Original Article

Intake of local vegetables and decreased risk of mortality and cancer incidence in Amami island regions, Japan

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Background and Objectives: There is emerging scientific evidence of the health benefits of traditional food plants at both molecular and folk remedy levels; however, epidemiological observations are limited. The Amami island region of Japan has a variety of unique traditions conserved till today, where a cohort study was conducted in 2005. The objective of this study was to investigate the associations between the intake of common and local vegetables and the risk of mortality and cancer incidence in Amami. **Methods and Study Design:** Participants were enrolled from the general population of Amami as part of the Japan Multi-institutional Collaborative Cohort (J-MICC) Study. In total, 5,015 participants (2,053 men and 2,962 women) aged 35-69 years were enrolled in this study. They were followed up to obtain information on movement, death, and cancer incidence. The hazard ratios (HRs) and 95% CIs were estimated using the Cox proportional hazard model after adjusting for potential confounding factors. **Results:** A significant inverse association was observed between cabbage intake and the HRs for overall mortality (p for trend=0.046) and lung cancer incidence (p=0.016). Intake of handama and togan as local vegetables was associated with decreased HRs for overall mortality (p=0.019 and 0.036, respectively). **Conclusions:** While the molecular and biochemical reasoning and residual confounding factors behind this association remain unclear, the findings of this study suggest that the dietary lifestyle in Amami has a positive impact on the residents, which can significantly decrease mortality risk.

Key Words: local vegetables, overall death, cohort study, cabbage, lung cancer

INTRODUCTION

Indigenous knowledge has repeatedly been the basis from which modern scientific knowledge has been derived. In particular, there is emerging scientific evidence of the health benefits of many traditional food plants at both molecular and folk remedy levels, and this ancestral knowledge has been repeatedly applied not only for the conservation of biodiversity and cultures, but also for drug development and community health.[1]

Amami islands (henceforth Amami) together with Okinawa, located southwest of Japan, forms a chain of islands known as the Ryukyu archipelago. The region has a variety of unique traditions that have been preserved due to its geographical isolation (Figure 1). While the residents of Amami have historically faced and still face many challenges of living on a remote island with limited access to healthcare, it has also become known for its high longevity rate, with a higher proportion of people living beyond 100 years compared with the average Japanese, even after accounting for its demographic structure, similar to the neighboring islands of Okinawa.[2-5] Although this "art of healthy human aging" has been extensively studied in Okinawa, very little scientific research has been conducted on the equally captivating and important, but smaller and more subtle regions of Amami.[3,6]

The "Amami Kodakara Project," conducted by Kagoshima Prefecture in an attempt to promote the uniqueness of the regional resources and culture in an ecological study design, highlighted several "longevity foods" that were more frequently consumed by healthy individuals over the age of 90 living in Amami.[7] A large proportion of the foods highlighted were local vegetables such as

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Figure 1. Amami is located southwest of Japan, and together with Okinawa forms a chain of islands known as the Ryukyu archipelago.

nira (local leek/Chinese chives), *imoduru* (sweet-potato vines), *handama* (local spinach), *togan*, unripe papaya consumed as a vegetable, and local fruits such as *shima-mikan* (island-mikan oranges), and passion-fruit. While the Japan Dietetic Association, approved by the Japanese Ministry of Health and Welfare, promotes the use of local food products in their dietary guidelines, and the "Amami Kodakara Project" studied the nutritional breakdown of the "longevity foods" they had raised, there has never been, to the best of our knowledge, an overarching epidemiological study on the protective effects of these "longevity foods" or specific local vegetables and fruits from Amami on death and/or cancer risk to date.

There have been extensive studies and suggestions that vegetable and fruit consumption work protectively to reduce overall mortality, certain cancers, and cardiovascular disease (CVD) worldwide, although specific associations are still controversial and some studies argue otherwise.[8-12] In particular, non-starchy vegetables and fruits contain a plethora of potential anti-tumorigenic agents, and many have proven to reduce the risk of specific cancers.[13] However, these international dietary studies and reports do not include traditional Amamian foods, which are less known globally.

We conducted a cohort study to investigate the associations of the intake of common and local vegetables with the risk of mortality and cancer incidence in Amami, where there is a greater longevity rate among the elderly population in comparison to the general Japanese population.

METHODS

Study subjects

Subjects were voluntarily enrolled individuals from the general population of Amami as part of the Japan Multi-institutional Collaborative Cohort (J-MICC) Study, which has already been described.[14] The baseline survey was conducted across five Amami islands between 2005 and 2008 among those who were undergoing routine health checkups conducted by the local government or private companies. In total, 5,015 participants (2,053 men and 2,962 women) aged 35–69 years gave their written consent and were enrolled in this study (response rate: 69.8%). The present study was approved by the Ethics Review Committee for Human Genome/Gene Analysis Research at our institution (No. 16 and No. 382).

The follow-up of this cohort is ongoing and 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 239 people and 243 deaths.

Information regarding the incidence and site of cancer was obtained from the regional cancer registry with permission from 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. Additional information on cancer incidence was collected through a direct interview 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 medical records at the respective hospitals. The final recorded number of cancer cases was 292. The proportion of those with death certificate notification (DCN) was 6.5% (19/292) and the mortality/incidence ratio (MI ratio) was 0.31 (90/292).

Lifestyle factors

Information on lifestyle factors was collected using a standardized, self-administered structured questionnaire used in J-MICC studies. This included information regarding sociodemographic characteristics, lifestyle habits such as smoking and alcohol habits, dietary habits, daily activity, habitual exercise, personal and family medical history, use of prescription medicines and supplements, reproductive history, and stress status. The food frequency questionnaire (FFQ) was used to collect information on dietary intake including 3 staple foods (rice, bread, and noodle), 43 food items, and 4 local vegetables (handama, nira, togan and papaya) that were picked out from the "longevity food stuffs" identified in the "Amami Kodakara Project".[7]

Handama (*Gynura bicolor*) is a green leafy vegetable with a purple-colored abaxial side (Figure 2a). It is commonly eaten boiled or raw with soy sauce as a side dish (Figure 3a). *Nira* (*Allium tuberosum*), is another green leafy vegetable with flat, narrow leaves and a strong fragrance (Figure 2b). It is eaten fried or boiled with other ingredients (Figure 3b). *Togan* (*Benincasa hispida*) is an edible perennial plant of the Cucurbitaceae family and can be preserved up to six months after harvest (Figure 2c). It is mostly eaten boiled (Figure 3c). Papaya (*Carica papaya*) is a common tropical fruit that can be found in backyards or side walks of Amami (Figure 2d). It is served before ripe as a vegetable, in the form of pickles, salad, or fried vegetables (Figure 3d).

Habitual consumption was ascertained with intake frequency of the 43 food items and 4 local vegetables divided into eight categories (almost never, 1-3 times/month, 1-2, 3-4, and 5-6 times/week, 1, 2, and ≥3 times/day), and the consumption frequency of the three staple foods divided 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 calorie and saturated fatty acid intakes were estimated using the FFQ and the alcohol intake questionnaire. Although the FFQ used in this study should not be interpreted as a measure of absolute intake values, previous validity studies conducted in two regions, including Amami, have shown it to be reflective of, and useful for, relative comparison among the participants.[15,16]

Statistical analysis

Food intake was categorized by intake frequency of <1, 1-2, and ≥3 times/week for vegetables, fruits, and red meat. Broccoli, handama, togan, and papaya were exceptions, as there were fewer participants consuming these foods at higher frequencies; these were sorted into the following categories: almost never, <1, and ≥1 time/week. Smokers were categorized as current, former, and never, while BMI was categorized as <18.5, 18.5-24.9 and ≥25. The Brinkman index was calculated using the average number of cigarettes per day and smoking years, and it

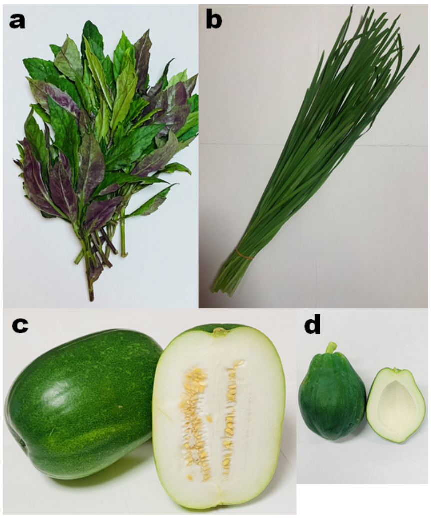

Figure 2. (a) *Handama* leaves are green on the adaxial surface, and reddish purple on the abaxial side; (b) *Nira* has flat and narrow leaves, and a strong fragrance; (c) *Togan* has a dark green rind and white, firm flesh; (d) Papaya as a vegetable is eaten while still green and young (unripe).

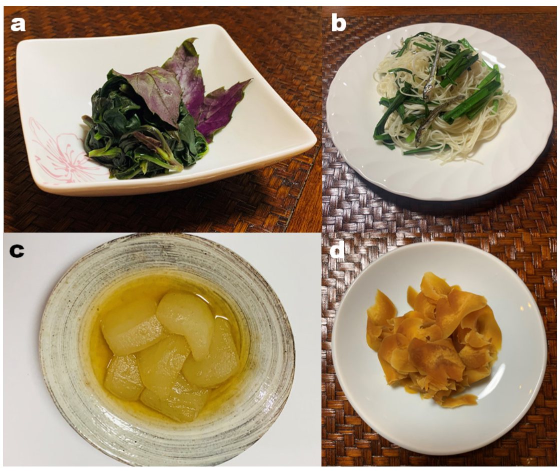

Figure 3. (a) *Ohitashi* (vegetables boiled in stock and served with soy-sauce) using *handama*; (b) A local Amami dish called *Abura-soumen*, which contains thin boiled noodles stir-fried with *nira*; (c) *Togan* is boiled in stock with soy-sauce; (d) Papaya pickled in soy-sauce, brown sugar, and white distilled liquor.

was included as an adjusting variable to calculate lung cancer risk. Drinking habits were classified as non-, ex-, or current drinkers. The total alcohol consumption amount was then estimated for current drinkers in the form of cumulative ethanol intake, using consumption frequency and intake amount of each beverage type (beer, Japanese sake, shochu, whiskey, and wine). Furthermore, total alcohol consumption was categorized as none, ≤20 g, and >20 g ethanol/day based on the recommended maximum intake of alcohol under Japanese governmental guidelines.16 Metabolic equivalents (METs) for habitual exercise and daily activity were calculated, accounting for intensity, frequency, and duration, as reported in the questionnaire. The estimation of METs/h/day was based on the duration and intensity of the exercise: 3.4 for light exercise, 7.0 for moderate exercise, and 10.0 for heavy exercise respectively.[18]

Habitual exercise, daily activity, and saturated fatty acids, were categorized by percentiles into three groups, and calorie intake into four groups. Age was also divided into four groups (35-44, 45-54, 55-64, and 65-69 years).

Person-years were calculated from the date when the baseline survey was conducted 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), depending on whichever occurred first. Hazard ratios (HRs) and their 95% confidence intervals (CIs) for death and cancer incidence according to the intake of vegetable (green leafy vegetables, green-yellow vegetables), cruciferous vegetables (cabbage, broccoli), fruits (fruits other than citrus, citrus fruits), and local vegetables (handama, nira, togan, papaya) were estimated using the Cox proportional hazard model. Age, sex, BMI, alcohol consumption, smoking habit, daily activity, habitual exercise, and intake of calories, red meat, and saturated fatty acids were used to control for confounding factors. Although CVD, including stroke, is also a major cause of death, this was not included in the present analysis due to the limited number of events (n=24).[11]

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

RESULTS

The age distribution was not apparently different between men and women, and slightly shifted to older populations in both sexes (Table 1). Women reported consuming vegetables and fruits more frequently, including local vegetables such as *handama*, *togan*, and papaya. Meanwhile, the consumption of meat, smoking, and drinking was more prevalent among men than among women.

A significant inverse association was observed between cabbage intake and the HRs for overall death, in which HR was 0.53 (0.36-0.77) for those with moderate intake (1-2 times/week) and 0.59 (0.37-0.95) for those with greater intake (≥3 times/week) (p=0.046) (Table 2). The HRs for cancer mortality in relation to cabbage intake did not show statistically significant differences. A decrease in HR (0.69, 0.48-0.99) was also observed among those with moderate broccoli intake (1-3 times/month), but was borderline (0.69, 0.47-1.02) among those with the greatest intake (≥1 times/week). Intake of other common vegetables and fruits were not associated with a significant decrease or increase in HR for overall or cancer mortality.

Intake of *handama* and *togan*, being local vegetables,

Table 1. Characteristics of subjects by sex

	Men (n=2053) N (%)	Women (n=2963) N (%)
Age (years)		
35-44	271 (13.2)	334 (11.3)
45-54	689 (33.6)	992 (33.5)
55-64	706 (34.4)	1135 (38.3)
65-69	387 (18.9)	501 (16.9)
Smoking (current)	661 (32.2)	144 (4.9)
Brinkman index (>400)	587 (28.6)	57 (1.9)
Alcohol consumption (>20 g ethanol/day)	1131 (55.1)	110 (3.7)
BMI (≥25)	913 (47.0)	956 (35.5)
Daily activity (>20.0 METs·h/day)	879 (43.1)	993 (34.0)
Habitual exercise (>3.25 METs·h/day)	440 (22.8)	448 (17.5)
Red meat intake (≥3 times/w)	644 (31.5)	1362 (46.3)
Fruit and vegetable intake		
Green leafy vegetables (≥3 times/w)	267 (13.1)	672 (22.9)
Green-yellow vegetables (≥3 times/w)	236 (11.5)	787 (26.7)
Cabbage (≥3 times/w)	315 (15.4)	727 (24.7)
Broccoli (≥1 times/w)	615 (30.0)	1379 (46.7)
Fruit (other than citrus) (≥3 times/w)	116 (5.7)	499 (16.9)
Citrus fruits (≥3 times/w)	143 (7.0)	564 (19.1)
Local foods intake		
Handama (≥1 times/w)	191 (9.4)	541 (18.4)
Nira (≥3 times/w)	136 (6.7)	487 (16.5)
Togan (≥1 times/w)	553 (27.1)	1009 (34.2)
Papaya (≥1 times/w)	482 (23.6)	885 (30.1)
Calorie intake (>1800 kcal/day)	1020 (49.7)	342 (11.5)
Saturated fatty acids intake (>12 g/day)	472 (24.9)	1172 (40.8)

BMI: body mass index; METs: metabolic equivalents; w: week; m: month.

Table 2. Hazard ratios and 95% confidence intervals of overall and cancer deaths according to intake of common vegetables and fruits in Amami

	Overall (n=242)			Cancer (n=77)		
	E/PY	HR†	95% CI	E/PY	HR†	95% CI
Green leafy vegetables						
<1 time/w	19/1928	1.00		26/15381	1.00	
1-2 times/w	135/31986	0.94	(0.67-1.30)	34/30922	0.96	(0.52-1.79)
≥3 times/w	88/23065	0.89	(0.57-1.39)	16/10676	1.19	(0.54-2.60)
p for trend		0.590			0.710	
Green-yellow vegetables						
<1 time/w	70/10417	1.00		21/10417		
1-2 times/w	132/35238	0.70	(0.50-1.00)	40/35238	0.81	(0.43-1.52)
≥3 times/w	40/11548	0.73	(0.46-1.18)	16/11548	0.90	(0.39-2.11)
p for trend		0.117			0.750	
Cruciferous vegetables						
Cabbage						
<1 time/w	48/6621	1.00		15/6621	1.00	
1-2 times/w	145/38581	0.53	(0.36-0.77)	49/38581	0.60	(0.30-1.19)
≥3 times/w	50/11933	0.59	(0.37-0.95)	13/11933	0.53	(0.22-1.30)
p for trend		0.046			0.183	
Broccoli						
<1 time/m	60/9440	1.00		19/9440	1.00	
1-3 times/m	96/25196	0.69	(0.48-0.99)	33/25196	0.97	(0.49-1.91)
≥1 time/w	87/22576	0.69	(0.47-1.02)	25/22576	0.74	(0.35-1.57)
p for trend		0.094			0.386	
Fruit other than citrus						
<1 time/w	134/26761	1.00		38/26761	1.00	
1-2 times/w	85/23747	0.85	(0.62-1.17)	31/23747	1.09	(0.62-1.91)
≥3 times/w	24/6801	0.94	(0.56-1.58)	8/6801	0.87	(0.32-2.35)
p for trend		0.515			0.965	
Citrus fruits						
<1 time/w	100/20958	1.00		31/20958	1.00	
1-2 times/w	108/28158	0.94	(0.68-1.29)	33/28158	0.93	(0.52-1.67)
≥3 times/w	33/8032	1.01	(0.61-1.66)	12/8032	1.18	(0.49-2.80)
p for trend		0.887			0.856	

E: events; PY: person-years; HR: hazard risk; CI: confidence interval; w: week; m: month; BMI: body mass index.
†Adjusted for age, sex, BMI, alcohol consumption, smoking habit, daily activity, habitual exercise, and intake of red meat, calorie and saturated fatty acids.

was associated with decreased HRs for overall death (*p*=0.019 and 0.036, respectively) (Table 3). Moderate intake of *nira* was also related to decreased HR (0.71, 0.51-0.98), although this inverse association was not maintained for those with the greatest intake or as an overall trend for consumption frequency. Decreased HR for cancer death was not observed for any of the four local vegetables.

Cabbage intake was also associated with decreased HRs for lung cancer incidence after adjusting for confounding factors, including the Brinkman index. HRs were 0.20 (0.06-0.64) for moderate intake (1-2 time/week) and 0.15 (0.03-0.85) for the greatest intake (≥3 times/week), with significant decreasing trend (*p*=0.016) (Table 4). Decreased HR (0.36, 0.14-0.96) for stomach cancer incidence with moderate intake of cabbage was also observed, but the decreasing trend was not significant. No significant association was observed between the intake of the four local vegetables and HRs for cancer (Table 5).

DISCUSSION

The present study investigated the association of the intake of common and local vegetables with the risk of mortality and cancer incidence in Amami, where there is a higher longevity rate among the elderly population. Intake of cabbage was associated with decreased HRs for overall death and lung cancer incidence. Consumption of local vegetables such as *handama* and *togan* was related to decreased HRs for overall death.

Intake of common vegetable, and death and cancer incidence

The decreased risk of total mortality with the intake of cabbage and cruciferous vegetables is consistent with previous studies that have reported decreased all-cause mortality in many countries.[19,20] A systematic dose-response meta-analysis of prospective studies on fruit and vegetable intake reported a negative association between all-cause mortality and cruciferous vegetable consumption. However, we found no study to date that has studied this association among the Japanese population. The present findings are in concordance with the findings from other studies conducted outside Japan, providing evidence on the protective function of cabbage against lung cancer and for reducing all-cause mortality in the Asian population.

A decreased HR with cabbage intake was observed for lung cancer incidence after adjusting for confounding factors, including the major known cause of lung cancer, smoking habits, based on the Brinkman index. This effect of cabbage has been reported in several studies on crucif-

Table 3. Hazard ratios and 95% confidence intervals of overall and cancer deaths according to intake of local foods in Amami

	Overall (n=242)			Cancer (n=77)		
	E/PY	HR†	95% CI	E/PY	HR†	95% CI
Handama						
<1 time/w	76/12791	1.00		37/12791	1.00	
1-2 times/w	100/28849	0.78	(0.55 -1.12)	30/28849	1.44	(0.82-2.54)
≥3 times/w	65/15486	0.57	(0.34 - 0.96)	19/15486	0.63	(0.24-1.64)
p for trend	0.019			0.805		
Nira						
<1 time/w	115/23770	1.00		37/23770	1.00	
1-2 times/w	90/26126	0.71	(0.51 - 0.98)	30/26126	0.71	(0.40 - 1.27)
≥3 times/w	37/7239	1.25	(0.81 - 1.92)	10/7239	0.93	(0.41 - 2.15)
p for trend	0.957			0.560		
Togan						
<1 time/w	49/7211	1.00		12/7211	1.00	
1-2 times/w	126/31805	0.69	(0.47 - 1.01)	45/31805	1.24	(0.54 - 2.83)
≥3 times/w	67/18081	0.61	(0.40 - 0.94)	20/18081	1.02	(0.42 - 2.51)
p for trend	0.036			0.852		
Papaya						
<1 time/m	84/16586	1.00		18/16586		
1-3 times/m	84/24643	0.77	(0.55 - 1.09)	34/24643	1.73	(0.85 - 3.52)
≥1 time/w	70/15826	0.93	(0.64 - 1.34)	24/15826	1.81	(0.85 - 3.85)
p for trend	0.662			0.133		

E: events; PY: person-years; HR: hazard ratio; CI: confidence interval; m: month; w: week; BMI: body mass index.
†Adjusted for age, sex, BMI, alcohol consumption, smoking habit, daily activity, habitual exercise, and intake of red meat, calorie and saturated fatty acids.

erous vegetables, which have suggested this to be the effect of glucosinolates, namely indoles and isothiocyanates which have anticarcinogenic properties.[21-23]

The aforementioned meta-analysis also reported a decreased risk of all-cause mortality with the intake of apples, pears, citrus fruits, green leafy vegetables, and salads. However, these associations were not observed in the present study. Dietary habits, including food types, consumption amounts, methods of cooking, and ingredient combinations, vary widely by country and region, even in Japan. This may have influenced the present results, although the comparative information is limited.

Local vegetable intake and risk of death

The intake of local vegetables such as *handama* and *togan* was associated with decreased HRs for overall death. To the best of our knowledge, there have been no previous reports on these specific associations (mainly due to the minimal studies that have been conducted fundamentally on these local foods), although the association between vegetable intake in general and decreased risk of total mortality has been reported in many studies.

Handama (otherwise known as Okinawa Spinach, *Gynura bicolor*, or *kinjisou*) is native to East Asian countries such as China, Taiwan, Myanmar, and Thailand, and is found to grow in open areas along rivers and roads. Its leaves, abaxially purple in color and green on the adaxial side, give it a distinctive look.[24] Very few studies have thus far been conducted on *G. bicolor*, although several recent molecular and mice studies have provided scientific evidence for its anti-diabetic and anti-inflammatory properties, attributed to its chemical components: dicaffeoylquinic acid or caffeic acid group and flavonoids, respectively.[25-27] *Togan* (otherwise known as white gourd, winter melon, *Benincasa hispida*, or *shibui*) belonging to the Cucurbitaceae family has equally been studied very little, but are used in Chinese oriental medicine as a diuretic, laxative, and a treatment for blood diseases.[28] Recent studies have also suggested its antiulcerogenic, antioxidant, and hypolipidemic effects, possibly due to its phytoconstituents, including flavone and sterols.[29-32]

A reduction in overall mortality is a composite measure that portrays the compound effect of different causes of death and a complex combination of different factors that increase or decrease the risk of each cause. It is difficult to clarify what the specific effect of *handama* and *togan* is with regard to decreasing the HR of overall death in the present observational study, but their protective effects against cancer may be relatively insignificant, because neither the HR for cancer nor that for death incidence was reduced through the intake of any of the vegetables. Furthermore, although possible known confounders were adjusted for, an unidentified confounding factor associated with a more traditional "Amamian lifestyle," that corresponds with or includes a greater consumption of *handama* and *togan*, may still exist. This additional unknown factor could be one that needs to be adjusted to truly comprehend the level at which these vegetables directly decrease the HR of death. Further follow-up with an increased number of different and specific causes of death is also required to clarify the effect of each vegetable on decreasing the risk of death.

Limitations

This study had several limitations. First, residual confounding factors that influence the HR of death and cancer may still exist, although common and known possible factors were adjusted for. As mentioned previously, this could be a factor that is based on or associated with local Amamian lifestyles and, possibly, even intertwined with the consumption levels of local vegetables, with the

Table 4. Hazard ratios and 95% confidence intervals of cancer incidence according to intake of common vegetables and fruits in Amami

	Men and Women														Women			
	PY	All (n=292)			Stomach (n=35)			Colorectum (n=40)			Lung (n=20)			PY	Breast (n=64)		
		E	HR†	95% CI	E	HR†	95% CI	E	HR†	95% CI	E	HR‡	95% CI		E	HR†	95% CI
Green leafy vegetables																	
<1 time/w	15381	81	1.00		12	1.00		9	1.00		11	1.00		7310	12	1.00	
1-2 times/w	30922	144	0.89	(0.66-1.20)	15	0.75	(0.30-1.87)	19	0.93	(0.40-2.15)	4	0.29	(0.08-1.04)	18661	32	1.19	(0.58-2.45)
≥3 time/w	10676	66	1.09	(0.74-1.59)	8	1.23	(0.42-3.55)	12	2.18	(0.85-5.60)	5	0.85	(0.23-3.22)	7673	20	1.59	(0.70-3.62)
p for trend		0.782			0.771			0.124			0.576				0.261		
Green-yellow vegetables																	
<1 time/w	10417	60	1.00		11	1.00		6	1.00		6	1.00		4137	6	1.00	
1-2 time/w	35238	170	0.83	(0.60-1.15)	19	0.44	(0.18-1.05)	23	1.08	(0.42-2.76)	9	0.46	(0.14-1.54)	20776	39	1.29	(0.50-3.32)
≥3 time/w	11548	62	1.02	(0.68-1.54)	5	0.62	(0.20-1.95)	11	2.73	(0.94-7.90)	5	0.76	(0.16-3.54)	8874	19	1.76	(0.64-4.86)
p for trend		0.948			0.284			0.050			0.648				0.208		
Cruciferous vegetables																	
Cabbage																	
<1 time/w	6621	40	1.00		8	1.00		3	1.00		6	1.00		3003	7	1.00	
1-2 time/w	38581	199	0.84	(0.58-1.21)	19	0.36	(0.14-0.96)	29	1.60	(0.47-5.44)	11	0.20	(0.06-0.64)	22430	43	0.85	(0.36-2.06)
≥3 time/w	11933	53	0.73	(0.46-1.16)	8	0.63	(0.20-1.98)	8	2.02	(0.51-8.03)	3	0.15	(0.03-0.85)	8287	14	0.77	(0.28-2.12)
p for trend		0.191			0.616			0.320			0.016				0.623		
Broccoli																	
<1 time/m	9440	46	1.00		8	1.00		3	1.00		5	1.00		4177	8	1.00	
1-3 times/m	25196	132	1.17	(0.80-1.70)	14	0.64	(0.24-1.66)	21	4.05	(0.94-17.44)	10	1.06	(0.27-4.13)	13999	27	1.10	(0.45-2.73)
≥1 time/w	22576	114	1.08	(0.73-1.60)	13	0.65	(0.23-1.78)	16	3.42	(0.76-15.43)	5	0.60	(0.13-2.85)	15609	29	1.14	(0.46-2.80)
p for trend		0.852			0.446			0.240			0.459				0.787		
Fruit other than citrus																	
<1 time/w	26761	129	1.00		16	1.00		21	1.00		11	1.00		12995	25	1.00	
1-2 time/w	23747	127	1.19	(0.91-1.57)	15	1.12	(0.48-2.59)	15	1.02	(0.49-2.13)	6	0.66	(0.20-2.13)	15355	26	0.91	(0.51-1.65)
≥3 time/w	6801	36	1.06	(0.68-1.66)	4	1.57	(0.47-5.23)	4	1.3	(0.41-4.09)	3	1.04	(0.20-5.49)	5577	13	1.08	(0.48-2.42)
p for trend		0.450			0.509			0.724			0.834				0.960		
Citrus fruits																	
<1 time/w	20958	109	1.00		12	1.00		20	1.00		12	1.00		9828	20	1.00	
1-2 time/w	28158	138	0.98	(0.74-1.30)	19	1.77	(0.71-4.44)	17	0.66	(0.32-1.34)	4	0.22	(0.06-0.85)	17490	28	0.91	(0.48-1.71)
≥3 time/w	8032	45	1.10	(0.73-1.67)	4	2.13	(0.58-7.87)	3	0.35	(0.08-1.60)	4	0.88	(0.20-3.80)	6427	16	1.2	(0.55-2.63)
p for trend		0.756			0.187			0.109			0.323				0.712		

HR: hazard ratio; CI: confidence interval; PY: person-years; E: events; w: week; m: month; BMI: body mass index.
†Adjusted for age, sex, BMI, alcohol consumption, smoking habit, daily activity, habitual exercise, calorie intake, red meat intake, and saturated fatty acids intake.
‡Adjusted for age, sex, BMI, alcohol consumption, smoking habit, daily activity, habitual exercise, calorie intake, red meat intake, and saturated fatty acids intake with Brinkman index.

Table 5. Hazard ratios and 95% confidence intervals of cancer incidence according to intake of local vegetables in Amami

	Men and Women													Women			
	PY	All (n=292)			Stomach (n=35)			Colorectum (n=40)			Lung (n=20)			PY	Breast (n=64)		
		E	HR†	95% CI	E	HR†	95% CI	E	HR†	95% CI	E	HR‡	95% CI		E	HR†	95% CI
Handama																	
<1 time/w	12791	51	1.00		5	1.00		9	1.00		5	1.00		6730	14	1.00	
1-2 times/w	28849	144	1.09	(0.81-1.46)	19	1.25	(0.51-3.08)	20	1.67	(0.77-3.61)	10	1.79	(0.60-5.31)	16734	26	0.71	(0.36-1.39)
≥3 time/w	15486	95	0.91	(0.62-1.33)	11	1.24	(0.40-3.84)	11	1.47	(0.56-3.83)	5	0.49	(0.06-4.03)	8332	24	0.78	(0.36-1.66)
p for trend		0.826			0.624			0.282			0.904				0.385		
Nira																	
<1 time/w	23770	125	1.00		20	1.00		19	1.00		12	1.00		11040	24	1.00	
1-2 time/w	26126	131	0.99	(0.74-1.30)	14	0.86	(0.38-1.92)	18	0.92	(0.45-1.88)	6	0.49	(0.15-1.56)	17076	34	0.91	(0.51-1.62)
≥3 time/w	7239	36	0.90	(0.58-1.39)	1	0.26	(0.03-2.06)	3	0.67	(0.19-2.43)	2	0.69	(0.14-3.44)	5649	6	0.49	(0.18-1.36)
p for trend		0.681			0.241			0.573			0.442				0.222		
Togan																	
<1 time/w	7211	34	1.00		4	1.00		6	1.00		5	1.00		3233	6	1.00	
1-2 time/w	31805	161	1.18	(0.77-1.80)	22	1.06	(0.35-3.22)	19	1.02	(0.34-3.08)	11	0.98	(0.25-3.86)	18831	37	1.06	(0.41-2.74)
≥3 time/w	18081	97	1.16	(0.74-1.81)	9	0.78	(0.22-2.75)	15	1.23	(0.39-3.84)	4	0.5	(0.09-2.61)	11675	21	0.87	(0.32-2.42)
p for trend		0.671			0.611			0.638			0.364				0.624		
Papaya																	
<1 time/w	16586	70	1.00		9	1.00		12	1.00		7	1.00		9192	17	1.00	
1-2 time/w	24643	123	1.19	(0.86-1.65)	16	1.19	(0.49-2.92)	15	0.73	(0.31-1.69)	8	1.71	(0.43-6.87)	14264	24	0.82	(0.42-1.61)
≥3 time/w	15826	98	1.32	(0.94-1.87)	10	0.82	(0.28-2.42)	13	1.31	(0.56-3.03)	5	1.99	(0.45-8.79)	10249	23	1.10	(0.55-2.21)
p for trend		0.112			0.758			0.497			0.369				0.740		

HR: hazard ratio; CI: confidence interval; PY: person-years; E: events; m: month; w: week; BMI: body mass index.
†Adjusted for age, sex, BMI, alcohol consumption, smoking habit, daily activity, habitual exercise, calorie intake, red meat intake, and saturated fatty acids intake.
‡Adjusted for age, sex, BMI, alcohol consumption, smoking habit, daily activity, habitual exercise, calorie intake, red meat intake, and saturated fatty acids intake with Brinkman index.

greater longevity rate among the elderly population. However, as there are few epidemiological studies that have examined the relationship between local vegetable intake and the risk of mortality and cancer incidence, the present findings provide fascinating evidence to reveal this association. Further studies are required to clarify the actual biological effects of these local vegetables and the confounding factors for mortality risk.

Second, the number of outcomes, especially for specific causes of death, is limited due to the limited size of the cohort population. Further data collected in this ongoing follow-up study will increase the statistical power on this topic. Third, genetic background is also a known factor that influences mortality risk and longevity, a factor that was not accounted for or adjusted for in this study.[33] However, comparative studies on the distribution of single nucleotide polymorphisms (SNPs) in Okinawa and Amami, compared to the mainland of Japan, did not present specific differences in SNPs associated with longevity, although SNP distributions were slightly different.[34,35] A comparison of the Amamian diet and health outcomes to those of Okinawa, also in the same archipelago, would be of considerable interest given its noted longevity.

Conclusion

This study evaluated the intake of common and local vegetables for the risk of mortality and cancer incidence in the Amami island regions of Japan. The results indicated that cabbage is a particularly remarkable food source, with a dose-dependent negative association with overall death and lung cancer. Intake of local vegetables, handama and togan, also showed an inverse relationship with overall death. While the molecular and biochemical reasoning and residual confounding variables behind this association remain unclear, it suggests that the dietary lifestyle of Amami has a positive impact on human health, significant enough to decrease the risk of death. This wisdom and brilliance of the Amami culture is one that should be preserved and spread to build a healthier society.

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AUTHOR DISCLOSURES

The authors declare no conflict of interest.

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