


A Japanese Box Lunch Bento Comprising Functional Foods Reduce Oxidative Stress in Men: A Pilot Study

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Abstract

The elder population has increased, introducing the profound medical and social challenge of maintaining health in aging seniors and the need for a medical approach to sustaining physical and mental health. The relationship between diseases and lifestyle-related factors such as diet and exercise are important. A health-conscious lifestyle improves one's health condition from a medical perspective, as indicated by new wellness monitoring using health devices and recent research into the efficacy of functional lunches incorporating utilitarian agricultural, forestry, and fishery products and foods. For a period of 3 months, and solely at lunchtime, 21 participants consumed the contents of a bento (Japanese box lunch), which incorporated functional (healthy) foods. A variety of factors were analyzed, including: weight, weight fluctuation rate, abdominal girth, triglycerides, total cholesterol value, and 8-OHdG (8-hydroxy-2'-deoxyguanosine). The bento comprising functional foods resulted in a reduction in both weight and abdominal girth without calorie restrictions. A reduction over time was observed in 8-OHdG, an oxidative stress marker, as compared to values prior to initiation of the study. Usage of a health device, exercise/dietary advice from a physician and nutritionist, and the availability of meals incorporating functional agricultural products might help prevent lifestyle disease and lead to improved health management.

Keywords

obesity, functional food, oxidative stress

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Introduction

A transformation in eating habits and a lack of exercise have led to metabolic syndrome and other lifestyle diseases which have intensified health concerns in Japan. The cancer has ranked as the leading cause of death in Japan since 1981, and the mortality rate increases annually. Prostate cancer disease and mortality rates are particularly notable; although low compared to those in Western countries, they have shown a remarkable increase. The high prostate cancer disease rate of Japanese who have migrated to the United States suggests a strong relationship between lifestyle and prostate cancer. The obesity rate of Japanese men doubled from 15% to 30% over a 30-year period (Tsugane, 2020). The impact of the Western diet rich in fatty foods

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Figure 1. An Example of Side Dishes of Japanese Lunch Box
 Note. The menu composed salmon steak, grilled oyster, salad with dressing, pickled radish, simmered taro in sweetened soy sauce, blueberry and boiled barley and rice.

and the lack of exercise cannot be ignored. This suggests a relationship between a high-calorie, high-fat diet (causing obesity and metabolic syndrome), and prostate cancer risk. A case study in Hawaii identified that 25% of prostate cancer cases were linked to a diet characterized by highly saturated fatty acids (Hankin et al., 1992). Obesity is known to be a strong risk factor in prostate cancer (Wilson et al., 2012). There are reports that metabolic syndrome, which is linked to obesity, is a likely risk factor in prostate cancer as well as in type-2 diabetes and cardiovascular disease. Obesity leads to an increase in insulin and inflammatory cytokines, and a decrease in adiponectin and testosterone. These changes are thought to participate in prostate cell carcinogenesis and malignant progression (Fujita et al., 2019). Body mass index (BMI) has an actual correlation with prostate cancer prognosis, with a BMI ≥ 30 kg/m² roughly doubling prostate cancer deaths (Chan et al., 2014).

Japan's Ministry of Agriculture, Forestry, and Fisheries (MAFF) is committed to the realization of a society in which individuals may enjoy a rich and healthy life based on eating habits derived from Japan's abundant foods. Meanwhile, the field of health devices has introduced the age of simplified lifelog monitoring with the increasing spread of mobile devices such as wearable sensors and iPhones which enable biodata and daily meal log oversight. The current study used healthy functional agricultural and processed foods, a wearable device application for recording aspects of daily life such as activity levels, meals, and weight, and a menu tailor-made for each individual's condition to create a system rendering a preventive effect on lifestyle disease through appropriate adherence to the relevant meals.

Materials and Methods

The current study targeted healthy males aged 30 to 65 familiar with the usage of mobile devices such as iPhones

and who provided written consent for participation. Individuals taking dietary/health supplements or consuming government-approved "food for specified health use" were excluded. All participants were Japanese. Approval was obtained from the Hospital Research Ethics Board (Approval number: 14-1822).

Participants consumed a bento (Japanese lunch box) planned by a certified nutritionist and incorporating functional foods at weekday lunchtime for a 3-month period. In order for the subjects to record their lifelogs on a daily basis, they used an activity meter linked with a mobile terminal and a meal recording application which uses a camera. Participants were surveyed regarding weight, abdominal girth, triglyceride values, total cholesterol value, and 8-hydroxy-2'-deoxyguanosine (8-OHdG) prior to the study, and at the 1-month, 2-month, and 3-month points. BMI was calculated as weight divided by height squared (kilograms per square meter). For detection of 8-OHdG, serum samples were prepared from whole blood samples, which were centrifuged at 1500 g for 10 min as soon as possible after collection from subjects and were kept at -80 C° until used. The procedure for detecting 8-OHdG in serum by Highly Sensitive 8-OHdG Check ELISA (KOG-HS10E, Japan Institute For the Control of Aging, Shizuoka, Japan) followed the instructions of the kit. Briefly, 50 ul of samples were used per well, mixed with an equal volume of the primary antibody and incubated overnight at 4°C. After washing and addition of the second antibody, absorbance was measured at a wavelength of 450 nm, and concentrations were calculated with the 4-PL program.

Bento meals centered around amylose-rich rice, barley abundant in β -glucan, and partially abraded brown rice grain. Bento caloric content ranged from 700 to 800 calories. No dietary restrictions were placed on subjects' breakfast and dinner meals. Functional agricultural products were utilized as bento ingredients in this study. Aside from essential nutrients, functional agricultural products also include chemical components which, when consumed in proper quantity, are anticipated to be effective in health promotion. They include

Dietary fiber: β -glucan, arabinoxylan, and fucoidan
 Polyphenols: catechin, rutin, quercetin, procyanidin, anthocyanin, and isoflavone
 Carotenoids: lycopene, β -cryptoxanthin, *astaxanthin*, and lutein
 Amino acids and peptides: alliin, anserine, and carnosine
 Other: allyl isothiocyanate, *capsaicin*, zinc, and so on.

Figure 1 indicated an example of Japanese lunch box.

For most participants of the study, venous blood was obtained in the morning and serum was separated immediately. Weight, abdominal circumference, total cholesterol, luteinizing hormone (LH), testosterone, and free testosterone were surveyed and/or collected from laboratory data.

Table 1. Changes of Clinical Variables After Taking Functional Bento.

Variable	Mean \pm SD		Mean difference	<i>p</i> value	95% confidence interval for difference	
	Initiation	Month 3			Lower	Up
Weight (kg)	83.38 \pm 17.89	81.80 \pm 17.97	-1.576	.018	-2.852	-0.301
Waist circumference (cm)	98.67 \pm 12.14	94.92 \pm 12.58	-3.738	<0.001	-4.922	-2.554
Hemoglobin (g/dL)	15.34 \pm 1.18	15.43 \pm 1.25	0.09	.438	-0.148	0.329
Total protein (g/dL)	7.41 \pm 0.33	7.42 \pm 0.26	0.005	.935	-0.116	0.126
Albumin (g/dL)	4.66 \pm 0.27	4.69 \pm 0.24	0.024	.600	-0.069	0.117
Total bilirubin (mg/dL)	1.01 \pm 0.51	0.93 \pm 0.42	-0.077	.290	-0.224	0.07
AST (U/L)	28.19 \pm 20.02	24.52 \pm 12.67	-3.667	.266	-10.348	3.015
ALT (U/L)	37.00 \pm 30.84	35.24 \pm 28.51	-1.762	.663	-10.063	6.54
LDH (U/L)	168.48 \pm 19.76	171.14 \pm 21.30	2.667	.378	-3.508	8.842
ALP (U/L)	218.00 \pm 58.22	218.05 \pm 54.13	0.048	.991	-8.924	9.019
γ GTP (U/L)	48.05 \pm 30.73	45.86 \pm 28.61	-2.19	.623	-11.335	6.954
Cholinesterase (U/L)	394.71 \pm 57.35	391.62 \pm 54.20	-3.095	.569	-14.245	8.055
Amylase (U/L)	64.76 \pm 22.83	65.86 \pm 25.12	1.095	.682	-4.399	6.59
Total Cholesterol (mg/dL)	207.67 \pm 32.27	207.71 \pm 30.65	0.048	.992	-9.401	9.496
Triglyceride (mg/dL)	182.48 \pm 111.69	222.10 \pm 223.33	39.619	.271	-33.399	112.637
HDL (mg/dL)	46.19 \pm 10.85	48.48 \pm 11.17	2.286	.078	-0.282	4.853
LDL (mg/dL)	161.48 \pm 33.32	159.24 \pm 29.76	-2.238	.639	-12.045	7.569
BUN (mg/dL)	13.51 \pm 2.60	12.87 \pm 2.38	-0.638	.188	-1.615	0.339
Creatinine (mg/dL)	0.87 \pm 0.10	0.86 \pm 0.11	-0.009	.570	-0.042	0.024
Uric acid (mg/dL)	6.70 \pm 1.38	6.55 \pm 1.21	-0.152	.384	-0.51	0.205
Na (mmol/L)	141.43 \pm 1.25	140.57 \pm 1.40	-0.857	.002	-1.362	-0.353
K (mmol/L)	4.3 \pm 0.25	4.17 \pm 0.25	-0.13	.070	-0.272	0.012
Cl (mmol/L)	104.81 \pm 1.60	103.48 \pm 1.63	-1.333	<0.001	-1.982	-0.684
Ca (mg/dL)	9.41 \pm 0.27	9.53 \pm 0.32	0.119	.093	-0.022	0.26
P (mg/dL)	3.48 \pm 0.44	3.59 \pm 0.51	0.114	.320	-0.12	0.348
Glucose (mg/dL)	102.52 \pm 19.76	102.71 \pm 15.26	0.19	.968	-9.686	10.067
HbA1C (%)	5.67 \pm 0.55	5.72 \pm 0.49	0.048	.241	-0.035	0.13
Cortisol (mg/dL)	10.18 \pm 3.54	11.06 \pm 4.21	0.881	.375	-1.146	2.908
LH (mIU/mL)	4.51 \pm 2.52	5.51 \pm 1.62	1.005	.168	-0.461	2.471
FSH (mIU/mL)	5.53 \pm 2.56	5.80 \pm 2.59	0.276	.193	-0.152	0.704
Testosterone (ng/dL)	452.39 \pm 167.40	415.30 \pm 161.92	-37.086	.208	-96.524	22.352
Free testosterone (pg/mL)	16.15 \pm 6.60	14.98 \pm 7.05	-1.171	.127	-2.708	0.365

Data are expressed as mean \pm SD. For analysis, we used repeated measures ANOVA (SPSS). A difference was considered significant at a value of $*p < .05$.

Results

Thirty individuals initially enrolled in the study, but once subjects who refused to consume bento meals or for whom blood samples could not be obtained at all time points were excluded, 21 remained to comprise the analysis set.

Study participants ranged in age from 24 to 64 years; the median age of all enrolled patients was 40 years. The mean age of participants was 41 years. The average BMI of all enrolled patients was 28.3 (± 4.81). Baseline characteristics were summarized in Table 1.

Participants, weighed an average of 1.576 kg less at the end of the study compared to measurements taken prior to study initiation, showing a statistically significant decrease, $p = .018$, $F(3, 60) = 4.593$. Abdominal girth decreased by an average of 3.738 cm, $p < .001$, $F(3, 60) = 24.499$, (Table 1). Blood tests showed consuming bento lunches incorporating functional foods have statistically significant difference on Na value, $p = .035$, $F(3, 60) = 3.047$, and Cl value, $p = .001$, $F(3, 60) = 6.434$, among baseline, 1-month, 2-month, and 3-month points. Pairwise comparisons between 3-month and baseline from repeated measure ANOVA demonstrating a significant decline in Na (-0.857 , $p = .002$) and Cl (-1.333 , $p < .001$).

8-OHdG has a structure of hydroxylated deoxyguanosine (dG) which is one of the “bases” forming DNA, and

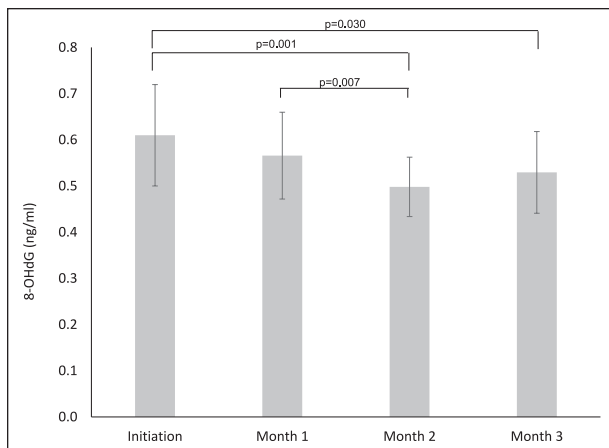


Figure 2. 8-OHdG Transitions Following Bento Meals Incorporating Functional Foods

Note. 8-OHdG was measured in serum prior to the study and at the 1-month, 2-month, and 3-month points. A statistically significant decline in 8-OHdG was observed at the 2-month ($p=.001$) and 3-month ($p=.030$) points compared to values prior to the study. A significant change ($p=.007$) was also observed between the 1-month and 2-month points. 8-OHdG; 8-hydroxy-2'-deoxyguanosin.

when oxidative stress occurs with active oxygen, the 8-OHdG is excreted in the healing process. Therefore, through the mechanism of active oxygen, 8-OHdG is a marker which keenly reflects influences on the body, and is measurable in blood, urine, and saliva. As a result of the functional bento, repeated measures ANOVA, $p = .001$, $F(3, 60) = 5.974$, revealed significant difference on 8-OHdG level. Pairwise comparisons test showed significant decline in 8-OHdG level was observed at the 2-month (-0.112 , $p = .001$) and 3-month (-0.08 , $p = .03$) points compared to the study pre-initiation point (Figure 2).

Discussion

Lifestyle improvements are effective in prevention of cancer and other diseases, but the key lies in the degree of continuation. The use of lifelogs is anticipated to help individuals manage their own health in various circumstances. The current study targeted healthy men and employed health devices to gather and monitor physical data which were used, together with bento lunches planned by certified nutritionists and incorporating functional foods, to investigate weight reduction and an inhibitory effect on oxidative stress. Following consumption of bento incorporating functional foods, reductions were observed in weight, abdominal girth, and 8-OHdG, an oxidative stress marker. Oxidative stress is closely related to carcinogenesis and malignant progression. Reactive oxygen stress (ROS) has been implicated in prostate carcinogenesis, and repair of oxidative DNA damage may be defective in prostate tissues as a result of uncontrolled

oxidative stress and increased oxidative DNA damage (Malins et al., 2003). An immunohistochemical study using 8-OHdG antibodies revealed positive staining in nuclei of prostate epithelial cells and prostate cancer cells (Ide et al., 2012). Our previous result indicated that the prostate may be particularly vulnerable to oxidative attack.

The incidence rate of prostate cancer is lower in Asian countries compared to Western nations, and dietary intake of polyphenols, which have a strong antioxidative action, may participate in the low incidence rate of prostate cancer (Horie, 2012). Guidance on prevention of cancer (and prostate cancer in particular) centers on appropriate exercise, avoidance of a high-fat diet, and foods rich in polyphenols such as vegetables (including tomatoes), fruits, soybeans, coffee, and green tea (Thapa & Ghosh, 2012). Results of the current study suggested that an intake of ingredients incorporating functional foods may help reduce oxidative stress on cells.

The bento comprising functional foods resulted in a reduction in both weight and abdominal girth without calorie restrictions. One of the reasons is the participants were consuming β -glucan daily. The intake of high β -glucan barley led to significant and safe reductions in body weight, BMI, and abdominal girth in individuals with visceral fat obesity (Aoe et al., 2017). Barley high β -glucan may contribute to loss the weight and abdominal girth in this study. Lower Na and Cl levels may indicate effective sodium restriction over the 3-month study period. These results show that functional food intake may help put the brakes on canceration with lower oxidative stress, and that weight loss may help prevent lifestyle disease such as metabolic syndrome and hypertension.

Attention is being increasingly paid to the relationship between telomeres, one factor determining cell longevity, and lifestyle factors such as exercise and diet. Telomeres, found in eukaryotes, are comprised of characteristic repetitive sequences of DNA at the chromosome end and various proteins, and have the role of preserving these chromosome ends. Telomeres are essential to normal chromosome division during cell division, grow short in cell deterioration which occurs with aging as chromosome instability increases, and are responsible for cell death and carcinogenesis. When telomere length shortens, the risk of bladder and lung cancer increases, and there are reports suggesting implication of this process in prostate cancer and prostatic intraepithelial neoplasia (Mirabello et al., 2009). On the other hand, telomere maintenance is enabled by an enzyme known as a telomerase. Ornish et al. divided subjects in a study into an active surveillance, low-risk prostate cancer group as the control group, and a lifestyle change group, and conducted follow-up for 2 years. The lifestyle change group consumed a low-fat diet of fruits and vegetables, walked for 30 min, did yoga, and enjoyed

the psychological care of social support. In the control group, 13 (27%) of the 49 subjects experienced progression of their prostate cancer requiring intervention (surgery, radiation treatment, etc.), while only 2 (5%) of the 43 subjects in the lifestyle change group required therapeutic intervention (Frattaroli et al., 2008). A comparative analysis of lifestyle changes using peripheral blood leukocytes reportedly reported significant improvements in elevated telomerase activity and controlled telomere length (Ornish et al., 2013). Exercise is known to yield physical and mental improvement in individuals, and at least 30 MET-hours/week of exercise reportedly cuts prostate cancer risk by about 40% (Patel et al., 2005). One report of a meta-analysis of 19 cohort studies and 24 case-control studies identified a weak inverse correlation between exercise and prostate cancer (Liu et al., 2011). There are some limitations to the design of this study. We could not monitor entire food intake. The system utilizing a wearable device to enable video recording of meals and caloric intake with real-time information sharing between the user and the monitor will contribute healthy longevity. However, we could not obtain enough data to analyze daily caloric intake and activity, because the subject did not record them continuously. Otherwise, the possibility of artificial effects due to the other confounding factors such as exercise cannot be excluded. This system has task to improve and promote health conditions by continuous action change without losing motivation. Another limitation of this study is its relatively small sample size. A future large-scale, long-term observational study is necessary, and usage of these health devices to gather further data including genetic information on what types of foods and exercise would aid in disease prevention might lead to development of strategic cancer prevention tools to partner with therapeutic exercise and targeted foods helpful in prevention of obesity and metabolic syndrome.

Our results demonstrated that ensuring healthy longevity for men requires an approach embracing disease prevention and anti-aging in addition to surgery and other forms of medical management.

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Declaration of Conflicting Interests

The author(s) declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

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