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Intake of Carbohydrate to Fiber Ratio Is a Useful Marker for Metabolic Syndrome in Patients with Type 2 Diabetes: A Cross-Sectional Study

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Keywords

Nutrition · Carbohydrate · Dietary Fiber · Type 2 diabetes · Metabolic syndrome

Abstract

Background/Aims: The effect of low carbohydrate diet on human health is still controversial. Whole grain, which is carbohydrate rich in fiber, has protective effects on human health. Thus, we assumed that intake of carbohydrate to fiber ratio has an important role in human health. ***Methods:*** This is a post-hoc analysis of a cross-sectional study of 164 patients with type 2 diabetes. Habitual food and nutrient intake were assessed and estimated by a self-administered diet history questionnaire. Intake of carbohydrate to fiber ratio was defined as carbohydrate (g)/fiber intake (g). Logistic regression analyses were performed to reveal the association between intake of carbohydrate to fiber ratio and metabolic syndrome (MetS). ***Results:*** Intake of carbohydrate to fiber ratio has closely associated with metabolic parameters, including triglycerides ($r = 0.21$, $p = 0.007$) and high-density lipoprotein cholesterol ($r = -0.23$, $p = 0.003$). Intake of carbohydrate to fiber ratio was associated with MetS (OR 1.06 [95% CI 1.00–1.13], $p = 0.047$) after adjusting for covariates, whereas carbohydrate intake (1.00 [0.99–1.01], $p = 0.752$) or carbohydrate energy/total energy (1.00 [0.94–1.07], $p = 0.962$) was not associated with MetS. ***Conclusions:*** Intake of carbohydrate to fiber ratio was associated with MetS, whereas carbohydrate intake was not.

Introduction

Type 2 diabetes is now increasing all over the world [1], and that is accompanied by overweight and obesity [2]. Weight reduction is important for reduction in cardiovascular disease risk in patients with type 2 diabetes [3].

Recent studies revealed that low carbohydrate diet (LCD) is useful for weight reduction [4, 5]. However, whether LCD is useful for human health, including all causes and cardiovascular disease mortality, or not is still controversial [6–8]. On the other hand, recent studies revealed that whole grain, which is carbohydrate rich in fiber, has a protective effect on all causes, cardiovascular

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disease, and cancer mortality [9, 10]. Therefore, we assumed that intake of carbohydrate to fiber ratio has an important role in human health. However, no previous studies reveled the association between the intake of carbohydrate to fiber ratio, and clinical and biochemical metabolic parameters. Therefore, we investigated the association between the intake of carbohydrate to fiber ratio, and clinical and biochemical metabolic parameters in this exploratory analysis of a previous cross-sectional study of patients with type 2 diabetes. Then, we also analyzed the association between the intake of carbohydrate to fiber ratio and metabolic syndrome (MetS).

Materials and Methods

Study Patients

We accessed a database of a previously reported study to evaluate the intake of carbohydrate to fiber ratio, and clinical and biochemical metabolic parameters [11]. Type 2 diabetes patients who performed a self-administered diet history questionnaire (DHQ) were included in this study. Exclusion criteria was as follows: the patients who did not complete the DHQ; the patients who had thyroid disease; adrenal tumor; turner syndrome; severe liver dysfunction, defined as raised aminotransferase levels and gamma-glutamyl transferase levels over 3 times the upper reference value [12]; severe renal dysfunction, defined as estimated glomerular filtration rate (eGFR) <30 mL/min/1.73 m^2 [13]; and the patients of missing data. This study was approved by the local research Ethics Committee of Kyoto Prefectural University of Medicine (Kyoto, Japan; RBMR-E-466–6) and written informed consent was obtained from each patient. Body mass index (BMI) was calculated as weight in kilograms divided by height in meters squared. After an overnight fast, venous blood was collected for the measurement of the concentrations of various factors, such as fasting plasma glucose, hemoglobin A1c, triglycerides (TG), and high-density lipoprotein (HDL) cholesterol. eGFR was calculated by the equation of Japanese Society of Nephrology: eGFR = 194 × Cre$^{-1.094}$ × age$^{-0.287}$ (mL/min/1.73 m^2; if women × 0.739) [14].

Estimation and Assessment of Habitual Food and Nutrient Intake

The details of estimation and assessment of habitual food and nutrient intake were reported previously [11]. Briefly, the usual dietary habits of the patients during the 1-month period were evaluated by the validated DHQ system [15]. DHQ is a questionnaire that investigates about the dietary intake situation of the past 1 month and consists of questions of the following 4 items: questions about day-to-day eating behavior, questions about each amount and frequency of intake of 149 foods, questions about each amount and frequency of essential foods and questions about each amount, and frequency of intake of food other than the aforesaid. Using DHQ and the nutritional value calculation program, we calculated dietary total energy intake (kcal), carbohydrate intake (g), protein intake (g), fat intake (g), fiber intake (g), carbohydrate energy/total energy (%), protein energy/total energy (%), and fat energy/total energy (%). Carbohydrates consist of sugar, starch, and fiber. We defined carbohydrate to fiber ratio as carbohydrate (g)/fiber intake (g). We also calculated potential renal acid load score (PRAL; mEq/day) and net endogenous acid production score (NEAP; mEq/day) [16], which are known as makers of dietary acid load [17].

Definition of MetS

MetS was defined by a joint interim statement of the International Diabetes Federation Task Force on Epidemiology and Prevention; the National Heart, Lung and Blood Institute; the American Heart Association; the World Heart Federation; the International Atherosclerosis Society; and the International Association for the Study of Obesity, using the criteria for Asians [18]. The patients were diagnosed as MetS when 3 or more of the following criteria were present: elevated blood pressure (BP; systolic BP ≥130 mm Hg and diastolic BP ≥85 mm Hg and/or medication for hypertension, in both sexes); hyperglycemia (fasting plasma glucose ≥5.6 mmol/L and/or medication for diabetes, in both sexes); hypertriglyceridemia (serum TG ≥1.70 mmol/L and/or medication for dyslipidemia, in both sexes); low HDL cholesterol levels (serum HDL cholesterol <1.03 mmol/L in men and <1.29 mmol/L in women); and abdominal obesity (waist circumference ≥90 cm in men and ≥80 cm in women). Because of lack of waist circumstance data, we submitted a BMI of ≥25 kg/m^2 as an index of obesity [19]. This definition was validated, previously [20–23].

Statistical Analysis

We used JMP version 10.0 software (SAS Institute Inc., Cary, NC, USA) for the statistical analysis and p value <0.05 was considered statistically significant. This study was an exploratory study of a previous cross-sectional study.

Mean or frequencies of potential confounding variables were calculated, and data were expressed as mean (SD) or absolute number. Student's t test or Pearson's chi-square test was conducted to assess the statistical significance of differences between patients without MetS and patients with MetS. Relationship between carbohydrate intake, carbohydrate energy/total energy, fiber intake or the intake of carbohydrate to fiber ratio, and clinical and biochemical metabolic parameters was examined by Spearman's rank correlation coefficient. We also investigated the association between carbohydrate intake or the intake of carbohydrate to fiber ratio and nutrition parameters by Pearson correlation coefficient. Then, logistic regression analyses were performed to reveal the association between intake of carbohydrate to fiber ratio, carbohydrate intake or carbohydrate energy/total energy, and MetS.

Results

In this study, 247 type 2 diabetes patients (134 men and 113 women) who received DHQ were enrolled. Among them, we excluded 83 patients (43 men and 32 women), 45 patients (28 men and 17 women) could not completed the questionnaire, 23 patients was incomplete information (13 men and 10 women), 4 patients had thyroid disease (1 men and 3 women), 1 woman had Turner syndrome, 1 man had adrenal tumor, 1 woman had severe

Table 1. Clinical characteristics of study patients

	Total	MetS (–)	MetS (+)	p value
n	164	72	92	–
Age, years	65.1 (10.0)	63.3 (10.2)	66.5 (9.7)	0.037
Gender, male/female	86/78	39/33	47/45	0.695
BMI, kg/m^2	24.0 (4.0)	22.0 (2.4)	25.5 (4.4)	<0.001
Systolic BP, mm Hg	130.3 (14.8)	124.5 (12.7)	134.9 (14.8)	<0.001
Diastolic BP, mm Hg	72.1 (10.7)	70.4 (10.2)	73.4 (10.9)	0.075
Hemoglobin A1c, %	7.2 (1.2)	7.3 (1.5)	7.2 (0.8)	0.828
Hemoglobin A1c, mmol/mol	56 (13)	56 (17)	55 (9.1)	0.828
FPG, mmol/L	8.3 (2.8)	7.7 (1.9)	8.7 (3.3)	0.034
TG, mmol/L	1.4 (0.9)	1.1 (0.6)	1.7 (1.0)	<0.001
HDL cholesterol, mmol/L	1.6 (0.4)	1.8 (0.5)	1.4 (0.4)	<0.001
Antihypertensive drug, –/+	83/81	58/14	25/67	<0.001
Diuresis usage, –/+	153/11	69/3	84/8	0.250
Insulin treatment, –/+	128/36	55/17	73/19	0.650
Metformin usage, –/+	116/48	58/14	58/34	0.014
Medication for dyslipidemia, –/+	91/73	51/21	40/52	<0.001
Number of metabolic risk factors	2.7 (1.0)	1.7 (0.5)	3.5 (0.6)	<0.001
Exercise, –/+	114/50	44/28	70/22	0.039
Smoking, none/past/current	101/43/20	44/20/8	57/23/12	0.884
Total energy intake, kcal	1,889.7 (627.7)	1,805.4 (610.0)	1,955.7 (636.8)	0.128
Carbohydrate intake, g	254.5 (80.6)	242.9 (79.5)	263.6 (80.7)	0.104
Carbohydrate energy/total energy, %	54.7 (8.5)	54.6 (8.8)	54.7 (8.3)	0.945
Protein intake, g	69.9 (26.7)	68.2 (25.8)	71.2 (27.4)	0.477
Protein energy/total energy, %	14.8 (2.7)	15.1 (2.8)	14.6 (2.6)	0.191
Fat intake, g	56.5 (27.5)	53.9 (25.6)	58.6 (28.9)	0.270
Fat energy/total energy, %	26.3 (6.4)	26.3 (6.3)	26.4 (6.4)	0.882
Fruit and vegetable intake, g	268.2 (226.2)	263.4 (224.4)	272.0 (228.7)	0.811
Fiber intake, g	14.1 (6.7)	14.5 (7.1)	13.9 (6.4)	0.589
PRAL, mEq/day	5.6 (13.8)	4.4 (13.8)	6.6 (13.8)	0.321
NEAP, mEq/day	49.9 (12.3)	48.9 (12.2)	50.7 (12.4)	0.356
Intake of carbohydrate to fiber ratio	20.1 (7.5)	18.8 (6.6)	21.2 (8.0)	0.041

Data are expressed as mean (SD) or absolute number.

Student's t test or Pearson's chi-square test was conducted to assess the statistical significance of differences between patients without MetS and patients with MetS.

MetS, metabolic syndrome; BP, blood pressure; FPG, fasting plasma glucose; HDL, high-density lipoprotein; PRAL, potential renal acid load score; NEAP, net endogenous acid production score; BMI, body mass index; TG, triglycerides.

liver dysfunction, and 7 patients (4 men and 3 women) had severe renal dysfunction. Therefore, 164 patients (86 men and 78 women) met the inclusion criteria.

Clinical characteristics of 164 patients are shown in Table 1. The carbohydrate intake or carbohydrate energy/total energy of patients with MetS and that of patients without MetS was not different. On the other hand, intake of carbohydrate to fiber ratio of patients with MetS was higher than that of patients without MetS.

Correlation between carbohydrate intake, carbohydrate energy/total energy, fiber intake or intake of carbohydrate to fiber ratio, and clinical and biochemical metabolic parameters is shown in Table 2. Intake of carbohydrate to fiber ratio has a close association with clinical and biochemical metabolic parameters, including TG (r = 0.21, p = 0.007) and HDL-cholesterol (r = –0.23, p = 0.003).

Carbohydrate intake was positively associated with fiber intake (r = 0.57, p < 0.001). Correlation between carbohydrate intake or intake of carbohydrate to fiber ratio and nutrition parameters is shown in Figure 1. Carbohydrate intake was associated with total energy intake (r = 0.86, p < 0.001). On the other hand, intake of carbohydrate to fiber ratio was not associated with total energy intake (r = 0.002, p = 0.759). Moreover, carbohydrate intake was positively associated with fruit and vegetable intake (r = 0.41, p < 0.001) and was not associated with

Table 2. Relationship between carbohydrate intake, carbohydrate energy/total energy, fiber intake or intake of carbohydrate to fiber ratio, and clinical and biochemical metabolic parameters

	Carbohydrate intake		Carbohydrate energy/ total energy		Fiber intake		Intake of carbohydrate to fiber ratio	
	r	*p* value	*r*	*p* value	*r*	*p* value	*r*	*p* value
Age	0.01	0.850	0.03	0.750	0.16	0.046	–0.17	0.032
BMI	0.20	0.009	–0.06	0.425	0.02	0.841	0.14	0.068
Systolic BP	0.07	0.398	0.03	0.739	–0.04	0.624	0.12	0.115
Hemoglobin A1c	0.02	0.797	0.06	0.422	0.10	0.218	–0.07	0.361
FPG	–0.03	0.685	–0.08	0.325	–0.05	0.549	0.06	0.476
TG	0.09	0.249	–0.05	0.561	–0.11	0.158	0.21	0.007
HDL-cholesterol	–0.24	0.002	–0.03	0.732	0.06	0.475	–0.23	0.003

Relationship between carbohydrate intake, carbohydrate energy/total energy, fiber intake or intake of carbohydrate to fiber ratio, and clinical and biochemical metabolic parameters was examined by Spearman's rank correlation coefficient.

HDL, high-density lipoprotein; BP, blood pressure; FPG, fasting plasma glucose; BMI, body mass index; TG, triglycerides.

PRAL ($r = 0.08$, $p = 0.338$) or NEAP ($r = 0.03$, $p = 0.673$). On the other hand, intake of carbohydrate to fiber ratio was negatively correlated with fruit and vegetable intake ($r = -0.42$, $p < 0.001$) and was positively correlated with PRAL ($r = 0.33$, $p < 0.001$) or NEAP ($r = 0.43$, $p < 0.001$).

Logistic regression analyses revealed that carbohydrate intake (OR 1.00 [95% CI 0.99–1.01], $p = 0.752$) or carbohydrate energy/total energy (OR 1.00 [95% CI 0.94–1.07], $p = 0.962$) was not associated with MetS (Table 3). On the other hand, intake of carbohydrate to fiber ratio was associated with MetS (OR 1.06 [95% CI 1.00–1.13], $p = 0.047$), after adjusting for age, sex, total energy intake, protein energy/total energy, fat energy/total energy, usages of metformin, usage of diuresis, exercise, and smoking status (Table 3).

Discussion

In this study, we showed that intake of carbohydrate to fiber ratio was associated with clinical and biochemical metabolic parameter and nutrition parameters. In addition, we also showed that intake of carbohydrate to fiber ratio was associated with the MetS.

The effect of LCD on human health is still controversial [6–8]. One of the possible examinations is that the other nutrition components were different among the studies. A previous study showed that an animal-based LCD was associated with all-cause mortality, whereas a LCD based on vegetable sources has a protective effect for all-cause mortality [8]. In this study, intake of carbohydrate to fiber ratio has a positive correlation with PRAL or NEAP, which has been known to be a risk factor for hypertension [24], type 2 diabetes [25, 26], and MetS [27]; and has a negative correlation with fruit and vegetable intake [28, 29], which has a protective effect on human health. On the other hand, the association between carbohydrate intake and this nutrition was not consistent. Moreover, only intake of carbohydrate to fiber ratio was associated with the MetS in this study. Furthermore, recent studies revealed that whole grain has the protective effect on all causes and cardiovascular disease mortality [9, 10]. Taking these findings together, not the carbohydrate intake or carbohydrate energy/total energy but the intake of carbohydrate to fiber ratio has an important role on human health.

The relationship between intake of carbohydrate to fiber ratio and TG or HDL-C was not strong. One of the possible reasons why the relationship was not strong is the usage of medication. In fact, the relationship between intake of carbohydrate to fiber ratio and TG ($r = 0.32$, $p = 0.002$ by Pearson correlation coefficient) or HDL-C ($r = -0.26$, $p = 0.013$) in patients without the usage of medication for dyslipidemia was higher than that in patients with the usage of medication for dyslipidemia (TG; $r = 0.05$, $p = 0.677$ or HDL-C; $r = -0.15$, $p = 0.200$).

The present study has several limitations that require consideration. First, this study was a cross-sectional design and this result did not permit the determination of causality. Thus, further studies are needed to better assess the relationships between the intake of carbohydrate to fiber ratio and MetS. Second, the data of food intake were obtained by the self-reported questionnaires; so the accuracy of diet survey depended on the memory power of patients. However, the data of DHQ was correlated with total en-

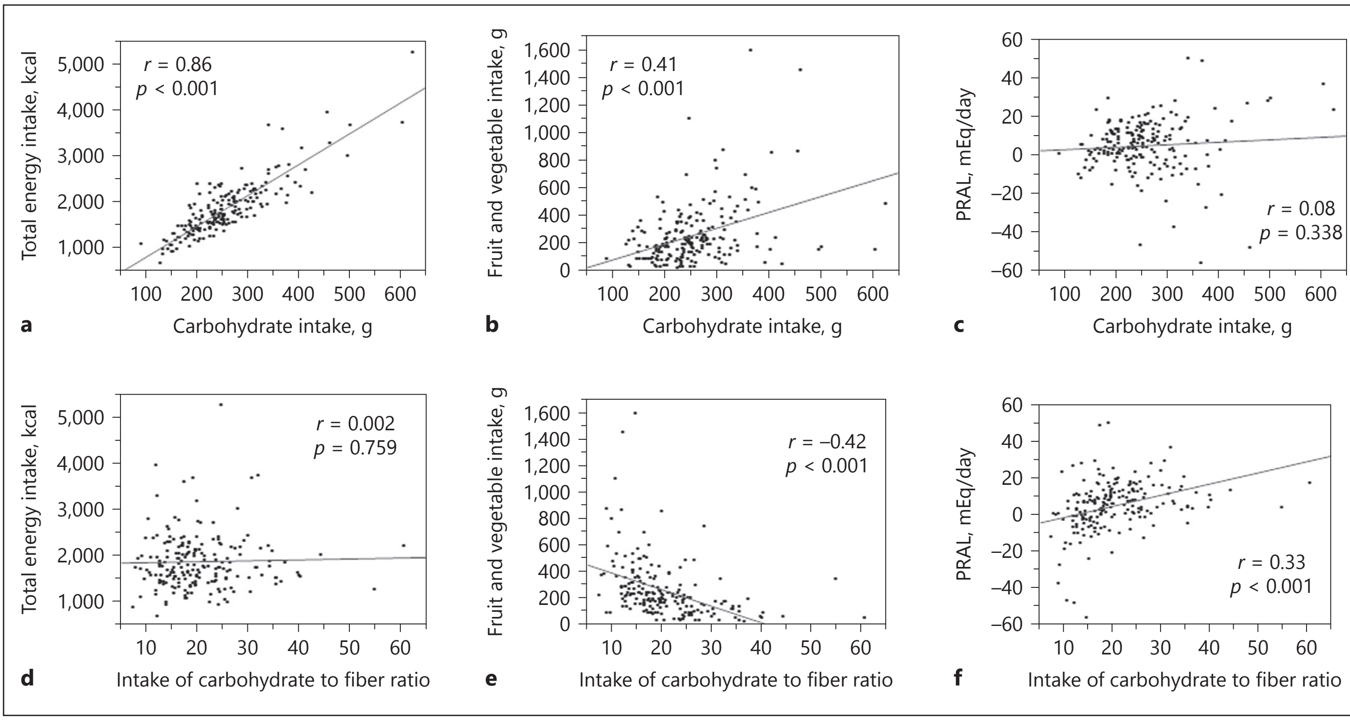

Fig. 1. Correlation between carbohydrate intake or intake of carbohydrate to fiber ratio and nutrition parameters by Pearson correlation coefficient. **a–c** The correlation between carbohydrate intake (g) and total energy intake (kcal), fruit and vegetable intake (g) or PRAL (mEq/day). **d–f** The correlation between intake of carbohydrate to fiber ratio and total energy intake (kcal), fruit and vegetable intake (g) or PRAL (mEq/day). PRAL, potential renal acid load score.

Table 3. Multiple regression analyses on prevalence MetS

	Model 1		Model 2		Model 3	
	OR (95% CI)	*p* value	OR (95% CI)	*p* value	OR (95% CI)	*p* value
Age, years	1.05 (1.01–1.10)	0.006	1.05 (1.02–1.10)	0.005	1.05 (1.02–1.10)	0.005
Gender, male	0.66 (0.28–1.56)	0.345	0.66 (0.27–1.56)	0.243	0.64 (0.27–1.50)	0.305
Total energy intake (per 100 kcal)	1.09 (0.94–1.27)	0.280	1.11 (1.02–1.22)	0.017	1.06 (1.00–1.14)	0.058
Protein energy/total energy, %	0.94 (0.79–1.11)	0.431	0.93 (0.78–1.10)	0.397	0.95 (0.80–1.12)	0.539
Fat energy/total energy, %	1.01 (0.94–1.10)	0.732	1.01 (0.93–1.10)	0.836	1.03 (0.96–1.10)	0.461
Exercise	0.54 (0.24–1.19)	0.124	0.53 (0.23–1.18)	0.120	0.61 (0.27–1.34)	0.220
Past smoker	1.06 (0.42–2.70)	0.900	1.04 (0.41–2.65)	0.933	1.10 (0.44–2.77)	0.840
Current smoker	1.62 (0.53–5.22)	0.397	1.63 (0.53–5.23)	0.395	1.63 (0.53–5.31)	0.396
Metformin usage	2.89 (1.33–6.53)	0.007	2.89 (1.34–6.53)	0.007	3.09 (1.42–7.03)	0.004
Diuresis usage	2.25 (0.58–11.2)	0.250	2.22 (0.57–11.1)	0.257	2.36 (0.61–11.8)	0.222
Carbohydrate intake, g	1.00 (0.99–1.01)	0.752	–	–	–	–
Carbohydrate energy/total energy, %	–	–	1.00 (0.94–1.07)	0.962	–	–
Fiber intake, g	0.94 (0.86–1.01)	0.085	0.94 (0.87–1.01)	0.100	–	–
Intake of carbohydrate to fiber ratio	–	–	–	–	1.06 (1.00–1.13)	0.047

Past and current smokers used none smoker as a reference.
MetS, metabolic syndrome.

ergy expenditure by the doubly labeled water [30] or semi-weighted dietary record [31], which is a standard method. Third, we could not take into account the glycemic index and glycemic load. Fourth, the lack of waist circumference data weakens the definition of MetS. However, BMI of ≥25 kg/m^2 was used as a cut-off for the diagnosis of obesity in Asian people [19] and was validated previously [20–22]. Fifth, we did not have data of gastrectomy or other gastrointestinal disease, which affected the metabolic condition. Sixth, we could clearly show the relationship between these data and prevalence rate of MetS, when we investigated it at the time of diagnosis before receiving dietary guidance. Then, the data of this study might be affected by dietary guidance for type 2 diabetes. We usually treat diabetic patients by diet therapy as well as diabetic medications. In general, dietary guidance is performed by a national registered dietitian at the onset of diabetes. Mean duration of diabetes in this study was 9.7 (7.2) years, which means that this study was carried out during the stable period after nutritional guidance was implemented. Therefore, intake of carbohydrate to fiber ratio could be a useful marker for MetS in patients with type 2 diabetes according to the results of this study, although the determination of causality was not permitted because of a cross-sectional design. Finally, the study population consisted of Japanese men and women; thus, it is unclear whether these findings are generalized in other ethnic groups.

In conclusion, this study showed that the intake of carbohydrate to fiber ratio was associated with MetS, whereas carbohydrate intake or carbohydrate energy/total energy was not. Therefore, we should focus not on the carbohydrate intake or carbohydrate energy/total energy but on the intake of carbohydrate to fiber ratio.

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Disclosure Statement

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Contributions

Y.H. designed the study, contributed to the data research, extraction, and analyses, and wrote the manuscript. M.T. designed the study, contributed to the data research, and contributed to the discussion. A.M., Y.K., S.W., M.K., Y.K., and M.Y. contributed to the data research and contributed to the discussion. M.F. contributed substantially to the study conception and design, data analysis, and interpretation, and drafting and critical revision of the manuscript for important intellectual content. M.F. is the guarantor of this work and, as such, had full access to all the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis. All authors were involved in the writing of the manuscript and approved the final version in this article.

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