Development and Comparability of a Short Food-Frequency Questionnaire to Assess Diet in Prostate Cancer Patients: The Role of Androgen Deprivation Therapy in CArdiovascular Disease – A Longitudinal Prostate Cancer Study (RADICAL PC) Substudy

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ABSTRACT

Background: There are few concise tools to evaluate dietary habits in men with prostate cancer in Canada.

Objective: The aim was to develop a short food-frequency questionnaire (SFFQ) in a cohort of prostate cancer patients.

Methods: A total of 130 men with prostate cancer completed the SFFQ and a validated comprehensive food-frequency questionnaire (CFFQ). Both questionnaires were administered at baseline and 6 mo later.

Results: We found good correlation between the SFFQ and the CFFQ for seafood, dairy, egg, fruits, potatoes, grains, soft drinks, and processed meat (Spearman rank correlation >0.5). Moderate correlation was found for meat, sweets, vegetables, protein, and carbohydrates (Spearman rank correlation: 0.3–0.5). We found a weaker correlation for total fat measured by SFFQ and CFFQ (Spearman rank correlation <0.3). There was adequate reproducibility during the 6-mo follow-up among all food groups and nutrients, with the exception of meat.

Conclusions: Our SFFQ can be considered an appropriate tool to be used for measuring the habitual dietary intake of prostate cancer patients. This trial was registered at www.clinicaltrials.gov as NCT03127631. *Curr Dev Nutr* 2021;5:nzab106.

Introduction

There have been several large epidemiologic studies in which the relationship between diet and outcomes in men with prostate cancer was evaluated (1–6). In an analysis of the Health Professionals Follow-Up study, Richman et al. (2) found that a daily increase of 1 serving (1 tablespoon) in oil-based dressing, post-diagnosis, was associated with a 29% decreased risk of lethal prostate cancer (HR: 0.71; 95% CI: 0.50,

0.98; *P* = 0.04). Additionally, well-done red meat was positively associated with advanced disease stage (T3), but not associated with disease progression (2). However, the optimal diet to reduce the risk of prostate cancer progression is still unknown.

Comprehensive food-frequency questionnaires (CFFQs) are costly, require participants' commitment, and limit the feasibility of measuring long-term intake (6). The Prostate Cancer Project (PCaP) Study modified the Diet History Questionnaire from 135 food and beverage items

(with an additional 26 dietary supplement questions) to 144 food and beverage questions in order to capture southern-specific food items of the catchment areas (5). The original Diet History Questionnaire included up to 263 foods or beverages and can be modified by removing items not frequently consumed (6). Similar in length, the Health Professionals Study food-frequency questionnaire (FFQ) was a 131-item semiquantitative FFQ (7, 8). A shorter but valid tool to measure diet in prostate cancer patients would be of value. However, prior research to develop a short FFQ (SFFQ) in this population has been limited. Neuhouser et al. (9) found that the use of a very short dietary screening questionnaire (13 questions) in prostate cancer patients from the Proscar drug study resulted in a loss of significant information (e.g., fat intake), and the authors suggested using a CFFQ. To our knowledge, there is no widely used, brief tool that adequately measures intake of major nutrients and food groups in prostate cancer patients. An SFFQ validated specifically in men with prostate cancer is needed because these individuals may have nuanced dietary habits that either predispose them to their cancer or result from their diagnosis with cancer and its treatment.

We undertook a prospective substudy of men recruited into the Role of Androgen Deprivation Therapy in CArdiovascular Disease—A Longitudinal Prostate Cancer Study (RADICAL PC). RADICAL PC is an ongoing prospective cohort study aimed at evaluating cardiovascular risk factors and morbidity in men with prostate cancer (1). An SFFQ limited to 50 questions would be valuable to enable the efficient collection of dietary data in the RADICAL PC cohort. Therefore, the objective of our study was to develop an SFFQ for RADICAL PC to quantify the intake of major food groups, namely fruits, vegetables, starchy foods, meats, and dairy products, and macronutrients in men with prostate cancer recruited in RADICAL PC.

Methods

Men were eligible for RADICAL PC if they were recently (within the past year) diagnosed with prostate cancer or if they had recently (within the past 6 mo) commenced or had a plan to soon commence (within the next month) androgen deprivation therapy, and individuals <45 y of age were excluded because the likelihood of the primary outcome of an adverse cardiovascular event is low among young adults (**Supplementary material [A]**). Every attempt was made to recruit an unbiased sample of eligible patients with sites instructed to screen consecutive men with prostate cancer. As of 3 May 2021, 2591 participants have been recruited from 16 Canadian sites (including both academic institutions and community uro-oncology centers) in the overall RADICAL PC study. In this nutritional substudy, we recruited consecutive participants enrolled in RADICAL PC between October 2016 and September 2017 at a single site in Hamilton, Canada. A single site was chosen for reasons of feasibility. All participants provided written informed consent. This study was approved by the Hamilton Integrated Research Ethics Board (HiREB), Hamilton Ontario, Canada.

Comprehensive compared with short FFQ content
For FFQ validation studies, biomarkers or food weighing records are used as the gold standard. However, budget and feasibility limited the use of biomarker or food weighing records and we chose to use a CFFQ as a comparison method, although both tools are prone to

the same measurement error. The purpose of the CFFQ implemented in RADICAL PC was to estimate the dietary intake of a wide range of foods and nutrients in a population of men with prostate cancer. The CFFQ includes a total of 161 food items for which respondents select the relevant portion sizes and frequency of consumption. For the reference method, we used the CFFQ, which has previously been validated (10) against 7-d diet records and has been used previously (11–13). The SFFQ was developed from the CFFQ by removing food items that were not frequently consumed, were not major sources of nutrient intake, and by creating summary food groups (**Supplementary material [B]**). The SFFQ includes 50 food items and takes ∼15 min to complete (as compared with the CFFQ that takes ∼45 min to complete). Portion sizes were selected based on average servings using the USDA food-composition database (version 2018) and the Canadian Nutrient File (version 2018) (14, 15). The frequency of consumption varied from *1*) never, <1 time/mo; *2*) 1–3 times/mo; *3*) 1 time/wk; *4*) 2–4 times/wk; *5*) 5–6 times/wk; *6*) 1 time/d; *7*) 2–3 times/d; to *8*) >4 times/d (**Supplementary material [C]**). We grouped food items into main food groups (**Supplementary material [D]**).

CFFQ and SFFQ implementation
Both the CFFQ and SFFQ were administered by phone at the same time at baseline and 6 mo afterward during the study follow-up call. The questionnaires were administered by trained research personnel who followed standardized instructions. The SFFQ was part of the 6-mo study data collection and was done first along with other RADICAL PC questionnaires, followed by the CFFQ at the end of the call. Participants were asked to report their average food consumption over the past year for the baseline, and their average consumption since the last visit at the 6-mo follow-up call. Participants were provided with examples of food groups (e.g., fish vs. seafood). A list of what each question included is part of the SFFQ and can be found in supplementary material (C). Alcohol intake was excluded from the SFFQ as it was collected on a different questionnaire as part of the RADICAL PC study.

Estimation of daily intake of foods and nutrients
We constructed a nutrient database to convert foods to nutrients. The nutrient database was developed using the USDA food-composition database (version 2018) and the Canadian Nutrient File (version 2018), which have extensive lists of food items available for purchase in Canada and their respective nutrient contents. We used the nutrient database to estimate daily energy and the nutrient intake of participants.

Sociodemographic variables
The following participant characteristics were collected: demographics, smoking (never, current, former) and alcohol use (never, current, former), prostate cancer characteristics, and comorbidities. Participants were stratified into high compared with low/intermediate prostate cancer risk using the criteria described by D'Amico et al and Heidenreich et al. (16, 17), which are based on the T-stage, blood concentration of prostate-specific antigen (PSA), and the Gleason histological grade. Demographic information included age, education (< high school, high school, college, university, trade school), ethnicity (White, non-White), and employment (employed with income, retired, or other). Physical activity was measured using the International Physical Activity Questionnaire and was classified as low, moderate, or high as previously

TABLE 1 Demographic characteristics of participants in the present substudy compared with the rest of the RADICAL PC study participants[1]

Characteristics	Substudy (n = 130)	RADICAL PC (not in substudy) (n = 2505)	P
Age, y	64.33 ± 6.40	68.29 ±7.98	0.001
Highest level of education achieved, n (%)			0.62
Less than high school	17 (13)	281 (12)	
High school	36 (28)	637 (27)	
College	31 (24)	477 (20)	
University	43 (33)	830 (36)	
Trade school	3 (2)	112 (5)	
Ethnicity, n (%)			0.29
White	120 (92)	2105 (89)	
Non-White	10 (8)	250 (11)	
Employment, n (%)			0.1
Employed with income	60 (46)	911 (39)	
Retired or other	70 (54)	1441 (61)	
Physical activity, n (%)			0.04
Low	43 (34)	520 (24)	
Moderate	43 (33)	777 (36)	
High	42 (33)	869 (40)	
Smoking, n (%)			0.95
Never	56 (43)	989 (42)	
Current	12 (9)	235 (10)	
Former	62 (48)	1136 (48)	
Alcohol, n (%)			0.12
Never	9 (7)	291 (12)	
Current	109 (84)	1825 (78)	
Former	12 (9)	240 (10)	
Diabetic, n (%)			0.05
No	80 (62)	1983 (84)	
Yes	50 (38)	390 (16)	
Coronary stent/PTCA, n (%)			0.63
No	123 (95)	2219 (94)	
Yes	7 (5)	153 (6)	
Stroke, n (%)			0.04
No	130 (100)	2296 (97)	
Yes	0 (0)	77 (3)	
Heart failure, n (%)			0.14
No	130 (100)	2332 (98)	
Yes	0 (0)	40 (2)	
Statin use, n (%)			0.04
No	117 (90)	1264 (53)	
Yes	13 (10)	1110 (47)	
Aspirin, n (%)			0.41
No	95 (73)	1654 (70)	
Yes	35 (27)	720 (30)	
ACE-I/ARB, n (%)			0.59
No	81 (62)	1423 (60)	
Yes	49 (38)	951 (40)	
BMI, kg/m^2	27.71 ± 3.84	28.42 ± 4.4	0.07
Healthy (20–25), n (%)	29 (22)	473 (20)	0.34
Underweight (<20), n (%)	2 (2)	29 (1)	
Overweight (25–30), n (%)	68 (52)	1089 (47)	
Obese (>30), n (%)	31 (24)	729 (32)	
Body circumference			
Waist, cm	106.39 ± 10.19	102.90 ± 12.10	0.01
Arm, cm	32.05 ± 3.27	30.62 ± 3.71	0.06
Waist-hip ratio	1.01 ± 0.05	0.99 ± 0.07	<0.001
PC risk category, n (%)			0.002
Low and intermediate	62 (48)	1164 (50)	
High	66 (52)	1000 (43)	
Metastasis	0 (0)	185 (7)	

[1]Values are means ± SDs or counts (%). ACE-I, angiotensin converting enzyme-inhibitors; ARB, angiotensin receptor blocker; PC, prostate cancer; PTCA, percutaneous transluminal coronary angioplasty; RADICAL PC, Role of Androgen Deprivation Therapy in CArdiovascular Disease—A Longitudinal Prostate Cancer Study.

TABLE 2 Mean intake of nutrients and foods measured by the CFFQ and SFFQ at baseline and 6-mo follow-up[1]

	CFFQ	SFFQ1	SFFQ2
Nutrients			
Energy (mean ± SD), kcal/d	1679 ± 544	1370 ± 386	1328 ± 452
Proteins, g/d	70.2	63.3	63.0
Total fats, g/d	50.9	60.8	56.8
Carbohydrates, g/d	209.6	137.2	135.0
Food groups, g/d			
Meat	52.1	63.8	67.0
Processed meat	12.6	24.3	25.5
Egg	47.8	30.6	29.1
Seafood	19.3	9.8	10.3
Soft drinks	89.2	81.3	73.0
Sweets	51.6	13.2	12.2
Dairy	324.4	311.4	272.6
Vegetables	246.2	106.6	108.8
Fruits	183.4	175.1	173.8
Potatoes	31.1	33.8	32.2
Grains	143.8	129.3	133.2

[1]CFFQ, comprehensive food-frequency questionnaire; SFFQ, short food-frequency questionnaire.

described ([18]). Waist, arm, and hip circumferences were measured by trained research personnel using a tape measure. The waist circumference was measured over the unclothed abdomen at the smallest diameter between the costal margin and iliac crest, the hip circumference was measured at the widest diameter around the buttocks, the arm circumference was measured at the midpoint of the right arm with arms hanging freely, and BMI was calculated as weight (kg) divided by height squared (m^2).

Statistical analysis

The mean (±SD), median, and IQRs of consumption of each food group were estimated for the SFFQ and the CFFQ for the food groups. We used ANOVA to compare characteristics of participants included in the substudy with all participants enrolled in the RADICAL PC study. This study sample ($n = 130$) falls within the minimum requirement of 50 participants for using the Bland–Altman plots to assess absolute agreement ([19]). The SFFQ was compared with the CFFQ for the aforementioned food groups and macronutrients using Spearman's rank correlation coefficient. A correlation coefficient >0.5 is considered to represent good correlation; moderate correlation is a correlation coefficient between 0.3 and 0.5, and poor correlation is <0.3 ([11], [13], [20], [21]). The agreement between the CFFQ and SFFQ for the main macronutrients and food groups was evaluated using Bland–Altman plots (1986), plotting mean differences between the 2 FFQs ([19]). We used the Bland–Altman plots to assess the level of agreement and whether differences between SFFQ and CFFQ estimated measurements were dependent on the magnitude of measurements. We have only reported Bland–Altman plots for main food groups (meats, starches, fruit and vegetables, and dairy products) because dietary advice is mostly based on main food groups. Using the residual method ([22]), energy-adjusted Spearman's correlation coefficients were calculated to allow for varying dietary composition. Additionally, reproducibility was evaluated by repeating the questionnaires at the 6-mo study visit. Using longer intervals between 2 questionnaires (3–6 mo) reduces the likelihood of participants

remembering their previous responses and includes seasonal variability ([1]). All data was analyzed in STATA version 14.0 (StataCorp).

Results

Participant characteristics

A total of 130 men with prostate cancer completed the SFFQ and the validated CFFQ, their characteristics compared with other participants in the RADICAL PC study are presented in **Table 1**. Both questionnaires were administered at baseline and six months later. The comparison between the 2 groups suggests that the individuals participating in this substudy are broadly similar to others in RADICAL PC, which is a large unbiased Canadian study.

The mean age of substudy participants was 60.3 ± 6.4 y. All participants were community-dwelling; $n = 113$ (87%) participants completed post-secondary school education; almost half the participants were former smokers ($n = 62$; 48%) and $n = 56$ (43%) participants had never smoked. There were 66 (52%) participants in the high-risk prostate cancer category (no participants had metastasis) and 62 (48%) in the low/intermediate prostate cancer category. Participants' mean BMI (kg/m^2) was 27.4 ± 3.8.

Comparisons of the SFFQ and the CFFQ

Table 2 shows the estimated mean daily intake of the specified food groups measured by the SFFQ and the CFFQ. The mean ± SD energy intake measured by the CFFQ and SFFQ were 1679 ± 544 kcal and 1370 ± 386 kcal, respectively. We found strong energy-adjusted correlations ($r > 0.5$) between the SFFQ and CFFQ for the following food groups: seafood ($r = 0.79$), dairy ($r = 0.76$), egg ($r = 0.74$), fruits and potatoes ($r = 0.72$ for both), and grains ($r = 0.70$). Moderate correlations ($r = 0.3$–0.5) for meat and sweets and for 2 nutrients—proteins and carbohydrates—were observed. We found acceptable agreements between the SFFQ and the CFFQ with respect to major food groups and macronutrients using the Bland–Altman plots. The differences in means between the SFFQ and CFFQ were between ±3 SDs and
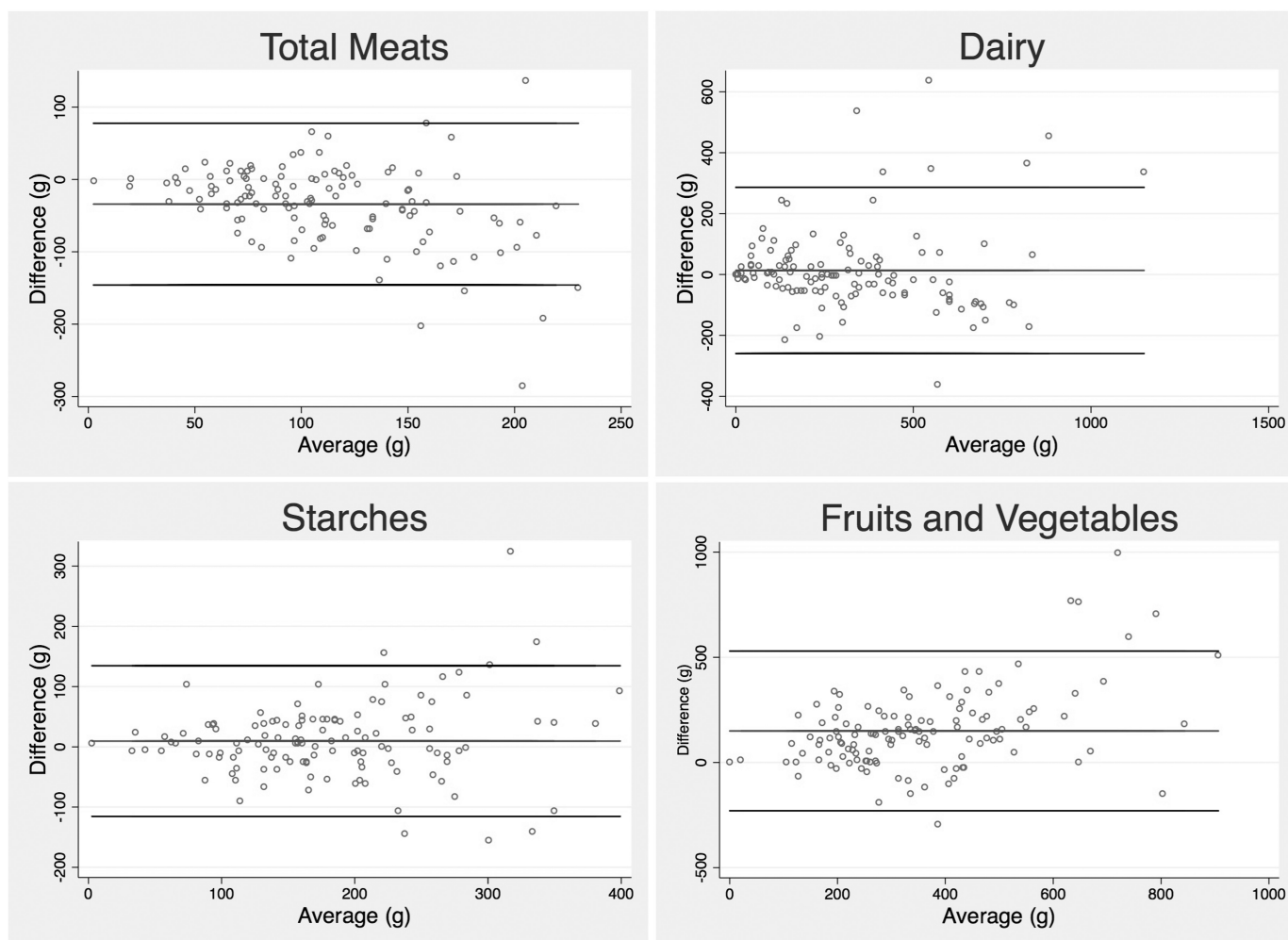
FIGURE 1 Bland–Altman plots of agreement between the SFFQ and CFFQ for daily intake of starches, total meats, fruits and vegetables, and dairy. The difference of mean estimates of each FFQ is plotted. CFFQ, comprehensive food-frequency questionnaire; FFQ, food-frequency questionnaire; SFFQ, short food-frequency questionnaire.

differences were not increased as intakes of foods or nutrients increased (**Figures 1** and **2**).

Reproducibility

Comparison of SFFQ food measurements at 2 time points showed strong intraclass correlation coefficient ($r > 0.5$) for sweets, processed meats, soft drinks, dairy, seafood, potatoes, eggs, fruits, vegetables, and grains. We found moderate correlation ($r = 0.3$–0.5) between all food groups, except for meat, as compared between the 2 time points (**Table 3**).

Discussion

In a cohort of men with prostate cancer, we found that the intake of several food groups (e.g., seafood, eggs, dairy, fruits, potatoes, vegetables, and grains) and nutrients (proteins and carbohydrates), as measured by an SFFQ, had good levels of agreement with the same food measured by the CFFQ.

The importance of specific foods and nutrients in prostate cancer

Most nutrition research in prostate cancer has focused on a single nutrient or food items. Previous studies have shown that a low intake of vegetable fat (2) and a high intake of red meat (3) and dairy (4) are associated with an increased risk of prostate cancer or worsening prostate cancer. The length of the FFQs implemented in previous studies is an obstacle for large epidemiological studies. The SFFQ developed for this study is able to reliably assess the intake of most food items that have been implicated in prostate cancer in other studies.

Previously, dietary recommendations have focused on the consumption of nutrients (e.g., fats and carbohydrates) as strategies to reduce chronic disease in populations. In the past 2 decades, however, the focus of dietary guidelines has shifted from nutrients to foods, because people's dietary choices are based on food types rather than on specific nutrients (23), and because nutrients have many different food sources that may have very different biological effects (e.g., polyunsaturated fat sources include nuts, fish, and vegetable oils, each of which may have differing effects on health). There is a need for an SFFQ tool that can
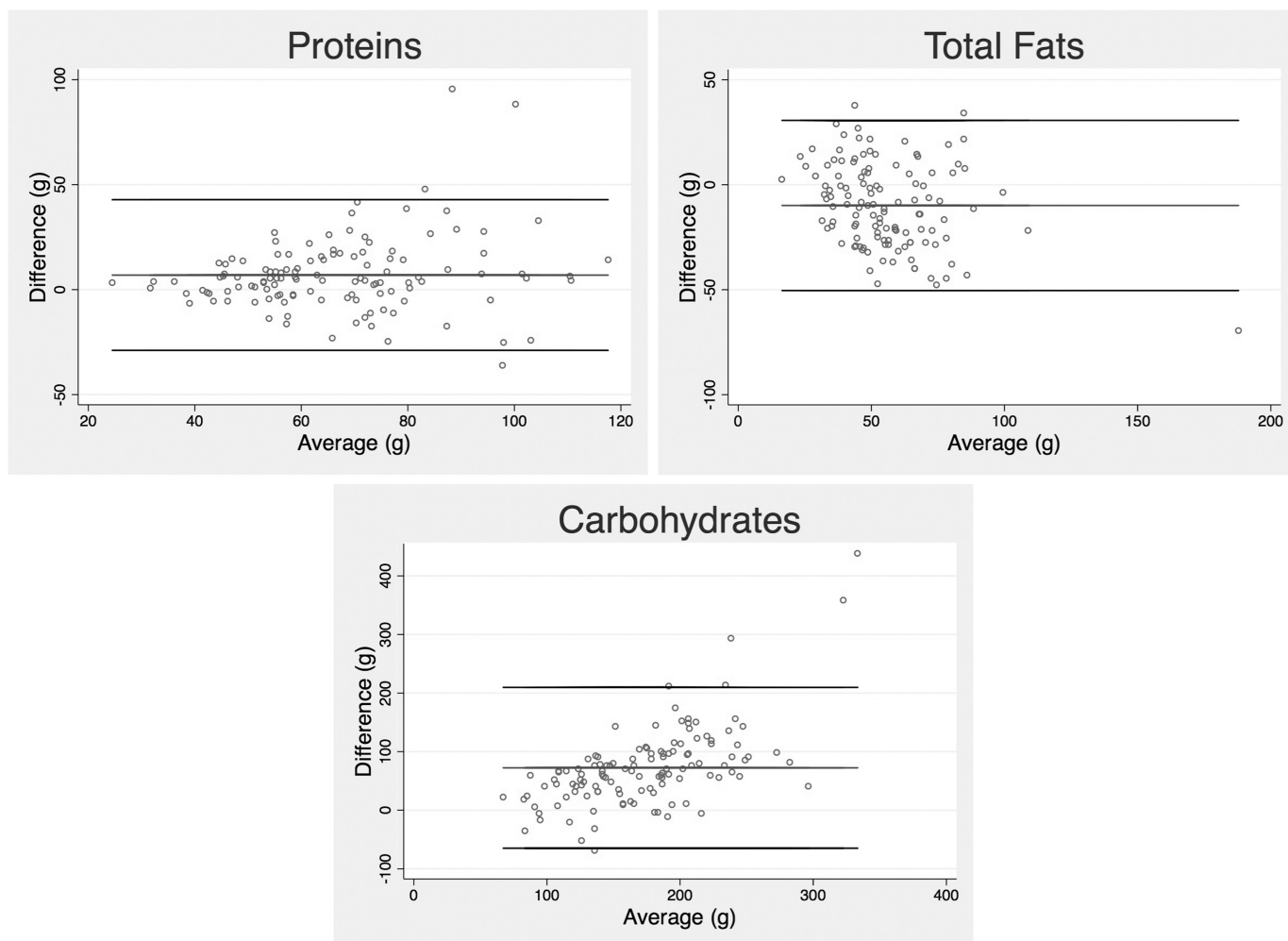
FIGURE 2 Bland–Altman plots of agreement between SFFQ and CFFQ for daily intake of protein, total fats, and carbohydrates. The difference of means estimates of each FFQ is plotted. CFFQ, comprehensive food-frequency questionnaire; FFQ, food-frequency questionnaire; SFFQ, short food-frequency questionnaire.

measure macronutrients (e.g., proteins, carbohydrates) and also commonly consumed foods. The SFFQ developed in our study is able to quantify the intake of macronutrients and most food groups in men with prostate cancer.

Comparability of the SFFQ to the CFFQ

Most previous comparability studies find ranges between 0.3 and 0.7 for major food groups and nutrients (9, 10, 24) measured by short and comprehensive FFQs. Almost all correlations that we observed between the SFFQ and the CFFQ varied between 0.3 and 0.85 and suggest that the SFFQ may be adequate for use in large epidemiological health studies for assessing the relation between diet and health outcomes (13, 20, 21), while substantially reducing the time and cost required for the collection of dietary data.

Bland–Altman method of agreement

The Bland–Altman (19) method was used to assess absolute agreement and found acceptable agreement among main food groups and nutri-

ents. Solely relying on correlation could result in misleading conclusions. Changing a scale of measurement does not affect correlation but does impact agreement. The limits of agreement for the Bland–Altman plots for major food groups and nutrients were similar or narrower than other comparability studies (10). FFQs are considered semi-quantitative and not used to predict absolute values, but rather rank individuals into percentiles or categories (9), and thus the discrepancies between the 2 FFQs identified by the Bland–Altman analysis may not preclude the use of the SFFQ in assessing individuals' long-term intake. It is important to note that carbohydrates showed a slight trend to overestimate higher intakes (and underestimate lower intakes), which has been noted in other studies (11).

Reproducibility of the SFFQ and CFFQ at 6 mo

The ability to successfully reproduce a questionnaire is an important characteristic of its performance (25). Most evaluations of FFQ reproducibility are performed by repeating the questionnaire within 3–12 mo: not so close together that participants are likely to recall their

TABLE 3 Comparability and reproducibility of the SFFQ for assessment of dietary intake[1]

Dietary intake	Correlation coefficient between CFFQ and SFFQ1		ICC between SFFQ1 and SFFQ2	
	Spearman correlation	Energy-adjusted correlation	ICC (95% CI)	P
Nutrients				
Energy (kcal/d)	0.60	—	0.60	<0.01
Protein	0.68	0.41	0.47	<0.01
Fat	0.47	0.09	0.60	<0.01
Carbohydrate	0.57	0.38	0.56	<0.01
SFAs	0.59	0.47	0.63	<0.01
MUFAs	0.40	0.11	0.57	<0.01
PUFAs	0.58	0.46	0.67	<0.01
Food groups (g/d)				
Seafood	0.85	0.79	0.59	<0.01
Dairy	0.87	0.76	0.61	<0.01
Egg	0.79	0.74	0.50	<0.01
Fruits	0.72	0.72	0.50	<0.01
Potatoes	0.74	0.72	0.55	<0.01
Grains	0.75	0.70	0.43	<0.01
Soft drinks	0.84	0.58	0.74	<0.01
Processed meat	0.57	0.50	0.75	<0.01
Meat	0.42	0.40	0.20	0.015
Sweets	0.55	0.38	0.75	<0.01
Vegetables	0.32	0.32	0.46	<0.01

[1]CFFQ, comprehensive food-frequency questionnaire; ICC, intraclass correlation coefficient; SFFQ, short food-frequency questionnaire.

previous responses, but not so far apart that dietary patterns are likely to change. Correlation coefficients for reproducibility between 0.5 and 0.7 are considered acceptable (26). According to these criteria, our SFFQ demonstrated adequate levels of agreement between SFFQs at baseline and 6-mo follow-up (correlation coefficients >0.40), indicative of adequate reproducibility. A high degree of reproducibility may be a result of correlated error and therefore does not ensure validity. A low degree of reproducibility is a definitive indication of the questionnaire's inability to adequately measure long-term intake (26). Therefore, our findings suggest that the reproducibility of our SFFQ is likely adequate to support its implementation in longitudinal studies of diet in men with prostate cancer.

Residual adjustment for energy
In our study, after adjusting for energy, most food items and nutrients remained in agreement except for total fats, which may be attributed to differences in physical activity, body size, and metabolic efficiency and result in attenuation of associations. The difference could also be due to measurement error because total energy intake is not measured as well as other nutrients due to difficulty in adequately representing portion sizes, which has often been a critique of adjusting for energy. However, in our study, even after adjusting for energy, most food groups remained in agreement.

Limitations
A limitation of this study is the length of time (∼1 h) it takes to complete both the CFFQ and the SFFQ during the phone call at baseline and 6-mo follow-up. This may have increased patient fatigue, potentially resulting in less accurate results. When adjusting for energy, we found that the level of agreement for some nutrients (carbohy-

drates, fats, and proteins) was slightly weaker and agreement was attenuated between fried foods and total fats. A loss in agreement for this food group and nutrient may weaken associations with disease due to confounding factors or extraneous variation in nutrient intake unrelated to disease. Last, we found a statistically significant difference in prostate cancer risk category between the overall RADICAL PC study and substudy sample, although the substudy includes a random sample of the large RADICAL PC trial, it is possible that there are some differences.

Conclusions
The SFFQ appears to be accurate enough to rank participants based on their intake of major food groups, and it may be useful to investigate the importance of dietary patterns in men with prostate cancer and to increase study feasibility.

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