFR 87.5 ±29.1 m l/min/1.73m^2，正常アルブミン尿974人，MA 433人]を解析対象とし，8年間経過観察した．1)全体的検討：年次eGFR低下が3 ml/min/1.73m^2 以上のΔGFR＞3群(n=201)でリスク因子を検討した．2)観察開始時のeGFRにより4群に分けた（G1:120 ml/min/1.73m^2 以上:n=157, G2:120-90:n=355，G3:90-60:n=735，G4:60未満:n=160）．3)観察開始時および終了時のACRとeGFRを比較した．4)4群のGFR低下速度を比較した．5)GFR低下速度と観察終了時のeGFR<60の頻度を検討した．【結果】1) GFR低下に関連するリスク因子は，観察開始時のACR高値，HbA1c高値およびeGFR高値およびDRの関与であった．2)観察開始時の年齢，性別，病悩期間，HbA1cは，4群間で有意に異なった．ACRは，観察開始時に比し，終了時に4群間とも有意に増加した．eGFRは，G1およびG2で観察開始時から終了時に有意に低下した．e GFRの年次低下率は4群で有意に異なり，G1が一番大であった．3) 年次eGFR 3 ml/min/1.73m^2 低下例は，G1に15.3%, G2に13.3%, G3に5.1%, G4に1.3%認め，当初のGFRが高値であればあるほど，年次GFR低下が大きい例の頻度が増加した．年次GFR低下3未満の群はむしろG4で多い傾向にあった．4)観察終了時にeGFR＜60になった例の頻度は，ΔGFR＞3群で有意に多かった．

【結論】日本人2型糖尿病において，1) 腎機能の低下には，観察開始時の尿アルブミン，血糖コントロールおよびGFRが関与するが，特にGFR高値例はGFRの低下速度が速い．2)GFR低下速度が大である群は，GFR＜60になる率が高い．したがって，GFR高値例をむしろ綿密に経過観察し，腎機能低下を早期に察知する必要がある．

今回の検討は，2015 年度の日本糖尿病学会と米国糖尿病学会(ADA)に報告予定で，さらに論文作成中である．ADA に提出した抄録を転記する．

The Japan Diabetes Complications Study (JDCS), a nation-wide, multicenter, prospective study of type 2 diabetic patients, reported that hemoglobin A1c (HbA1c), systolic blood pressure (SBP), or smoking were risk factors for the onset of macroalbuminuria. However, risk factors for GFR decline remain unclear, while increased albuminuria and progressive renal function decline are clinical manifestations of diabetic nephropathy in types 1 and 2 diabetic patients. We explored clinical factors affecting the GFR course and renal function decline rate in the JDCS of 1,407 patients (667 women, mean age 58 yrs, HbA1c 66.7±14.0 mmol/mol) whose urinary albumin-to-creatinine ratio (ACR) and eGFR were determined at baseline with an 8-yr follow-up. Advanced age, high HbA1c, eGFR, and ACR, or diabetic retinopathy at baseline, were risk factors for patients with annual eGFR decline ≥3 ml/min/1.73 m^2 (ΔG≥3 group; n=201). SBP and diastolic BP did not affect GFR. Baseline eGFR in the ΔG≥3 group (114±40) was higher than in patients with GFR decline<3 (non-decliner; 83±24, p<.001) and decreased to 68±25 at follow-up (p<.001). The frequency of GFR<60 at the follow-up was higher in the ΔG≥3 group than in the non-decliners (χ^2 15.31, p<.0005). We divided the patients into 4 groups according to baseline eGFR: G1 (120≤baseline eGFR), G2 (90≤baseline eGFR<120), G3 (60≤baseline eGFR<90), G4 (baseline eGFR<60). The eGFRs in groups G1 and G2 were decreased at follow-up compared to baseline (p<.01 for both). G1 group's annual GFR decline rate was significantly higher than that in the other groups. In 974 normo- and 433 low-microalbuminuric Japanese type 2 diabetic patients, increased GFR at baseline resulted in rapid GFR decline followed by lower GFR below normal at the final observation. GFR should be continually measured and extra careful attention should be paid to patients with eGFR>90 ml/min/1.73 m^2 to detect cases with rapidly decreased GFR under normal range.

おわりに

糖尿病診療の目標の 1 つは様々な慢性血管合併症の発症予防・進展抑制さらには緩解にある．腎症に関しては，如何に尿アルブミンを増加させないか，そして腎機能低下を阻止するかが重要である．その観点から，今回は

GFR低下に対するrisk factor の同定を行った.

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平成２６年度　分担研究報告書

糖尿病網膜症

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糖尿病網膜症は糖尿病性腎症、糖尿病性神経障害と並ぶ糖尿病の３大合併症であり、その中でも最も頻度が高い合併症と言われている。Japan Diabetes Complications Study (以下、JDCS)は40-70歳の２型糖尿病患者を対象とした多施設無作為臨床試験である。生活習慣介入による糖尿病合併症の発症予防を目的とした臨床研究であるが、同時に、我が国の糖尿病専門施設に通院する典型的な２型糖尿病患者の糖尿病網膜症の有病率、発症率、また、臨床経過を知る重要な疫学資料である。JDCS研究では糖尿病網膜症の存在と重症度の判定は１年おきに各施設の眼科専門医によって調査用の記録用紙に病変の有無を記入、それを元に中央で国際重症度分類に準拠した重症度を決定した。施設ごとの判定の違いを評価するために診察時に撮影された眼底写真を合わせて収集し、精度管理を行った。

今回、糖尿病網膜症及び糖尿病黄斑浮腫についてその程度をより定量的な判定法で分類するために、収集された眼底写真のデジタルアーカイブ化を行った。特に、紙媒体へのプリントアウト画像やポラロイド写真については経年変化により脱色や変色の危険もあり、また、フィルム画像やデジタル画像についても簡便に閲覧できるよう統一した画像アーカイブの作成を行った。デジタル画像のアーカイブ化により、定性的

な判定に加え、定量的な網膜症関連アウトカムを得ることも可能になる。

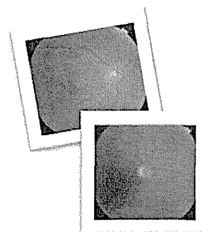
ベースライン調査から8年次追跡までの眼底画像23443枚について、イメージスキャナーGTX-970（EPSON社TIFF-Bitmap形式; 24bit, 圧縮なし, 1800DPI相当)を用いデジタル化を行った。デジタル化された画像は耐障害性と読み出し書き込み性能を確保するためRAID10で冗長化されたネットワークアタッチトストレージ（QNAP社TS-869 Pro）に保管した（**図1**）。平成27年3月9日眼底写真をデジタルアーカイブ化する作業が終了した（**表1**）。アーカイブ化された画像を用い、糖尿病黄斑浮腫に関して画像解析ソフトを用い、「黄斑浮腫の有無と重症度」、「硬性白斑の定量的測定」、また、糖尿網膜症や糖尿病との関連が知られる網膜血管径測定などの定量的評価を行う予定である。

図1　眼底写真のデジタルアーカイブ化の流れ

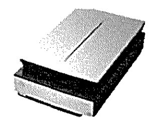
表1　眼底写真のデジタルアーカイブ化（平成27年3月9日終了）

眼底写真のデジタルアーカイブ化の流れ

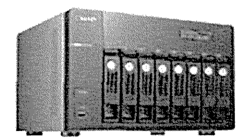
それに伴い得られる網膜症関連アウトカム

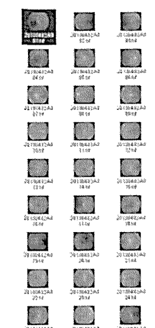


JDCSで収集された
様々なフォーマットの眼底写真



イメージスキャナーを用いデジタル化GTX-970（EPSON社）
（TIFF-Bitmap形式; 24bit, 圧縮なし, 1800DPI相当）

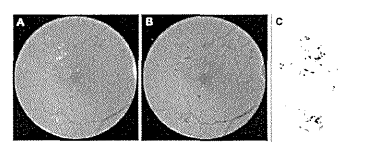




RAID10で冗長化された
NAS装置にアーカイブ化
（QNAP社TS-869 Pro）

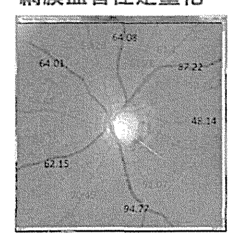
糖尿病黄斑症の定性判定

硬性白斑の定量化手法の導入



Sasaki M, Kawasaki R, et al.
(Invest Ophthalmol Vis Sci. 2013)

網膜血管径定量化



眼底写真のデジタルアーカイブ化
（平成27年3月9日終了）

デジタル化	23,443枚
1年次調査	3,327枚
2年次調査	3,331枚
3年次調査	3,255枚
4年次調査	3,537枚
5年次調査	3,016枚
6年次調査	2,225枚
7年次調査	1,594枚
8年次調査	1,447枚
（撮影年照合中	*1,698枚）*

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平成26年度　分担研究報告書

食事療法について

－肉摂取量と心血管疾患発症との関係－

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研究要旨

肉摂取量と糖尿病発症に関する研究は多くみられるものの、2 型糖尿病患者における肉摂取量と CVD 発症リスクの関連性は未解明の点が多い。そこで、本研究では JDCS の 40-70 歳の日本人 2 型糖尿病患者 1588 名を対象として、両者の関連性を縦断的に検討した。1996 年に食物摂取頻度調査を実施し、8 年後の CVD 発症（冠動脈疾患と脳卒中を含む）をエンドポイントとした。Cox 比例ハザードモデルにより、肉摂取量で四分位に分けた 4 群のうち最小摂取群（Q1）を基準として疾患発症リスクのハザード比を算出した。

四分位における肉摂取量の平均値は、10-98g/日の範囲であった。CVD 発症リスクは、肉摂取量と有意に関連しなかったが、冠動脈疾患発症リスクについては、肉摂取量増加に伴い有意なリスク増加が見られた(Q2:3.0[95%信頼区間, 1.3-6.7], Q3:3.3[1.4-7.6], Q4:3.3[1.4-8.1], いずれも p= 0.01)。脳卒中については、肉摂取量と有意な関連性は見られなかった。本研究より、2 型糖尿病患者における肉摂取量と CVD 発症リスクとの関係が明らかとなった。

A. 研究目的

本研究では、Japan D iabetes Complications S tudy のデータを用いて、日本人 2 型糖尿病患者における 2 型糖尿病患者における肉摂取量と CVD 発症リスクの関連を明らかにする。

B. 研究方法

本研究の対象者は、JDCS に登録された 2 型糖尿病患者のうち、合併症の既往のない 40-70 歳の患者 1588 名とした。主要な評価項目は、CVD 発症リスクであり、登録後 8 年後の冠動脈疾患・脳梗塞発症をアウトカムとして検討した。解析方法は、Cox 比例ハザードモデルを用いた。

C. 結果

観察期間中、各合併症の発症者は、CVD: 132 名、CHD: 96 名、脳卒中: 68 名であった。四分位における肉摂取量の平均値は 10-98g/日の範囲であり、（表 1）欧米 2 型糖尿病患者の約半量の摂取であった。CVD 発症リスクは、肉摂取量の増加と有意な関連は見られなかったが、アウトカムを CHD 発症に限定した場合、肉摂取量増加と共に有意なリスク増加が見られた（Q2: 3.0[95%信頼区間, 1.3 -6.7], Q 3: 3.3[1.4-7.6], Q 4: 3.3[1.4-8.1], いずれも p= 0.01）（表 2）。また、肉摂取量 10g 増加ごとに、CHD 発症リスクは 9 % の増加がみられた（1.09 [1.02-1.16] p= 0.01）（表 3）。一方、脳卒中発症リスクについては、肉摂取量とは有意な関連性が見られなかった。

D. 結論

最近海外で報告された肥満が死亡率を減少させるという傾向は、日本人 2 型糖尿病患者では見られなかった。その理由として、現在の BMI は食事指導などによる生活習慣の変化により修飾されている可能性が考えられた。

E. 研究発表

特になし

表 1. 調査開始時における肉摂取量と臨床像との関係.

	Q1 (N=279) mean SD	Q2 (N=357) mean SD	Q3 (N=351) mean SD	Q4 (N=366) mean SD
肉摂取量 (g)	±6.0	28.8±4.9	50.3±7.6	±35.6
年齢 (歳)	60.2±6.5	58.7±6.5	58.2±6.9	57.8±7.4
女性 (%)	52.0%	49.6%	49.6%	39.3%
糖尿病罹病期間 (年)	11.1±6.8	11.1±7.0	10.5±7.0	11.3±7.3
HbA1c (%)	8.2±1.2	8.3±1.4	8.3±1.3	8.4±1.4
随時血糖 (mg/dL)	160.9±42.8	161.8±45.6	156.5±42.0	164.0±43.9
BMI (kg/m^2)	22.8±2.9	23.0±3.1	22.9±2.9	22.9±3.0
SBP (mmHg)	130.4±15.6	132.6±15.6	131.8±17.4	130.6±15.6
LDL-C (mg/dL)	122.0±31.5	124.9±35.3	121.8±30.6	121.3±31.0
HDL-C (mg/dL)	53.5±16.0	53.6±17.3	55.7±17.1	55.5±16.9
Triglyceride (mg/dL)	97.5±60.0	101.5±78.0	100.0±67.0	101.0±70.0

表 2. 肉摂取量の違いによる 8 年後の心血管疾患発症リスク.

	Q1	Q2			Q3			Q4		
	HR	HR	95%CI	p	HR	95%CI	p	HR	95%CI	p
肉摂取量 (g)	±6.0		28.8±4.9			50.3±7.6			±35.6	
CHD										
Events/Patients	10/279		29/357			27/351			30/366	
Not adjusted	ref		(1.2 - 5.6)			(1.2 - 5.3)			(1.3 - 5.9)	
Adjusted †	ref		(1.3 - 6.7)			(1.5 - 7.6)			(1.4 - 8.1)	
脳卒中										
Events/Patients	15/279		15/357			14/351			19/366	
Not adjusted	ref	0.8	(0.4 - 1.5)	0.42	0.7	(0.3 - 1.4)	0.33	0.9	(0.5 - 1.8)	0.73
Adjusted †	ref	0.8	(0.4 - 1.6)	0.50	0.9	(0.4 - 1.9)	0.71	1.3	(0.6 - 3.2)	0.54
CVD										
Events/Patients	19/279		39/357			33/351			38/366	
Not adjusted	ref	1.7	(1.0 - 2.9)	0.06	1.4	(0.8 - 2.4)	0.28	1.6	(0.9 - 2.7)	0.12
Adjusted †	ref	1.7	(1.0 - 3.1)	0.06	1.7	(1.0 - 3.2)	0.07		(1.1 - 4.0)	

† 年齢・性別・BMI・糖尿病罹病期間・HbA1c・SBP・血中脂質・血糖降下薬の使用有無・インスリンの使用有無・降圧薬の使用有無・脂質改善薬の使用有無・喫煙歴・運動習慣・アルコール摂取量・エネルギー摂取量・食品摂取量（穀類・魚類・野菜類）・ナトリウム摂取量で調整した。

表 3. 量-反応関係で見た、肉摂取量の違いと 8 年後の心血管疾患発症リスク

	Linear analysis		
	10g ごとの HR	95%CI	p
CHD			
Not adjusted	1.06	(1.01 - 1.11)	0.01
Adjusted †	1.09	(1.02 - 1.16)	0.01
Stroke			
Not adjusted	0.96	(0.89 - 1.04)	0.30
Adjusted †	0.99	(0.90 - 1.09)	0.80
CVD			
Not adjusted	1.02	(0.97 - 1.06)	0.47
Adjusted †	1.05	(0.99 - 1.12)	0.09

† 年齢・性別・BMI・糖尿病罹病期間・HbA1c・SBP・血中脂質・血糖降下薬の使用有無・インスリンの使用有無・降圧薬の使用有無・脂質改善薬の使用有無・喫煙歴・運動習慣・アルコール摂取量・エネルギー摂取量・食品摂取量（穀類・魚類・野菜類）・ナトリウム摂取量で調整した。

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ORIGINAL ARTICLE

Dietary intake in Japanese patients with type 2 diabetes: Analysis from Japan Diabetes Complications Study

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ABSTRACT

Aims/Introduction: Though there are many differences in dietary habits and in the metabolic basis between Western and Asian people, the actual dietary intake in Asian patients with diabetes has not been investigated in a nationwide setting, unlike in Western countries. We aimed to clarify dietary intake among Japanese individuals with type 2 diabetes, and identify differences in dietary intake between Japanese and Western diabetic patients.

Materials and Methods: Nutritional and food intakes were surveyed and analyzed in 1,516 patients with type 2 diabetes aged 40–70 years from outpatient clinics in 59 university and general hospitals using the food frequency questionnaire based on food groups (FFQg).

Results: Mean energy intake for all participants was 1737 ± 412 kcal/day, and mean proportions of total protein, fat, and carbohydrate comprising total energy intake were 15.7, 27.6 and 53.6%, respectively. They consumed a 'low-fat energy-restricted diet' compared with Western diabetic patients, and the proportion of fat consumption was within the suggested range that has been traditionally recommended in Western countries. As a protein source, consumption of fish (100 g) and soybean products (71 g) was larger than that of meat (50 g) and eggs (29 g). These results imply that dietary content and food patterns among Japanese patients with type 2 diabetes are quite close to those reported as suitable for prevention of obesity, type 2 diabetes, cardiovascular disease, and total mortality in Europe and America.

Conclusions: A large difference was shown between dietary intake by Japanese and Western patients. These differences are important to establish ethnic-specific medical nutrition therapy for diabetes.

INTRODUCTION

Medical nutritional therapy is an essential constituent in managing existing diabetes and preventing, or at least slowing, the development of diabetes complications[1]. Thus, it is necessary to determine and assess dietary patterns in diabetes patients. However, there have been no large-scale studies of dietary patterns in nationwide settings from Asian regions except a recent study of elderly diabetic patients[2], although there have been many such studies among populations with diabetes in Western countries, such as the Diabetes Nutrition and Complications Trial, Strong Heart Study, National Health and Nutrition

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Examination Survey, and European Diabetes Centers Study of Complications in Patients with Insulin-Dependent Diabetes Mellitus Complications Study Group[3–6].

Dietary patterns in Asia are quite different from those of Western countries because of differences in food culture, food supply, dietary consumption and nutritional intake. For example, according to a report of the Food and Agriculture Organization (FAO) of the United Nations in 2007[7], the total energy supply and the energy supply from animal products in Asia were lower than those in Western regions (2668 and 402 kcal/day in Asia, 3748 and 1028 kcal/day in the USA, and 3406 and 942 kcal/day in European regions, respectively), although the percentage of energy from vegetable products was higher than in Western regions (85% in Asia, 73% in the USA and 72% in European regions).

In addition, in their joint position statement on the treatment of hyperglycemia, the American Diabetes Association and European Association for the Study of Diabetes encourage the development of individualized treatment plans built around racial and ethnic differences[8]. We reported previously that Japanese type 2 diabetic patients had a much lower body mass index (BMI) than Western patients, even though energy intake was the same, and both groups were similar with regard to age, diabetes duration, hemoglobin A1c (HbA1c) and other clinical variables[9,10]. This suggests a different metabolic basis between East Asians and Western patients with diabetes, such as the degree and influence of insulin deficiency and resistance[11]. Furthermore, it was reported that the profiles of the incidence of complications in diabetic patients differ between Asian and Western countries, such as much lower risks of myocardial infarction, stroke and congestive heart failure in Asian patients compared with Western patients, despite a higher risk of end-stage renal disease in Asian patients[12]. It could be possible that differences in eating patterns influence, at least partly, the differences in profiles of complications between the two groups.

Thus, given the differences in dietary habits and metabolic basis between Western and Asian people, it is necessary to clarify the actual dietary intake among Asian individuals with type 2 diabetes and compare it with that of Western diabetic patients in order to rationally develop effective medical nutritional therapy for diabetes. Our aim of the present study was to elucidate the actual dietary intake among Japanese middle-aged individuals with type 2 diabetes who participated in a nationwide cohort study, and to identify differences between Japanese and Western diabetic patients' dietary intake.

METHODS

Study Population

The Japanese Diabetes Complications Study (JDCS) is a nationwide cohort study of Japanese patients with type 2 diabetes from outpatient clinics in 59 university and general hospitals. Participants were previously diagnosed patients with type 2 diabetes aged 40–70 years whose HbA1c levels were ≥6.5%. Details of the study procedure were published elsewhere[13]. The protocol for the study, which is in accordance with the Declaration of Helsinki and the Ethical Guidelines for Clinical/Epidemiological Studies of the Japanese Ministry of Health Labor and Welfare, received ethical approval from the institutional review boards of all of the participating institutes. Written informed consent was obtained from all patients enrolled. A dietary survey was carried out in the baseline year of 1996. Nutrition and food intakes were assessed by the Food Frequency Questionnaire based on food groups (FFQg). A total of 1,516 of the eligible 2,033 patients completed the FFQg, and their data were analyzed in the present study.

Dietary Assessment

Nutrition and food intakes were assessed by the FFQg. The FFQg is composed of items on 29 food groups and 10 kinds of cookery, and elicits information on the average intake per week of each food or food group in commonly used units or portion sizes. After participants completed the questionnaire, a dietician reviewed the completed questionnaire with the participant. The FFQg was externally validated by comparison with weighed dietary records for seven continuous days of 66 subjects aged 19–60 years[14].

The correlation coefficients between the FFQg and dietary records for energy, protein, fat, carbohydrate, and calcium intakes were 0.47, 0.42, 0.39, 0.49, and 0.41, respectively. Intakes of 26 of the 31 nutrients were not significantly different between the two methods by paired *t*-tests. We used standardized software for population-based surveys and nutrition counseling in Japan (EIYO-KUN v.4.5, manufactured at the site of the Shikoku University Nutrition Database)[15] to calculate nutrient and food intakes, which were based on Japan Dietary Reference Intakes in 1996.

Other Assessments

Other measurements in addition to the dietary survey included a physical examination, blood pressure measurement, neurological/ophthalmological examination, and laboratory tests that included HbA1c, fasting plasma glucose/insulin/C-peptide, serum lipids/creatinine/urea nitrogen and urine analyses[13]. HbA1c assays were standardized by the Lab Test Committee of the Japan Diabetes Society (JDS)[13]. HbA1c values were converted from JDS values into National Glycohemoglobin Standardization Program (NGSP) equivalent values. NGSP equivalent values were calculated using the following formula: NGSP equivalent value (%) = JDS value (%) + 0.4[16]. Physical activity and smoking status were determined by a detailed questionnaire.

Statistical Analysis

All data are presented as means ± standard deviation unless otherwise stated. Differences in the major characteristics between participants who completed and did not complete the FFQg were examined by *t*-tests. All *P*-values are two-sided, and the significance level is 0.05. All statistical analyses were carried out using SAS packages version 9.1 (SAS Institute, Cary, NC, USA).

RESULTS

Table 1 shows the characteristics of the 1,516 type 2 diabetes patients. Their mean BMI was 22.7 kg/m^2, and 23% of the patients had a BMI ≥25 kg/m^2. Their mean age was 59 years, and mean HbA1$_C$ value was 7.9%.

Table 1 | Characteristics of 1,516 diabetic patients who participated in the nutritional and food intake survey of the Japanese Diabetes Complications Study

	Men (*n* = 807)		Women (*n* = 709)		Total (*n* = 1,516)	
	Mean	SD	Mean	SD	Mean	SD
Age (years)	58.4	±7.0	59.0	±6.8	58.7	±6.9
Diabetes duration (years)	11.5	±7.4	10.4	±6.7	11	±7.1
Weight (kg)	62	±8.6	54.2	±8.3	58.4	±9.3
BMI (kg/m^2)	22.7	±2.6	23.2	±3.3	22.9	±3.0
<18.5 kg/m^2	4.0%		6.8%		5.3%	
≥25 kg/m^2	19.3%		28.1%		23.4%	
Waist circumference (cm)	81.9	±7.8	76.6	±9.4	79.4	±9.0
Waist-to-hip ratio	0.89	±0.06	0.83	±0.07	0.86	±0.1
Fasting plasma glucose (mmol/L)	8.9	±2.4	9.0	±2.5	8.9	±2.4
HbA1c (%)	7.7	±1.2	8.1	±1.3	7.9	±1.3
Systolic blood pressure (mmHg)	131	±15.7	131	±16.3	131.4	±16.0
Diastolic blood pressure (mmHg)	77	±9.8	76	±9.9	76.6	±9.9
Total serum cholesterol (mmol/L)	5.0	±0.9	5.4	±0.9	5.2	±0.9
Serum LDL cholesterol (mmol/L)	3.0	±0.9	3.3	±0.8	3.2	±0.8
Serum HDL cholesterol (mmol/L)	1.4	±0.4	1.5	±0.5	1.4	±0.4
Serum triacylglycerol† (mmol/L)	1.2	±0.8	1.1	±0.8	1.1	±0.8
eGFR† (mL/min per 1.73 m^2)	79.4	±33.0	81.8	±36.6	80.3	±33.7
Treated by insulin (%)	18.1%		22.1%		20.0%	
Treated by OHA without insulin (%)	64.7%		67.1%		65.8%	
Current smoker (%)	46.4%		8.7%		28.7%	

eGFR, estimated glomerular filtration rate; HbA1c, hemoglobin A1c; HDL, high-density lipoprotein; LDL, low-density lipoprotein; OHA, oral hypoglycemic agent; SD, standard deviation. †Median and interquartile range.

Table 2 shows the nutritional intake per day and the percentage of participants who met nutritional recommendations[17–19]. The mean daily energy intake for all participants was 1737 ± 412 kcal/day, and the mean proportions of total protein, fat and carbohydrate comprising total energy intake were 15.7, 27.6, and 53.6%, respectively. Saturated fatty acid intake comprised 28.6% of total fat intake. Additionally, we evaluated energy and nutritional intakes, respectively, by patients grouped according to sex, age, intensity of physical activity during work, HbA1C level and diabetes duration. Features of energy intake and nutritional intake, and the percentage of participants who met the nutritional recommendations by Japan and major Western guidelines were similar for each comparison with the exception that the men consumed 180 kcal/day more energy than the women (1820 and 1640 g/day, respectively; Table 2). As for intake of selected food groups per day, the mean total vegetable intake for all participants was 324 g/day (Table 3). As a protein source, consumption of fish (100 g) and soybean products (71 g) was larger than that of meat (50 g) and eggs (29 g). The male patients consumed approximately eightfold more alcoholic beverages than the female patients (115 and 14 g/day, respectively), but the characteristics of food intake did not differ greatly among the patient groups.

Table 4 summarizes the dietary composition of various study populations with diabetes, including the current JDCS participants. The JDCS patients had higher carbohydrate consumption and lower fat consumption than reported among diabetic patients in Western countries (37–50% energy and 35–45% energy, respectively)[3–6]. However, it is necessary to note differences in methods for measurement of dietary intake among the studies. In contrast, the JDCS patients had lower carbohydrate consumption and higher fat consumption than reported for type 2 diabetic patients in Korea[20] and South Africa[21]. The energy intake of JDCS patients was similar to that for Western diabetic patients[3–6], although the Western diabetic patients had a higher BMI than the Japanese diabetic patients.

DISCUSSION

In the present study, we determined the actual dietary intake among Japanese with type 2 diabetes in a nationwide large-scale setting. We clarified that the JDCS patients consumed a 'high-carbohydrate low-fat' diet compared with Western diabetic patients, and that their energy intake was similar to that of Western diabetic patients. In addition, the features of energy intake, and nutritional and food intake among the JDCS patients were similar regardless the differences in sex, age, intensity of physical activity during work, HbA1C level, and diabetes duration.

According to the National Health and Nutrition Survey[22] carried out the same year as the dietary survey of JDCS, energy intake by Japanese men and women aged 40–69 years in the general population ranged from 2214 kcal/day to 2319 kcal/day and

Table 2 | Nutritional intake per day, and percentage of participants who met the nutritional recommendations of the Japan Diabetes Society, Canadian Diabetes Association and American Diabetes Association

	Men (*n* = 807)		Women (*n* = 709)		Age <60 years (*n* = 755)		Age ≥60 years (*n* = 761)	
	Mean	SD	Mean	SD	Mean	SD	Mean	SD
Nutritional intake								
Energy								
kcal	1819	400	1643	405	1760	420	1714	403
Carbohydrate								
% Energy	53.0	6.8	54.2	6.3	52.9	6.7	54.2	6.5
g	239.6	55.4	220.1	48.5	230.9	54.4	230.0	52.0
Protein								
% Energy	15.2	2.3	16.2	2.4	15.6	2.4	15.8	2.4
g	69.7	20.8	67.2	22.7	69.0	22.1	68.0	21.4
Fat								
% Energy	26.7	4.9	28.7	4.8	28.1	5.1	27.2	4.8
g	54.3	17.1	53.2	18.9	55.3	18.5	52.3	17.3
SFAs								
% Energy	7.6	1.7	8.3	1.6	8.0	1.7	7.9	1.6
MUFAs								
% Energy	8.8	2.0	9.3	2.0	9.3	2.1	8.8	2.0
PUFAs								
% Energy	6.4	1.5	6.9	1.5	6.8	1.6	6.5	1.5
n6								
% Energy	5.2	1.3	5.5	1.4	5.5	1.4	5.2	1.3
n3								
% Energy	1.5	0.4	1.6	0.4	1.6	0.4	1.6	0.4
Cholesterol								
mg	316.9	116.9	306.9	118.1	313.1	116.5	311.3	118.6
Ca								
mg	619.6	228.3	661.0	229.5	628.9	228.3	648.9	230.8
Fe								
mg	8.0	2.5	8.2	2.7	8.1	2.6	8.1	2.5
Dietary fiber, total								
g	14.1	5.3	15.4	5.3	14.5	5.4	14.9	5.2
Sodium								
g	4.1	1.5	4.3	1.6	4.1	1.6	4.3	1.5
Recommendation met								
Carbohydrate†								
<55% Energy	61%		55%		61%		55%	
55–60% Energy	24%		29%		25%		27%	
≥60% Energy	15%		17%		13%		18%	
Fat†								
<25% Energy	38%		21%		27%		33%	
SFAs‡								
<7% Energy	35%		17%		26%		27%	
Fiber (total)†								
≥20 g	13%		17%		14%		16%	
Sodium†								
<3.9 g	50%		45%		50%		46%	

Table 2 | (Continued)

	Sedentary occupation (*n* = 1,032)		Non-sedentary occupation (*n* = 366)		HbA1c <7% (*n* = 1,266)		HbA1c ≥7% (*n* = 250)	
	Mean	SD	Mean	SD	Mean	SD	Mean	SD
Nutritional intake								
Energy								
kcal	1,714	400	1,774	436	1,736	407	1,739	437
Carbohydrate								
% Energy	53.6	6.5	53.9	6.9	53.4	6.7	54.6	6.2
g	227.7	51.1	237.2	59.1	229.5	52.1	235.4	57.9
Protein								
% Energy	15.7	2.4	15.3	2.4	15.7	2.4	15.5	2.2
g	67.9	21.0	68.6	23.1	68.6	21.7	67.9	21.7
Fat								
% Energy	27.7	4.8	27.1	5.3	27.6	5.0	27.8	4.8
g	53.2	17.3	53.9	19.0	53.7	17.9	54.2	18.2
SFAs								
% Energy	8.0	1.6	7.7	1.8	7.9	1.7	8.2	1.7
MUFAs								
% Energy	9.0	2.0	8.8	2.1	9.0	2.1	9.1	2.0
PUFAs								
% Energy	6.6	1.5	6.6	1.6	6.7	1.5	6.5	1.4
n6								
% Energy	5.3	1.3	5.3	1.4	5.4	1.4	5.2	1.2
n3								
% Energy	1.6	0.4	1.5	0.4	1.6	0.4	1.5	0.4
Cholesterol								
mg	311.8	116.2	305.0	118.6	312.2	117.8	312.2	116.2
Ca								
mg	637.4	222.5	631.2	242.4	637.2	232.4	648.0	215.6
Fe								
mg	8.1	2.4	8.1	2.7	8.1	2.6	8.1	2.5
Dietary fiber, total								
g	14.7	5.2	14.4	5.5	14.6	5.3	15.1	5.5
Sodium								
g	4.2	1.5	4.2	1.6	4.2	1.5	4.2	1.6
Recommendation met								
Carbohydrate†								
<55% Energy	58%		57%		59%		52%	
55–60% Energy	26%		26%		26%		28%	
≥60% Energy	16%		17%		15%		20%	
Fat†								
<25% energy	28%		36%		31%		28%	
SFAs‡								
<7% Energy	26%		30%		27%		23%	
Fiber, total†								
≥20 g	16%		12%		15%		17%	
Sodium†								
<3.9 g	49%		50%		48%		48%	

Table 2 | (Continued)

	Diabetes duration <10 years (*n* = 737)		Diabetes duration ≥10 years (*n* = 779)		Total (*n* = 1516)	
	Mean	SD	Mean	SD	Mean	SD
Nutritional intake						
Energy						
kcal	1,762	425	1,708	397	1,737	412
Carbohydrate						
% Energy	53.3	6.5	53.9	6.7	53.6	6.6
g	232.8	55.2	228.0	51.0	230.5	53.2
Protein						
% Energy	15.6	2.4	15.7	2.4	15.7	2.4
g	69.5	22.6	67.3	20.7	68.5	21.7
Fat						
% Energy	27.9	4.9	27.3	5.0	27.6	5.0
g	55.1	18.3	52.4	17.5	53.8	18.0
SFAs						
% Energy	7.9	1.7	7.9	1.7	7.9	1.7
MUFAs						
% Energy	9.1	2.0	8.9	2.0	9.0	2.0
PUFAs						
% Energy	6.7	1.5	6.5	1.5	6.6	1.5
n6						
% Energy	5.4	1.4	5.2	1.3	5.3	1.4
n3						
% Energy	1.6	0.4	1.5	0.4	1.6	0.4
Cholesterol						
mg	316.1	120.2	307.2	114.1	312.2	117.5
Ca						
mg	644.5	238.8	632.3	220.2	639.0	229.7
Fe						
mg	8.3	2.6	7.9	2.5	8.1	2.6
Dietary fiber Total						
g	15.0	5.4	14.4	5.2	14.7	5.3
Sodium						
g	4.3	1.6	4.1	1.5	4.2	1.5
Recommendation met						
Carbohydrate†						
<55% Energy	59%		57%		58%	
55–60% Energy	27%		25%		26%	
≥60% Energy	13%		19%		16%	
Fat†						
<25% Energy	28%		32%		30%	
SFAs‡						
<7% Energy	27%		27%		27%	
Fiber, total†						
≥20 g	17%		13%		15%	
Sodium†						
<3.9 g	48%		49%		48%	

MUFAs, mono-unsaturated fatty acids; n3, n-3 fatty acids; n6, n-6 fatty acids; PUFAs, poly-unsaturated fatty acids; SD, standard deviation; SFAs, saturated fatty acids. †Carbohydrate intake, 50–60% of total energy; fat intake, <25% total energy; fiber, >20 g/day; and sodium, <3.9 g (<10 g as salt) were recommended by the Japan Diabetes Society[17]. ‡Saturated fat intake should be <7% of total energy as recommended by the Canadian Diabetes Association[18] and the American Diabetes Association.[19]

Table 3 | Intake of selected food groups per day

	Men (*n* = 807)		Women (*n* = 709)		Age <60 years (*n* = 755)		Age ≥60 years (*n* = 761)	
	Mean	SD	Mean	SD	Mean	SD	Mean	SD
Grains (g)	207	58	173	40	194	54	189	52
Potato/aroid (g)	50	40	58	50	50	41	57	49
Soybeans/soy products (g)	68	49	75	54	71	51	72	52
Fruits (g)	121	101	148	108	126	107	140	103
Green-yellow vegetables (g)	130	69	147	66	136	67	140	68
Other vegetables (g)	174	103	200	99	184	100	188	104
Meat (g)	52	37	47	39	54	40	46	36
Fish (g)	103	61	97	59	101	61	100	60
Eggs (g)	30	18	28	16	29	16	29	17
Milk/dairy products (g)	165	109	177	94	168	108	173	97
Sweets/snacks (g)	16	20	20	21	18	21	17	20
Oil (g)	17	9	17	9	18	9	16	8
Alcoholic beverages (g)	155	195	14	48	99	180	80	142
Other beverages (g)	44	85	28	67	41	84	33	70

	Sedentary occupation (*n* = 1032)		Non-sedentary occupation (*n* = 366)		HbA1c <7% (*n* = 1266)		HbA1c ≥7% (*n* = 250)	
	Mean	SD	Mean	SD	Mean	SD	Mean	SD
Grains (g)	187	50	202	62	191	53	194	54
Potato/aroid (g)	53	42	55	45	53	42	57	58
Soybeans/soy products (g)	70	49	72	57	72	53	67	44
Fruits` (g)	139	105	118	109	132	104	141	112
Green-yellow vegetables (g)	139	68	132	67	137	67	143	70
Other vegetables (g)	188	102	176	100	184	102	195	103
Meat (g)	49	37	48	39	49	38	52	42
Fish (g)	99	60	100	62	102	61	93	58
Eggs (g)	29	17	28	16	29	17	30	16
Milk/dairy products (g)	170	101	169	107	168	102	184	105
Sweets/snacks (g)	18	20	19	22	17	20	20	23
Oil (g)	17	9	17	9	17	9	17	9
Alcoholic beverages (g)	83	160	103	166	96	169	54	116
Other beverages (g)	35	77	45	83	36	76	41	85

	Diabetes duration <10 years (*n* = 737)		Diabetes duration ≥10 years (*n* = 779)		Total (*n* = 1,516)	
	Mean	SD	Mean	SD	Mean	SD
Grains (g)	191	54	192	53	191	53
Potato/aroid (g)	56	45	51	45	54	45
Soybeans/soy products (g)	73	55	69	48	71	52
Fruits (g)	138	116	129	93	133	105
Green-yellow vegetables (g)	141	67	135	69	138	68
Other vegetables (g)	191	100	181	104	186	102
Meat (g)	51	39	48	37	50	38
Fish (g)	102	62	98	58	100	60
Eggs (g)	29	17	29	16	29	17
Milk/dairy products (g)	169	107	172	98	170	103
Sweets/snacks (g)	19	22	17	19	18	21
Oil (g)	18	9	16	9	17	9

Table 3 (Continued)

	Diabetes duration <10 years (*n* = 737)		Diabetes duration ≥10 years (*n* = 779)		Total (*n* = 1,516)	
	Mean	SD	Mean	SD	Mean	SD
Alcoholic beverages (g)	91	174	86	147	89	162
Other beverages (g)	38	81	35	73	37	77

HbA1c, glycated hemoglobin; SD, standard deviation.

1836 kcal/day to 1916 kcal/day, respectively. Thus, the JDCS patients consumed an energy-restricted diet reduced by 400–500 kcal/day in men and 200–300 kcal/day in women compared with Japanese men and women in the general population.

In addition, the energy intakes by the JDCS patients and Western patients with type 2 diabetes were similar. However, the mean BMI of the JDCS patients was within the normal range, and was much lower than in Western diabetic patients[3–6]. The differences in energy intake between the two groups were too small to explain the large difference in BMI. In terms of the biological aspects of ethnic differences, it is known that Asian people are more susceptible to pancreatic β-cell secretory defects and pronounced dysfunction in early insulin secretion than Western people[23]. In contrast, among Asian populations, the proportion of body fat and prevalence of prominent abdominal obesity are higher than in individuals of European origin with similar BMI values[23]. Also, ethnic differences in biological factors based on genetics, such as the basal metabolic rate, are assumed between Asian and Western people. Further studies are required to clarify the mechanism of the development of type 2 diabetes in consideration of an ethnic-specific constitution, and it should be investigated whether results of dietary assessments and actual food intake differ consistently between Asian and Western patients with diabetes.

The proportions of protein, fat and carbohydrate consumed by JDCS patients met the major current Western guidelines (American Association of Clinical Endocrinologists[24], European Association for the Study of Diabetes[25], Canadian Diabetes Association[18]), which recommend carbohydrate intake ranging from 45 to 65%, fat intake <30–35% and protein intake from 10 to 20%. Furthermore, mean carbohydrate intake as a percentage of energy intake (53.6%) met the current recommendations of the JDS (50–60%)[17], and mean fat intake (27.6%) was 2.6% higher than the recommendation (25% or less)[17]. Therefore, it was clarified that Japanese type 2 diabetic patients consumed a 'low-fat energy-restricted diet', which has been traditionally recommended in Western countries (generally 25–35% of energy from fat)[18,26,27], although the guidelines of the American Diabetes Association for 2011[19] stated the possibility of the effectiveness of both a low-carbohydrate and a low-fat calorie-restricted diet. These proportions of intake by the JDCS patients did not differ much according to sex, age, intensity of physical activity during work, HbA1C level and diabetes duration. In addition, the proportion of fat consumption by the JDCS patients met the definition of low fat intake reported in the recent systematic review by the American Diabetes Association, which might improve glycemic control, total cholesterol and low-density lipoprotein (LDL) cholesterol, but might also lower high-density lipoprotein (HDL) cholesterol[26]. However, the JDCS patients and Western type 2 diabetic patients had similar HDL cholesterol levels (1.4 mmol/L and 1.1–1.2 mmol/L, respectively)[3,4], which is probably a result of the fact that the serum level of HDL cholesterol is naturally higher in East Asians than in Western populations.

The proportions of protein, fat and carbohydrate as percentages of energy supply in the JDCS patients were similar to those reported in elderly Japanese type 2 diabetic patients (fat/carbohydrate: 25.6/59.0%)[2], the general Japanese population (25.8/59.3%)[27], and a comprehensive picture of the pattern of the country's food supply reported in the FAO Balance Sheet (27.3/59.5%)[7]. Furthermore, according to the report of the FAO in 1996[7], fat and carbohydrate as percentages of energy supply in the USA, European region, Spain, Korea, and South Africa were 34.5/53.1%, 33.5/54.4%, 39.5/47.5%, 20.0/68.9%, and 22.0/67.7%, respectively. Thus, the proportions of protein, fat and carbohydrate consumed by diabetic patients in each country were similar to those reported in the FAO Balance Sheet, which reflects dietary patterns for each country[7]. As well as in these countries, it can be estimated that Japanese type 2 diabetes patients' 'low-fat energy-restricted diet' is deeply ingrained in the ethnic-specific dietary pattern of Japan.

As a protein source, consumption of fish and soybean products was larger than that of meat and eggs, and this pattern was similar without regard to sex, age, intensity of physical activity during work, HbA1C level and diabetes duration. These results imply that dietary content and food patterns among Japanese patients with type 2 diabetes were quite close to those in Western countries that have been reported as decreasing the risk of obesity[28], type 2 diabetes[29] and mortality as a result of cardiovascular disease[29], which is known to be higher in Western countries than in Japan. Conversely, the American Diabetes Association noted that soy-derived supplements were not associated with a significant reduction in glycemic measures or risk factors for cardiovascular disease, and that there is limited evidence in relation to protein sources[26].