Examining the Beneficial Aspects of Nutritional Guidance Using Estimated Daily Salt Intake in Cancer Patients with Ischemic Heart Disease

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Background:
The outcomes associated with nutritional guidance for patients with ischemic heart disease undergoing cancer treatment have not been explored. We examined the effects of nutritional guidance using estimated daily salt intake in cancer patients with ischemic heart disease.

Material/Methods:
We examined the data from physical examinations and laboratory assessments of 27 patients with suspected excessive salt intake who underwent coronary angiography for the first time and received nutritional guidance on their next visit to the Department of Cardiology of Shizuoka Cancer Center between May 2018 and March 2020. Salinity measurement was not used in the nutritional guidance method, but the patients were instructed to reduce consumption of salt-containing foods. We compared the frequency of the estimated daily salt intake with the frequency of categories requiring salt control (food, cooking, and table salts).

Results:
The median age of the participants was 74 (range, 63–86) years. The estimated daily salt intake and the rate of change in the triglyceride level were negatively correlated (r=–0.61, *P*<0.01). The estimated daily salt intake was reduced in 16 cases; there was a relative decrease in the frequency of food intake among categories requiring salt control compared with that in the nonimproved cases (*P*<0.01). No difference was found between the cancer stage and the affected site of the digestive system in either group (*P*=0.64, *P*=0.39).

Conclusions:
Nutritional guidance on dietary habits without using salinity measurement was beneficial in preventing ischemic heart disease and food intake reduction in cancer patients.

MeSH Keywords:
Cancer Care Facilities • Coronary Angiography • Nutrition Assessment

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Background

Heart storage disease has the second highest mortality rate after cancer [1]. The prevalence of cancer increases with age [2], but the epidemiological statistics for heart disease are not clear [3]. Medical guidelines indicate a daily salt intake of 3.8 g due to the role of salt intake in the development of this illness [4–6]. Although there is evidence that a reduction in dietary salt results in nutritional deficiency and loss of appetite [7], there has been no discussion concerning the effects on triglycerides (TGs) [8], which reflect the oral intake quantity of nutrients. No significant effects have been reported for the effects of sodium and the Dietary Approaches to Stop Hypertension (DASH) diet on serum lipids [9]. However, the adverse effects of high TG levels on the heart are well known [10]. In recent years, guidelines for hypertension have been presented [11], but there has been no report focusing on the actual dietary habits of patients. The methodologies and outcomes of nutritional guidance for patients with ischemic heart disease undergoing cancer treatment have not been explored. This could be because there are many ready-made food options in cities, latent variations in salt content that cannot be aggregated, and several available resources on the salt content of foods. Furthermore, because there are no evaluation tools, it is likely that the salinity calculation method of each patient and dietitian would not be consistent. In addition, salinity measurement is probably infeasible in cancer patients with suspected ischemic heart disease who have adverse events [12] and a psychological burden [13] due to cancer treatment. The key to the therapeutic effect may lie in the subjective assessment of each patient [14]. According to the National Nutrition Survey, salt intake is the highest for men and women in their 60s [15]. The estimation of daily salt intake [16] can be easily evaluated from voluntary urine using salt intake evaluation methods [11], and it has been shown to be useful for hypertensive patients. Although this phenomenon has been reported, it has not been discussed as a nutritional guidance for patients with heart disease who are undergoing cancer treatment and its outcomes have not been considered. The purpose of this study was to explore the benefit of voluntary urine (estimated daily salt intake) in the nutritional guidance regarding the dietary habits of cancer patients undergoing coronary angiography (CAG).

Material and Methods

Participants

We conducted a retrospective subset analysis. The study was approved by the Institutional Review Board (IRB) of the Shizuoka Cancer Center (SCC) (SCCIRB approval number: 30-J78) and performed in accordance with the principles of the Declaration of Helsinki. Patient consent was obtained using the in-hospital bulletin board of the SCCIRB for a retrospective study.

We enrolled 27 patients who underwent CAG for the first time and accepted nutritional guidance during the study period from May 2018 to March 2020. Patients were excluded if they received cancer treatment during the evaluation period, had renal cancer, or were judged to be ineligible for this clinical study by the attending physician.

Nutritional guidance

The baseline evaluation (T1) was the morning before CAG or the day of CAG (day of admission), and the follow-up evaluation (T2), in which nutritional guidance was implemented, was performed the morning on the day of the next department's medical examination. **Figure 1** shows a patient interview sheet filled by medical staff during nutritional guidance.

The following variables were evaluated from T1 to T2. Estimated daily salt intake [16] was calculated from voluntary urine (from the second urine after waking for the day and onward, once, >10 mL), as follows:

Estimated daily salt intake (g/d)=$1.29 \times$(Na: mEq/L/Cr: mg/dL/$10 \times$ expected creatinine excretion)$^{0.392}$

Male/female creatinine excretion (mg/d)=$14.89 \times$body weight (kg)+$16.14 \times$height (cm)$-2.04 \times$age-2244.45 (Equation 1)

where Na is the urine sodium concentration (mEq/L), and Cr is the urine creatinine concentration (mg/dL).

Body composition (skeletal muscle mass, fat mass, body water, and phase angle) was evaluated using the body weight and bioelectrical impedance analysis (In Body S20®), which examined fasting and used bioelectrical impedance analysis, respectively [17,18]. Blood biochemical values (total cholesterol [TC], TGs, high-density lipoprotein cholesterol [HDL-C]) were evaluated to examine fasting.

The rate of change of these variables from T1 to T2 was calculated, and the relationship with estimated daily salt intake was investigated. We also investigated the relationship between the estimated daily salt intake and changes in the skeletal muscle mass, and the relationship between the cancer stage in T2 and the rate of change in skeletal muscle mass from T1 to T2.

The method for nutritional guidance method was as follows. The categories listed below requiring salt control [19] (food, cooking, and table salt) were subjectively evaluated by the patients at T1 based on their dietary habits and patterns. Guidance for healthy food substitutions was provided, and each category was reevaluated at T2.

Nutritional guidance for cardiology patients
Questionnaire
Living alone: Yes   No
There are suppotters in the neighborhood: Yes   No
• Cooking home-made foods: cook it myself rate=   :   (   )
• Do you eat out?   Frequency   times a week   Where and what
• Do you eat home meal replacements? Frequency   times a week   Where and what • Checking salt content   I do not check
☆ Dietary Habit

Food salt
• Bread: Once a day   1–3 times a week   4–6 times a week   Twice a day   Every meal
• Noodles: Once a day   1–3 times a week   4–6 times a week   Twice a day   Evety meal
  Type: Cup   Noodle   Soba   Udon
• Soup   Once a day   1–3 times a week   4–6 times a week   Twice a day   Every meal
• Pickles   Once a day   1–3 times a week   4–6 times a week   Twice a day   Evety meal
• Salted (ham, dried fish, salted salmon, etc.)
  Once a day   1–3 times a week   4–6 times a week   Twice a day   Every meal
• Bran floor   Yes   No

Cooking salt
Cooking salt
• Use of Dashi   Natural (   ) Commercial soup stock (   ) Both natural and commercial
• Soy sauce   reduced salt   salt   sugar
• Frequency of fried food   times a week
  Seasoning   I measure seasoning   I do not measure seasoning

Table salt
• Seasoning   Frequently used ready-made foods

Daily meal pattetn
Wake-up time
Breakfast time

10:00

Lunch time

15:00

Dinner time

Late-night snack

Bedtime

Exercise of 30 minutes or more →2 times a week   Yes   No
Tobacco and drinking
Eat fast and eat until full
Defecation
Excerpts from the Shizuoka Cancer Center electronic medical records

Figure 1. Patient interview answer sheet for medical personnel

Food salt included salted products (e.g., pickles, meat/fish processed food, dried goods, bread, and noodles) for which the T1 alternatives were raw vegetables, boiled vegetables, tofu, egg dishes, rice, unsalted noodles (e.g., soba), and white fish. At the T2 evaluation, the frequency of use improved by >80% compared with T1. The substitution of ready-made products was not assessed.

The cooking salt category included commercial soup with added salt, consumed multiple times a day. The T1 alternative instruction was natural or commercial dashi without added salt, consumed once a day. The T2 evaluation assessed whether the alternative guidance had been adopted.

The table salt category included use of a soy sauce dispenser (frequent use) and ready-made products. The T1 alternative

instruction was to use a push-type soy sauce dispenser, how to read the amount of salinity of ready-made products (400 mg of sodium corresponds to approximately 1.0 g of salt), and preparation of homemade lunches that provide balanced nutrition with limited cooking salt. The T2 evaluation assessed adoption of alternative guidance.

Through dietary records and interviews, the frequency of use of the categories requiring salt control in eating habits were investigated during the past 3 days in all patients. Patients were divided into 2 groups, with and without reduced estimated daily salt intake at T2 (improved and nonimproved groups, respectively), and intake was compared with the frequency of use at T1. The cancer stage at T2 of both groups was also compared based on the cancer site (digestive and nondigestive systems).

Table 1. Comparison of the parameters*.

	T1 (n=27)		T2 (n=27)		*P***
Body weight, kg	62.4	(44.2–81.2)	61.8	(44.0–81.2)	0.94
Bioelectrical impedance analysis***					
Skeletal muscle mass, kg	23.9	(15.0–35.0)	24.7	(14.7–31.8)	0.93
Fat mass, kg	17.7	(7.6–35.9)	18.3	(8.2–36.6)	0.07
ECF/TBF	0.35	(0.26–0.36)	0.35	(0.32–0.37)	0.25
ECW/TBW	0.39	(0.30–0.41)	0.39	(0.38–0.41)	0.26
Phase angle, degree	4.85	(3.62–6.39)	4.86	(3.42–6.30)	0.75
Biochemical examination (blood)					
Total cholesterol, mg/dL	177	(87–267)	168	(85–261)	0.99
Triglycerides, mg/dL	106	(44–293)	114	(44–395)	0.35
HDL-C, mg/dL	49	(29–91)	49	(30–79)	0.73
Biochemical examination (voluntary urine)					
Creatinine urine, mg/dL	58.2	(13.1–338.3)	84.4	(15.9–276.6)	0.36
Sodium urine, mEq/L	105	(52–218)	90	(12–195)	0.93
Estimated daily salt intake, g	9.7	(3.8–14.9)	9.7	(3.1–14.0)	0.79

ECF – extracellular fluid; ECW – extracellular water; HDL-C – high-density lipoprotein cholesterol; TBF – total body fluid; TBW – total body water. * The data are expressed as median (range); ** *P* values are based on *t* tests; *** Edema value based on bioelectrical impedance analysis: ECF/TBF ≥0.39; ECW/TBW ≥0.43.

Statistical analysis

All variables were expressed as medians. The comparison of study variables was performed using *t* test and the Wilcoxon/Kruskal-Wallis test. Associations were analyzed by correlation analysis. Fisher's exact test was used for comparison of ratios. Calculations were performed using the statistical software, JMP® PRO12 (SAS Institute Inc., Cary, NC, USA) and R (version 3.5.1; R Foundation for Statistical Computing, Vienna, Austria). A significance level of 5% (2-tailed testing, *P*<0.05) was used in all analyses.

Results

The participants included 20 men and 7 women. Their median age was 74 (range, 63-86) years. The body mass index at T1 was 24.1 (range, 20.3–32.4) kg/m^2. The median period from T1 to T2 was 35 (range, 7–122) days, and all patients were diagnosed as having ischemic heart disease at T1 after undergoing CAG (24 cases of angina pectoris, 2 of coronary artery sclerosis, and 1 of myocardial infarction).

There was no difference in the estimated daily salt intake, body composition, and biochemical test values (**Table 1**) between T1 and T2. The change in the estimated daily salt intake from T1 to T2 and the rate of change of TGs were negatively correlated (r=−0.61, *P*<0.01; **Figure 2**). However, there was no association

between the rate of change of TC, HDL-C, body weight, and body composition (skeletal muscle mass/fat mass) (r=0.04, *P*=0.83; r=0.34, *P*=0.09; r=0.32, *P*=0.11; r=0.17, *P*=0.40). The cancer stage (I, 10; II, 7; III, 2; IV, 7; unknown, 1) and the rate of change of skeletal muscle mass (I, −1.7; II, −1.5; III, −4.0; IV, −1.1; unknown, −0.7) did not show any significant difference in the multivariate analysis (*P*=0.83; Wilcoxon/Kruskal-Wallis test). All cases had no exercise habits.

In 16 of the 27 cases, the estimated daily salt intake improved at T2 following nutritional guidance at T1. A significant difference was found in the rate of TG change and the estimated daily salt intake (**Table 2**). Compared with the nonimproved group (11 cases), the frequency of consuming foods, such as salted food, bread and noodles etc., decreased by >80% per day in the improved group (16 cases, *P*<0.01). However, there was no difference in the cooking category including the frequency of consuming natural dashi or the frequency of using soy sauce dispensers in the table salt category (**Table 3**). There was no difference in the cancer stages and sites involving the digestive system and other systems between the 2 groups (*P*=0.64, *P*=0.39; **Table 2**).

Discussion

We tested blood biochemical values related to nutrient metabolism and found that TGs were negatively correlated with the

Table 2. Comparison between the improved group and the nonimproved group for estimated daily salt intake*.

	Improved group (n=16)	Nonimproved group (n=11)	P^{**}
Male: Female	12: 4	8: 3	1.00^{***}
Age, years	74 (63–85)	74 (67–86)	0.80
Assessment period, days	31 (7–111)	43 (21–122)	0.19
BMI, kg/m^2: T1	24.3 (20.2–32.4)	22.5 (21.5–27.8)	0.52
Bioelectrical impedance analysis			
%LBW loss of body weight: T1→T2	−0.2 (−3.0–3.3)	0.0 (−5.3–3.2)	0.94
%LSMM: T1→T2	−0.6 (−20.1–10.1)	1.8 (−14.8–10.2)	1.00
%LFM loss fat mass: T1→T2	1.6 (−24.2–36.8)	6.1 (−11.9–85.1)	0.60
Biochemical examination (blood)			
TC rate of change, %: T1→T2	−7.9 (−43.0–17.7)	−6.0 (−32.5–28)	0.69
TG rate of change, %: T1→T2	27.1 (−39.7–101.3)	−40.3 (−60.6–50)	<0.01
HDL-C rate of change, %: T1→T2	−3.4 (−42.9–37.1)	2.2 (−13.2–27.9)	0.37
Estimated daily salt intake rate of change, %: T1→T2	−25.0 (−75.2−−5.4)	12.4 (2.7–173.7)	<0.01
Stage of cancer	I: 4 II: 5 III: 1 IV: 5 Unknown site: 1	I: 6 II: 2 III: 1 IV: 2	0.64^{***}
Cancer site (digestive# and nondigestive)	Lung: 5 Colon: 3# Prostate: 2 Larynx: 2# Bladder: 1 Stomach: 1# Liver: 1# Esophagus: 1#	Stomach: 3# Liver: 2# Lung: 2 Colon: 2# Uterus: 1 Thyroid: 1	0.39^{***}

BMI – body mass index; HDL-C – high-density lipoprotein cholesterol; LBW – loss of body weight; LFM – loss fat mass; LSMM – loss skeletal muscle mass; TC – total cholesterol; TG – triglyceride. * The data are expressed as median (range); ** P values are based on Mann-Whitney test unless otherwise noted; *** P value is based on Fisher's exact test.

Table 3. Frequency ratio of categories requiring salt control in improved and nonimproved groups of daily estimated salt intake.

	Improved group (n=16)		Nonimproved group (n=11)		P^*
	T1	T2	T1	T2	
Food salt	38	7	21	19	<0.01
Cooking salt	15	6	10	4	1.00
Table salt	8	6	5	1	0.35

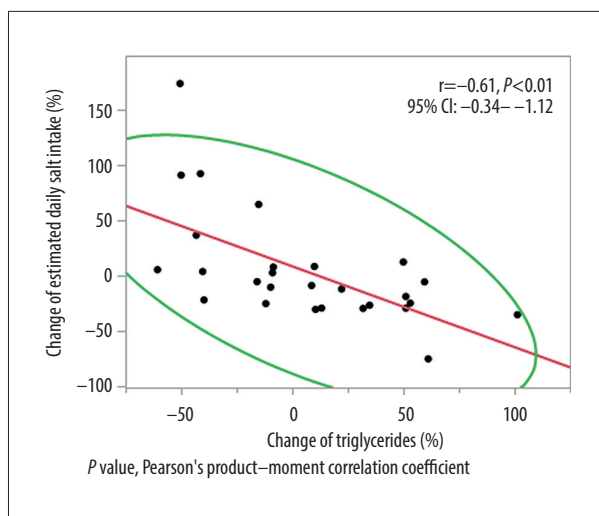T1 – baseline evaluation; T2 – follow-up evaluation. * P values are based on Fisher's exact test.

Figure 2. Relationship between estimated daily salt intake and rate of change of triglycerides

estimated daily salt intake (r=–0.61, P<0.01; **Figure 2**). While it has been reported that guidance for low salt intake can lead to decreased food intake [7], a meta-analysis found that TGs reflected an excessive oral intake of salt [8]. This finding suggested that patients with a lower salt intake at T2 had a higher oral nutritional intake resulting in increased TG levels. However, we found no significant difference in the body weight and body composition changes. Our findings suggested that reduced salt intake led to increased oral nutritional intake that resulted in high TG levels. This finding was contrary to those of a previous report [7]. Of the genes that have increased expression in response to feeding, the TG gene group has the highest rate of increase and the greatest fluctuation in expression due to diet [20]. Furthermore, in 1990, Iso et al. [21] showed a relationship between TGs and ischemic heart disease. In addition, a causal relationship has been shown between TG-related pathways and heart disease [10,22]. The fact that only TGs were associated with estimated daily salt intake may be due to the effects of nutritional metabolism other than the Warburg effect of cancer [23]. As TGs are involved in the DASH diet in cancer patients, we propose that guidance should be given in view of adherence in cancer patients whose TG levels exceed 150 mg/dL before and after receiving nutritional guidance focused on salinity control.

However, 2 crucial questions arise. Does the taste of salt in foods reflect salt intake? Is a salty taste equal to the salt content? The estimated daily salt intake at T1 was 9.7 g. This value was comparable to the salt intake of people in their 70s of the same generation (9.8 and 11.1 g/d in women and man participants, respectively) from the National Health and Nutrition Survey [15]. This finding indicated that the global intake of salt is high and suggested the need to support the treatment [24–26]. From T1 to T2, there was a relative decrease in the frequency of foods that the patients consumed,

which resulted in improved estimated daily salt intake (P<0.01, **Table 3**). In addition, no relationship was observed between the cancer stage and site at T2 and the estimated daily salt intake in the improved and nonimproved groups. Therefore, it was likely that the motivation of cancer patients affected the impact that nutritional guidance had on their dietary habits. Our results found that the nutritional guidance (i.e., reduction of salty food consumption frequency to <80% per day) in the subjective evaluation of each patient has a low burden on the patient and a scientific guidance effect, and is suitable, as a nutritional intervention method, for cancer patients. However, the guidance method and results of each patient's dietary habits for estimated daily salt intake (**Figure 1, Table 3**) were limited to relative evaluations [19]. It is likely necessary to evaluate the salt content in meals with measuring instruments.

Skeletal muscle mass and bioelectrical impedance analysis [27] were expected to affect nutritional metabolism. However, our results did not change during the course of the study (**Table 1**) and did not correlate with the rate of change in the estimated daily salt intake (r=0.32, P=0.11). In addition, there was no significant difference in the rate of change between the cancer stage and the skeletal muscle mass (P=0.83). Thus, it was likely that the effect on creatinine (a skeletal muscle mass metabolite that indicates the progression of cachexia [28,29]) was small.

This research aimed to support cancer patients who wanted to be treated without bias from the viewpoint of a registered dietitian. It proposed a new nutritional guidance method that can be widely applied even to patients without cancer. However, while we discussed the topic of ischemic heart disease and cancer, the effects in the context of salinity and nutrition aspects (e.g., saturated fatty acids, potassium) and exercise are not clear.

This study had some limitations. It was based on dietary habit adherence [6], evaluated through subjective evaluation of individual patients, and had a small sample size; however, it had a scientific guidance effect. This suggested that it was a suitable method of nutritional intervention for cancer patients [30–34]. Furthermore, this study involved a disease with a low prevalence, we did not include a comparison group of patients without cancer, and the outcome could not be traced back.

Conclusions

This study suggested that estimation of daily salt intake and nutritional guidance using dietary habits for cancer patients with ischemic heart disease had beneficial aspects. Considering the burden on cancer patients, nutritional guidance based on adherence (i.e., reduction of salty food consumption frequency to <80% per day) that does not require salt measurement may be sufficient.

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