Original Article

Association between brown sugar intake and decreased risk of cancer in the Amami islands region, Japan

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Background and Objectives: Although excess white sugar intake imposes various health burdens, brown sugar is high in minerals, polyphenols, and polycosanol. However, few epidemiological studies have assessed brown sugar intake for health benefit. People in the Amami islands region, with a relatively high proportion of individuals with longevity, consume brown sugar as a type of refreshment. This cohort study was conducted in Amami to clarify the association of brown sugar intake with mortality risk and cancer incidence. **Methods and Study Design:** Participants were recruited from the general population of Amami as part of the Japan Multi-Institutional Collaborative Cohort Study. The number of eligible participants was 5004 (2057 men and 2947 women). During the median follow-up period of 13.4 years, 274 deaths and 338 cases of cancer were observed. HRs and 95% CIs were estimated using the Cox proportional hazard model, after adjusting for sugar-related and other variables. **Results:** After adjusting for their related confounding factors, brown sugar intake was associated with decreased HRs and a decreasing trend for all-site and stomach cancer incidence (p = 0.001 and 0.017, respectively) in women and men, and for breast cancer incidence (p = 0.034) in women. Additionally, a decreasing trend in the HRs for lung cancer incidence was observed among never and ex-smokers (p = 0.039). Decreased HRs for overall death, cancer, and cardiovascular disease were not apparent. **Conclusions:** Brown sugar intake was associated with decreased risk of all-site, stomach, and breast cancer incidences in the Amami population.

Key Words: brown sugar, mortality, cancer risk, cohort study

INTRODUCTION

The average life expectancy in Japan is the second highest in the world after that in Hong Kong;[1] this longevity has been attributed to the benefits of Japanese food.[2] However, regional differences in the distribution of long-lived people have been observed even within Japan; particularly, the proportion of long-lived people is high in Okinawa and the Amami Islands.[3-5] Although this "*art of healthy human aging*" has been extensively studied in Okinawa, scarce scientific research has been conducted on the equally captivating and important, but smaller and subtler regions of Amami.[4,6,7]

The Amami islands region has a subtropical climate and is located southwest of Japan. The diet in this region mainly comprises of Japanese food, such as rice, fish, soybean products. However, some other foods, such as green papaya and stir-fry dish, are common to Southeast Asia.[8] We are conducting a cohort study in the Amami island region, in which the baseline questionnaire inclu-

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des items on region-specific food intake, in addition to items on the general dietary habits of Japanese people. Recently, we have reported that consumption of the region-specific vegetables, handama and togan, was associated with a reduced risk of all-cause mortality in the Amami population.[9] These foods were concordantly reported in the "Amami Kodakara Project," an investigation conducted by the Kagoshima Prefecture to promote the uniqueness of the regional resources and culture using an ecological study design. This study highlighted several "longevity foods" that were more frequently consumed by healthy individuals over the age of 90 years living in the Amami Islands.[10] Furthermore, ecological surveys related to longevity, conducted in the Amami islands region, revealed that brown sugar, produced by taking advantage of the subtropical climate, is consumed as a type of refreshment (Figure 1), and was also listed as one of the "longevity foods."[10]

Brown sugar is high in minerals, such as potassium, calcium, magnesium, and sodium, as well as in polyphenols and polycosanol.[11] Among sugar cane derivatives, brown sugar contains several polyphenols that show higher antidiabetic potential at higher levels than does white sugar. In an *in vitro* study, brown sugar demonstrated 1, 1-diphenyl-2-picrylhydrazyl radical scavenging activity, which correlated with a moderate inhibition of yeast α-glucosidase; additionally, no significant effect was shown on porcine pancreatic α-amylase activity. Thus, it may inhibit key enzymes relevant to type 2 diabetes.[12] The effect of brown sugar on intestinal absorption of glucose has also been reported.[13] The non-sugar fraction of crude brown sugar prepared from sugarcane was found to inhibit the elevation of levels of serum triglycerides, lipid peroxides, and insulin in rats.[14] Furthermore, brown sugar polyphenols showed antioxidative activities[15] and antibacterial activity against cariogenic bacteria.[16] Furthermore, brown sugar intake led to reduced development of atherosclerosis in an experimental animal model.[17]

However, few epidemiological studies have assessed the relationship between brown sugar intake and health risks in humans. Therefore, this study aimed to clarify the association of brown sugar intake with mortality risk and cancer incidence in the residents of the Amami Islands.

METHODS

Study participants

Voluntary participants were recruited from the general population of the Amami Islands, as part of the Japan Multi-institutional Collaborative Cohort (J-MICC) Study, which has already been described elsewhere.[18] The baseline survey was conducted in five Amami islands among those who were undergoing routine health checkups conducted by the local government or private companies between 2005 and 2008. In total, 5015 participants aged 35–69 years provided written consent and were enrolled in the study (response rate: 69.8%). Eleven participants were excluded due to lack of information on brown sugar intake. Finally, the number of eligible participants was 5004 (2057 men and 2947 women). The present study was approved by the Ethics Review Committee for Human Genome/Gene Analysis Research at Kagoshima University Graduate School of Medical and Dental Sciences (No. 16 and 382).

The follow-up of this cohort is ongoing, and the follow-up data are added and revised every 2 years, which will continue until 2025. The present study accounted for deaths and the movement of people out of the study region based on local government records until December 2019, which revealed the movement of 299 people out of the region and 274 deaths. Information on the cause of death was also obtained from death certificates and vital statistics data after obtaining permission from the Ministry of Health, Labour and Welfare. The cause of death was defined using ICD-10 codes for cancer (n = 110; C00–D48) and for CVD (n = 48; I00–I99).

Information regarding the incidence and site of cancer was obtained from the regional cancer registry with permission from the Kagoshima Prefecture. Furthermore, additional surveys were conducted 5 and 10 years after the baseline survey, because some hospitals had not reported to the regional cancer registry system during the first half of the follow-up period. Additional information on cancer incidence was collected through a direct inter-

Figure 1. Brown sugar is habitually taken as a kind of refreshments with Japanese tea at the snack time in Amami island regions.

view of the study participants and through a mail-in questionnaire or telephone interview among those who did not attend the direct interview. The diagnosis of these self-reported cancer cases was then confirmed based on the medical records of the respective hospitals. Six participants who had a history of cancer before the baseline were excluded from the analysis on cancer incidence (n = 4998). The final number of cancer cases recorded was 338. The proportion of those with death certificate notification (DCN) was 15.4% (52/338) in the overall follow-up period (0.07–14.2 years) and 10.2% (31/304) in the early 10-year follow-up period, because of the time-lag of the cancer registration system, in which data was updated every 2 years, including previous cases.

Lifestyle factors

Information on lifestyle factors was collected using a standardized, self-administered, structured questionnaire used in the J-MICC studies. This included information regarding sociodemographic characteristics; lifestyle habits such as smoking and alcohol consumption; dietary habits; daily activity; habitual exercise; personal and family medical history; use of prescription medicines and supplements; reproductive history; and stress status. The FFQ was used to collect information on dietary intake of three staple foods (rice, bread, and noodles), 43 food items, and several vegetables, local fish, and brown sugar, which were selected from the "longevity food stuffs" identified in the "Amami Kodakara Project."[10]

Habitual consumption was ascertained by dividing the intake frequency of the 43 food items and four local vegetables into eight categories (almost never; 1–3 times/month; 1–2, 3–4, and 5–6 times/week; and 1, 2, and ≥ 3 times/day), and that of the three staple foods into six categories (almost never, 1–3 times/month; 1–2, 3–4, and 5–6 times/week; every day), followed by specific intake amounts per meal (breakfast, lunch, and dinner).

Daily energy, carbohydrate, and fatty intakes were estimated using the FFQ and the alcohol intake questionnaire. Although the present FFQ was not interpreted as a measure of absolute intake values, previous validity studies conducted in two different regions, including the Amami Islands, have shown it to be reflective of and useful for relative comparisons among participants.[19,20]

Clinical characteristics

Clinical data were collected as part of the health examinations in the J-MICC Study. They included determination of systolic blood pressure (SBP), diastolic blood pressure (DBP), triglyceride (TG), total cholesterol, HDL-C, and fasting blood glucose (FBG) levels.

Blood pressure was measured by a nurse or trained staff, with the participant in a sitting position, using a standard mercury sphygmomanometer or automated blood pressure measurement monitor. Biochemical tests were performed in each study region. LDL-C levels were calculated according to the Friedewald formula using a TG level < 400 mg/dL when LDL-C examination was not included in the routine health checkup.[21]

Statistical analysis

Age was divided into three groups (35–49, 50–59, and 60–69 years). Food and beverage intake was categorized into three groups according to a similar number of participants. Brown sugar intake was categorized as lowest (< 1 time/week, Q1), medium (1–6 times/week, Q2), and highest (≥ 1 time/day, Q3). Smoking and drinking were each categorized as current vs. former and never. Pack-years of smoking was calculated using the number of packs and duration of smoking among current smokers. BMI was categorized as < 18.5 kg/m^2, 18.5-24.9 kg/m^2, and ≥ 25 kg/m^2. Metabolic equivalents (METs) for habitual exercise and daily activity were calculated, accounting for intensity, frequency, and duration, as reported in the questionnaire.[22] Then, the estimation of METs h/day was categorized into three groups according to a similar number of participants as < 0.17, 0.17-2.17, and ≥ 2.18 for habitual exercise, and < 7.0, 7.0-21.0, and ≥ 21.0 for daily activity. Energy-adjusted intakes of carbohydrates and fat were estimated using the residual method.[23] The intakes of energy, carbohydrate, and fat were also categorized by percentiles into three groups.

Hypertension was defined as SBP ≥ 140 mmHg, DBP ≥ 90 mmHg, or intake of antihypertensive medication. Dyslipidemia was defined as TG level ≥ 150 mg/dL, LDL-C level ≥ 140 mg/dL, or HDL-C level < 40 mg/dL or the use of lipid-lowering agents. Glucose intolerance was defined as FBG level ≥ 110 mg/dL or the use of antidiabetic medication.

Person-years was calculated from the date at baseline (October 12, 2005, for the first participant) to the date of death or cancer incidence, the date of movement out of the region, or the last date of follow-up (December 31, 2019), whichever occurred first. The median follow-up period was 13.4 years (0.07–14.2 years) for death events and 13.5 years (0.07–14.2 years) for cancer incidence events. Cases of death and cancer that occurred within 1 year from the baseline survey were excluded from the analysis to minimize the effects of potential reverse causality. HRs and their 95% CIs for death and cancer incidence, according to the intake of brown sugar, were estimated using the Cox proportional hazard model after adjusting for confounding factors in three models: model 1: adjusted for age and sex; model 2: adjusted for age, sex, smoking, pack-years, drinking, daily activity, habitual exercise, BMI, hypertension, dyslipidemia, glucose intolerance, intake of meat, fish, green vegetables, fruits except citrus, citrus, Western sweets, Japanese sweets, coffee, and green tea; model 3: adjusted for age, sex, smoking, drinking, daily activity, habitual exercise, BMI, hypertension, dyslipidemia, glucose intolerance, intake of meat, fish, green vegetables, fruits except citrus, citrus, western sweets, Japanese sweets, coffee, green tea, and soft drink, and energy-adjusted intakes of carbohydrates and fat. The variables used for the adjustment were categorized into three groups according to a similar number of participants. Model 3 was used to estimate the HRs for cancer incidence. The HR for breast cancer was estimated with adjustment for additional reproductive factors (menarche age, delivery, breastfeeding, and menopause age), because these risk factors were breast cancer-specific. Cancer sites of the stomach, colon, lung, breast, and prostate were selected for subgroup analysis on cancer incidence, as these included enough cases for analysis. As the number of deceased cancer cases was limited for each site, subgroup analyses on cancer death were not performed.

The characteristics of study participants according to brown sugar intake at the baseline were tested using chi square test. Furthermore, the relationship between brown sugar intake, and hypertension, dyslipidemia and glucose intolerance at the baseline was also tested using p-value for trend on the odds ratios by logistic regression model after adjusted for the confounding variables of the model 3.

Differences were considered statistically significant when *p*-values were less than 0.05. All statistical analyses were performed using Stata software (version 16; Stata Corp., College Station, TX, USA).

RESULTS

The older age group and women consumed brown sugar more frequently (Table 1). Various lifestyles and dietary habits were associated with brown sugar intake at the baseline. Frequent intake of brown sugar was positively associated with daily activity; habitual exercise; intake of meat, fish, tofu, green vegetables, fruit except citrus, and nutrient intake of energy and fat. Brown sugar intake was also negatively associated with smoking, drinking, and glucose intolerance, and positively associated with hypertension. It was not related to dyslipidemia. However, the *p*-values for the trend on the odds ratios of brown sugar intake for hypertension, dyslipidemia and glucose intolerance were not statistically significant after adjusted for the confounding variables of the model 3 (*p* for trend: 0.743, 0.176, 0.795, respectively).

Medium intake of brown sugar was associated with a decreased HR for overall death in model 1 (HR1), but the deceasing trend was not statistically significant, and the HRs in models 2 and 3 (HR2 and HR3, respectively), after adjusting for other variables, were also not significant (Table 2). The decreasing trend in HR1 for cancer death was statistically significant, but the trends in HR2 and HR3 were non-significant. Decreased or increased HRs for CVD, based on brown sugar intake, were not observed.

Decreased HRs (0.73, 95% CI: 0.56–0.94 in the medium; 0.59, 95% CI: 0.43–0.81 in the highest) and their decreasing trend (*p* = 0.001) for all sites of cancer incidence according to brown sugar intake were observed in men and women after adjusting for their related confounding factors, similar to HR3 (Table 3). The decreas-

Table 1. Characteristics of study participants from the Amami islands region, according to brown sugar intake

	Brown sugar intake						*p*
	Q1		Q2		Q3		
	N	(%)	N	(%)	N	(%)	
Age in years							<0.001
35–49	789	40.6	422	22.7	145	12.1	
50–59	764	39.3	754	40.5	372	31.0	
60–69	390	20.1	686	36.8	682	56.9	
Total	1943	100	1862	100	1199	100	
Gender							<0.001
Women	946	48.7	1148	61.7	853	71.1	
Men	997	51.3	714	38.4	346	28.9	
Smoking (current & former)	811	41.7	500	26.9	240	20.0	<0.001
Drinking (current & former)	1277	65.7	1007	54.1	499	41.6	<0.001
Daily activity (≥ 21.0 METs x h/day)	644	33.1	628	33.7	480	40.0	<0.001
Habitual exercise (≥ 2.18 METs x h/day)	537	27.6	613	32.9	427	35.6	<0.001
BMI (≥ 25.0 kg/m^2)	849	43.7	861	46.2	537	44.8	0.047
Hypertension	756	38.9	742	39.9	499	41.6	0.001
Dyslipidemia	954	49.1	881	47.3	571	47.6	0.087
Glucose intolerance	337	17.3	246	13.2	152	12.7	<0.001
Food intake							
Meat (≥ 3 times/week)	714	36.8	761	40.9	522	43.5	<0.001
Fish (≥ 5 times/week)	302	15.5	395	21.2	316	26.4	<0.001
Milk (≥ 1 times/day)	454	23.5	552	29.8	471	39.4	<0.001
Tofu (≥ 3 times/week)	628	32.6	721	39.0	624	52.1	<0.001
Green vegetables (≥ 3 times/week)	634	32.6	758	40.7	615	51.3	<0.001
Fruits except citrus (≥ 3 times/week)	344	17.7	488	26.2	471	39.3	<0.001
Citrus (≥ 3 times/week)	448	23.1	644	34.6	541	45.1	<0.001
Western sweets (≥ 1 times/week)	213	11.0	353	19.0	249	20.8	<0.001
Japanese sweets (≥ 1 times/week)	370	19.0	654	35.1	547	45.6	<0.001
Coffee (≥ 2 cups/day)	666	34.3	629	33.8	410	34.2	0.746
Green tea (≥ 3 cups/day)	434	22.3	615	33.0	631	52.6	<0.001
Soft drinks (≥ 3 cups/day)	596	30.7	612	32.9	521	43.5	<0.001
Nutrient intake							
Energy (≥ 1697 kcal/day)	633	32.6	615	33.0	420	35.0	0.180
Energy-adjusted carbohydrate (≥ 240.4 g/day)	693	35.7	578	31.0	397	33.1	<0.001
Energy-adjusted fat (≥ 47.2 g/day)	594	30.6	614	33.0	460	38.4	<0.001

Q1. lowest intake; Q2. medium intake; Q3. highest intake; METs. metabolic equivalents.

Table 2. Hazard ratios and 95% confidence intervals for the overall deaths and deaths due to cancer and cardiovascular disease, according to brown sugar intake

	Brown sugar intake								*p* for trend
	Q1		Q2			Q3			
	E/PY	HR	E/PY	HR	95%CI	E/PY	HR	95%CI	
Overall									
HR1†	114/23642	1.00	88/22823	0.69	0.52–0.92	72/14715	0.79	0.57–1.08	0.092
HR2‡		1.00		0.79	0.59–1.06		0.93	0.66–1.31	0.574
HR3§		1.00		0.79	0.59–1.06		0.93	0.66–1.31	0.566
Cancer									
HR1†	50/23642	1.00	39/222823	0.69	0.45–1.07	21/14715	0.52	0.30–0.89	0.013
HR2‡		1.00		0.78	0.49–1.22		0.63	0.36–1.12	0.107
HR3§		1.00		0.77	0.49–1.21		0.62	0.35–1.11	0.098
CVD									
HR1†	16/23642	1.00	17/222823	0.90	0.45–1.81	15/14715	1.03	0.49–2.19	0.938
HR2‡		1.00		0.97	0.47–2.02		1.11	0.50–2.52	0.788
HR3§		1.00		0.97	0.47–2.02		1.13	0.50–2.55	0.764

Q1, lowest intake; Q2, medium intake; Q3, highest intake; E, events; PY, person-years
†Adjusted for age and sex
‡Adjusted for age, sex, smoking, pack-years, drinking, daily activity, habitual exercise, body mass index, hypertension, dyslipidemia, glucose intolerance, intake of meat, fish, green vegetables, fruits except citrus, citrus, Western sweets, Japanese sweets, coffee, green tea, and soft drinks
§Adjusted for age, sex, smoking, pack-years, drinking, daily activity, habitual exercise, body mass index, hypertension, dyslipidemia, glucose intolerance, intake of meat, fish, green vegetables, fruits except citrus, citrus, Western sweets, Japanese sweets, coffee, green tea, soft drinks, energy-adjusted carbohydrates, and energy-adjusted fat

ing trend in the HR for selected sites of cancer incidence according to brown sugar intake was statistically significant in stomach cancer (p = 0.017) and breast cancer in women (p = 0.035). The decreasing trend in the HRs for lung cancer incidence seemed to be decreased, but was not statistically significant. However, subgroup analysis showed a significant decreasing trend in the HRs for lung cancer incidence only among never and ex-smokers (number of events: 23, p = 0.039).

DISCUSSION

The present cohort study observed the association between brown sugar intake and the risk of death and cancer incidence. Decreased HRs for cancer incidence were found for all cancer sites including stomach and breast. The increased or decreased HRs for overall, cancer, and CVD deaths were not apparent.

White sugar intake is generally considered to be harmful to health, but epidemiological studies have not fully supported such effects.[24] The association between sugar intake and obesity is controversial.[24] Some studies on sweetened beverages have observed a positive association with obesity, but the same studies emphasized methodological and accuracy issues of dietary intake assessment, especially associated with sugar consumption. A large prospective study reported that total fructose intake was weakly positively associated with all-cause mortality in both women and men, whereas added sugar, sucrose, and added sucrose intakes were inversely associated with other-cause mortality in men.[25] A Japanese cohort study observed that the high intake of starch reduced mortality, whereas the high intake of sugars, including glucose,

Table 3. Hazard ratios and 95% confidence intervals for all-site and selected sites of cancer, according to brown sugar intake

	Brown sugar intake								*p* for trend
	Q1		Q2			Q3			
	E/PY	HR†	E/PY	HR†	95%CI	E/PY	HR†	95%CI	
Women and men									
All site	144/23315	1.00	122/23165	0.73	0.56–0.94	72/14870	0.59	0.43–0.81	0.001
Stomach	19/23315	1.00	17/23165	0.60	0.29–1.26	6/14870	0.28	0.09–0.83	0.017
Colorectum	14/23315	1.00	12/23165	0.80	0.35–1.87	7/14870	0.75	0.27–2.08	0.554
Lung	17/23315	1.00	11/23165	0.52	0.22–1.24	5/14870	0.37	0.12–1.11	0.055
Women									
Breast‡	29/11870	1.00	21/14414	0.53	0.28–0.98	15/10674	0.48	0.23–0.98	0.035
Men									
Prostate	10/12445	1.00	10/8751	0.92	0.35–2.42	7/4195	0.90	0.29–2.79	0.848

Q1, lowest intake; Q2, medium intake; Q3, highest intake; E, events; PY, person-years
†Adjusted for age, sex, smoking, pack-years, drinking, daily activity, habitual exercise, body mass index, hypertension, dyslipidemia, glucose intolerance, intake of meat, fish, green vegetables, fruits except citrus, citrus, Western sweets, Japanese sweets, coffee, green tea, soft drinks, energy-adjusted carbohydrates, and energy-adjusted fat
‡Adjusted for age, smoking, drinking, daily activity, habitual exercise, body mass index, hypertension, dyslipidemia, glucose intolerance, intake of meat, fish, green vegetables, fruits except citrus, citrus, Western sweets, Japanese sweets, coffee, green tea, energy-adjusted carbohydrates, energy-adjusted fat, and menarche, delivery, breast feeding, and menopause

fructose and sucrose, increased mortality in men.[26] A positive association between added sugar intake and CVD diseases was reported in the US.[27-29]

The epidemiological evidence for the association between sugar-sweetened beverage consumption and cancer risk is limited, but several prospective studies have suggested that a high intake might increase the risk of obesity-related cancers as well as breast and prostate cancer.[30] Furthermore, studies have associated colorectal cancer with sugar, but a residual confounding effect by energy intake and glycemic load was emphasized.[31]

Brown sugar has high mineral content, such as potassium, calcium, magnesium, and sodium, as well as in polyphenols and polycosanol.[11] Several in vitro and in vivo studies have shown the effects of brown sugar on the inhibition for porcine pancreatic α-amylase activity, which is relevant to several factors including: type 2 diabetes;[12] intestinal absorption of glucose;[13] the elevation of serum triglyceride, lipid peroxides, and insulin of rats;[14] antioxidative activities;[15] antibacterial activity against cariogenic bacteria;[16] and the reduced development of atherosclerosis in an experimental animal model.[17] However, few epidemiological study observed its protective effect on heath. People in the present study region of the Amami Islands habitually consume brown sugar as a type of refreshment. This dietary habit makes it an appropriate region to investigate the effect of brown sugar intake on health after controlling for the intake of other sugars. Actually, the association between brown sugar intake and CVD was not observed in the present study, although a positive association between added sugar intake and CVD diseases was reported in the US.[27-29]

The present study found that brown sugar intake was associated with decreased HRs for all sites of cancer incidence, especially stomach and breast cancers. Furthermore, a decreased HR for lung cancer was observed among never and ex-smokers. The HRs for cancer-related death with brown sugar intake seemed to decrease but were not statistically significant. The decreased HRs may suggest the hypothetical effect of brown sugar intake may be involved in cancer prevention. Sweetened food items, beverages, and carbohydrates were carefully adjusted to control for confounding factors. Furthermore, an increased HR for colon cancer was not observed, although a previous study reported a positive association between sugar-sweetened beverage intake and early onset colorectal cancer among women.[31] Thus, the sugar itself in the ingested brown sugar may have a lesser influence on the present results. Decreased HRs for several sites of cancer suggest that brown sugar intake may interact with common protective pathways associated with different cancers, or may be associated with another confounding factor that has not been adjusted for in this study.

The mechanisms underlying the association between brown sugar intake and decreased cancer risk was not clear, but several potential explanations can be listed. Brown sugar has polyphenols,[11,32] and showed antioxidative activities[15,32] and antibacterial activity against cariogenic bacteria[16] in *in vitro* and *in vivo* studies. Flavonoids identified from sugarcane juice also showed *in vitro* antiproliferative activity against several human cancer cell lines, with higher selectivity toward cells of the breast.[33] A lot of studies reported preventive effects for cancer by polyphenols[34] and flavonoids.[35] Another potential mechanism is an inhibitory effect for increase in blood glucose level. Several in vitro and in vivo studies have shown the effects of brown sugar on the inhibition for porcine pancreatic α-amylase activity, which is relevant to type 2 diabetes;[12] intestinal absorption of glucose;[13] and insulin of rats.[14] An intervention study among 14 healthy Malay individuals reported that the participants with minimally refined brown sugar jelly intake revealed lower levels in satiety profiles (peptide tyrosine and C-peptide) and glycemic profile (glucagon) than those with refined sugar jelly intake.[36] Potential causal associations were identified for genetically predicted type 2 diabetes mellitus and fasting insulin concentrations and risk of endometrial, pancreas, kidney, breast, lung, and cervical cancers.[37]

Limitations

This study had several limitations. First, residual confounding factors might have been present, although adjustments were made for known possible confounders. Although intake of sugar was not completely adjusted, surrogate items, such as Western sweets, Japanese sweets, soft drinks and carbohydrate were used for the adjustment. Sweetened beverages were the representative food item for total sugar intake in the Japanese cohort study.[26] Furthermore, participants who frequently consumed brown sugar had relatively healthy lifestyles, which might have led to an underestimation of the health burden risk. However, the effect thereof was likely small, because the HRs for overall and CVD deaths were not increased, and decreased HRs were observed only for cancer incidence. Second, the HRs for cancer death and incidence could not be compared due to the limited number of cancer deaths. As this cohort study is ongoing, further follow-up will increase the number of events, allowing comparisons of the HRs.

Conclusions

We identified an association between brown sugar intake and the risk of cancer incidence in the Amami islands region, where brown sugar is ingested as a type of refreshment. Brown sugar intake was associated with decreased all-site, stomach, and breast cancer incidences. Furthermore, a decreased risk for lung cancer was also associated with brown sugar intake among never and ex-smokers in this region. Further studies should be conducted to confirm the specific impacts of brown sugar on health benefits before recommended for its effectiveness. Furthermore, excess intake of brown sugar should be avoided, due to the excess intake of the energy.

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CONFLICT OF INTEREST AND FUNDING DISCLOSURES

The authors declare no conflict of interest.

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