RESEARCH COMMUNICATION

Japanese versus Mediterranean Diets and Cancer

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Abstract

   Morbidity and mortality statistics, including incidences of fat-related cancers (FRCs), and dietary intake and sources of fats and oils were compared for Japanese, Mediterranean and American people. Incidences of FRCs, except for steeply increasing colon cancer, have remained low in Japan. Similarly, Mediterranean people enjoy relatively low risks of FRCs compared with American people. The low risks of FRCs in Japanese may be explained by limited intake of fats and oils as a whole, and a low ratio of n-6 polyunsaturated fatty acids (PUFAs) versus n-3 PUFAs through consumption of the latter from marine foods. They also frequently consume vegetables and fruit, and dietary fiber. Mediterranean people moderately consume fats and oils from a large amount of olive oil, containing not only oleic acid but also polyphenols (including flavonoids), α-tocopherol and carotenoids (including β-carotene), which are antioxidants and anti-carcinogenic as in red wine, vegetables (including herbs) and fruit. The diet also features medium intake of fish and shellfish along with cereals/pasta/bread. From the standpoint of intake of total fat, the low risks of FRCs in Japanese seem "plausible," while the low risks in Mediterranean people may be termed "paradoxical." In summary, limited consumption of fats and oils, moderate intakes of marine foods, and vegetables and fruit, in line with a modest intake of energy may be advocated for promoting health, prolonging life and prevention of lifestyle-related diseases including FRCs.

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Key words: fat-related cancers, intake of fats and oils, Japanese diet, Mediterranean diet, n-6 PUFA vs. n-3 PUFA, sources of fats and oils

Introduction

   Cancer is caused by interaction between host and environmental factors and is associated with activation of oncogenes and inactivation of suppressor genes. Carcinogenesis progresses together with the contribution of multiple factors, multiple hits and multiple stages with a long latent period. Environmental factors appear to play major roles in the pathogenesis of cancer, generally exerting greater influence than genetic factors. Fat-related cancers (hereafter FRCs) at sites in the colon, breast, prostate, corpus uteri and ovary may be good examples in this respect (Prentice and Sheppard, 1990; Wynder et al., 1992; Giovannucci et al., 1994; WCRF/AICR, 1997).

   As is known, Japanese and Mediterranean people enjoy low risks of FRCs (Doll and Peto, 1981; Prentice and Sheppard, 1990; Wynder et al., 1992; Giovannucci et al.,

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Table 1. Morbidity/Mortality Statistics for Selected Diseases and Life Expectancy in Japan, Italy and USA

	Male			Female		
	Japan	Italy	USA	Japan	Italy	USA
Age-adjusted cancer incidence (/100,000) of						
colon	24.9[1]	16.0[2]	30.4[3]	15.7	12.9	21.6
breast	0.3	0.5	0.8	31.1	50.3	93.3
prostate	9.0	12.9	79.1	-	-	-
corpus uteri	-	-	-	4.1	8.6	18.4
ovary etc.	-	-	-	6.1	7.0	11.6
Age-adjusted mortality (/100,000)[4] from						
ischemic heart disease	27.7	80.3	137.3	14.3	34.6	70.3
cerebrovascular disease	55.6	55.4	30.8	38.4	43.2	26.3
Life expectancy(years) [4]	76.5	74.4	72.1	83.1	80.8	79.0

[1] Miyagi Cancer Registry, Japan during 1988-1992 in *Cancer Incidence in Five Continents Vol. VII*, Lyon, IARC, 1997.
[2] Latina Province, Italy during 1988-1992 in *ibid*.
[3] Connecticut Cancer Registry, USA, White during 1988-1992 in *ibid*.
[4] Data in 1993 based on *1994 World Health Statistics Annual,* 1995 and *1996 World Health Statistics Annual* , 1998.

1994; WCRF/AICR, 1997). We here compared morbidity and mortality statistics, including incidences of FRCs, mortality from coronary/ischemic heart disease (hereafter CHD) and life expectancy, in combination with similarities and differences of dietary intake and sources of fats and oils in Japanese, Mediterranean and Western (American) people.

Materials and Methods

Using data compiled by IARC and WHO (WHO, 1995; IARC/IACR, 1997; WHO, 1998), we assessed morbidity and mortality statistics, including incidences of FRCs, mortality from CHD and life expectancy, and reviewed literature in terms of the similarities and dissimilarities in absolute intake of major nutrients, composition of fatty acids, sources of selected fatty acids and cholesterol, and other relevant factors in the Japanese and Mediterranean diets compared with the American diet (Hirayama, 1978; Fidanza,1980; Block et al., 1985; Ferro-Luzzi and Sette,1989; Lands et al., 1990; Wynder et al., 1992; Freudenheim et al., 1993; Anti et al., 1994; de Lorgeril et al., 1994; Ferro-Luzzi and Branca, 1995; Sugano, 1996; Ernst et al., 1997; de Lorgeril et al., 1998; Tsuji and Tsuji, 1998; Alberti-Fidanza et al., 1999; Ferro-Luzzi, 1999; Lands, 1999; Simopoulos, 1999; Tokudome et al., 1999). The Mediterranean diet appears to be more diverse than that prevailing in Japan with traditional variation with the area of the region. However, both information on morbidity and mortality statistics and dietary intake was only available for Italy or Southern Italy and therefore we here employed these data as a surrogate index for the Mediterranean people and diet in general.

Results

Incidences of FRCs during 1988-1992, except for steeply increasing colon cancer, and mortality from CHD in 1993 have remained low in Japan (WHO, 1995; IARC/IACR, 1997; WHO, 1998) and life expectancy is the longest in the world (Table 1). In contrast, the mortality rate from cerebrovascular disease in Japanese males is high, in line with the continued high incidence of gastric cancer (Moore et al., 1999). Relatively low risks of FRCs and a low mortality from CHD are similarly enjoyed by Mediterranean people.

A comparison of intake of major nutrients among the Japanese, Mediterranean and American diets in the 1970s and 80s is given in Table 2 (Hirayama, 1978; Fidanza,1980; Ferro-Luzzi and Sette,1989; Lands et al., 1990; Wynder et al., 1992; Anti et al., 1994; de Lorgeril et al., 1994; Ferro-Luzzi and Branca, 1995; Sugano, 1996; Ernst et al., 1997; de Lorgeril et al., 1998; Tsuji and Tsuji, 1998; Alberti-Fidanza et al., 1999; Ferro-Luzzi, 1999; Lands, 1999; Simopoulos, 1999). These were chosen as suitable, given the latent period of at least 20 years necessary for cancer development. Over the last few decades decreased consumption of carbohydrates, more or less stable intake of protein, and increased intake of fats and oils, in particular, have been reported in the developed countries worldwide, including Japan, Mediterranean and other Western countries like the United State.

Table 2. Approximate Intake of Major Nutrients and Composition of Fatty Acids in Japanese, Mediterranean and American Diets[1] in the 1970s~80s.

	Japanese diet	Mediterranean diet	American diet
Total energy (kcal/day)	2,000	2,300	2,300
Protein in grams/day (energy %)	60~70 (10~15%)	70~80 (10~15%)	90~100 (15~20%)
Carbohydrate in grams/day (energy %)	300~350 (60~65%)	300~350 (50~55%)	250~300 (45~50%)
Total fat in grams/day (energy %)	40~50 (20~25%)	70~80 (30~35%)	80~90 (35~40%)
Animal fat : Vegetable fat : Marine fat	4 : 5 : 1	2 : 6 : 1	7 : 3: < 0.1
SFAs : MUFAs : PUFAs	1 : 1 : 1	2 : 5 : 2	2 : 2 : 1
n-6 PUFAs : n-3 PUFAs	4	6~8	10

[1] Hirayama, 1978; Fidanza,1980; Ferro-Luzzi and Sette,1989; Lands et al., 1990; Wynder et al., 1992; Anti et al., 1994; de Lorgeril et al., 1994; Ferro-Luzzi and Branca, 1995; Sugano, 1996; Ernst et al., 1997; de Lorgeril et al., 1998. Tsuji and Tsuji, 1998; Alberti-Fidanza et al., 1999; Ferro-Luzzi,1999; Lands, 1999; Simopoulos, 1999

Table 3. Sources of Selected Fatty Acids and Cholesterol in Japanese, Mediterranean and American Diets

Rank	Japan[1] Foods	%[4]	Italy[2] Foods	%	USA[3] Foods	%
Saturated fatty acids						
1.	Eggs, chicken	12.2	Olive oil	15.4	Hamburgers, cheesebgs, meat loaf	9.3
2.	Milk, whole	10.2	Whole milk	10.7	Whole milk, whole milk beverages	9.1
3.	Well-milled rice	5.3	Medium cheese: Swiss, provolone, caciocavallo	7.7	Cheeses, excluding cottage cheese	7.3
4.	Pork, Boston butt	4.4	Soft cheese: Bel Paese, Gorgonzola	6.3	Beef steaks, roasts	7.3
5.	Beef, chuck loin	2.9	Butter	5.9	Hot dogs, ham, lunch meats	7.0
Oleic acid						
1.	Eggs, chicken	12.5	Olive oil	52.7	Hamburgers, cheesebgs, meat loaf	8.3
2.	Salad oil, mixed	10.4	Peanut oil	4.6	Hot dogs, ham, lunch meats	7.4
3.	Mayonnaise	5.1	Sunflower, corn, soy and mixed seed oils	3.8	Doughnuts, cookies, cake	6.7
4.	Vegetable oil, mixed	4.4	Beef, medium fat	3.6	Beef steaks, roasts	6.5
5.	Milk, whole	3.8	Sausage and salami	3.4	Margarine	5.6
Linoleic acid						
1.	Salad oil, mixed	11.9	Sunflower, corn, soy and mixed seed oils	25.4	Mayonnaise, salad dressings	14.9
2.	Vegetable oil, mixed	8.2	Olive oil	24.5	Margarine	10.2
3.	*Tofu* (Soybean curd)	7.2	Peanut oil	8.4	French fries, fried potatoes	7.5
4.	Well-milled rice	6.7	Chicken and turkey	5.5	White bread, rolls, crackers	6.7
5.	Mayonnaise	5.9	Potatoes	2.9	Salad and cooking oils	6.5
Cholesterol						
1.	Eggs	51.9	Eggs	32.0	Eggs	35.9
2.	Whole milk	3.0	Beef, medium fat	10.4	Beef steaks, roasts	8.7
3.	Squid	2.7	Chicken and turkey	7.5	Hamburgers, cheesebgs, meat loaf	7.3
4.	Salmon	2.5	Whole milk	5.8	Whole milk, whole milk beverages	5.4
5.	Mayonnaise	2.4	Fish	5.5	Hot dogs, ham, lunch meats	4.3

[1] Tokudome et al.,1999. [2] Freudenheim et al., 1993. [3] Block et al., 1985. [4] Percentage contribution.

Total fat intakes were approximately 40~50, 70~80 and 80~90 grams per day, in the Japanese, mediterranean and American diets, respectively. Fat percentages were about 20~25%, 30~35% and 35~40%, in that order. The ratios of animal fat: vegetable fat: marine fat were 4 : 5 : 1, 2 : 6 : 1 and 7 : 3 : < 0.1, respectively. The ratios of saturated fatty acids (hereafter SFAs) : monounsaturated fatty acids (hereafter MUFAs) : polyunsaturated fatty acids (hereafter PUFAs) were 1 : 1 : 1, 2 : 5 : 2 and 2 : 2 : 1. The ratios of n-6 (ω6) PUFAs to n-3 (ω3) PUFAs in the Japanese, Mediterranean and American diets were 4, 6~8 and 10, respectively.

Next, we picked up three representative reports from Japan (Tokudome et al., 1999) , Italy (Freudenheim et al., 1993), and USA (Block et al., 1985) and compared the foods contributing to intake of selected fatty acids and cholesterol in the Japanese, Mediterranean and American diets. Admittedly, neither the methods of the dietary survey nor the calendar years were the same. Furthermore, neither sex nor age were adjusted, and food categorization was not identical. However, we may nevertheless generate a global idea of the food sources of fats and oils.

SFAs were provided by eggs, milk, rice and then meat in the Japanese diet; by olive oil, milk and dairy products in the Mediterranean diet; and by meat, milk and cheese in the American diet (Table 3). Oleic acid, a major component of MUFAs, was largely supplied by eggs and vegetable oils in the Japanese diet; typically by olive oil in the Mediterranean diet; and mostly by meat and foods cooked with vegetable oils in the American diet. Linoleic acid, a principal constituent of n-6 PUFAs, has a common origin from vegetable oils, irrespective of the diet type. Olive oil was again a main source of linoleic acid in the Mediterranean diet, but not from linoleic acid-rich margarine. Of the n-3 PUFAs, α-linolenic acid was provided by vegetable oils, irrespective of the diet type, and strikingly by olive oil again in the Mediterranean diet. Eicosapentaenoic acid (hereafter EPA) and docosahexaenoic acid (hereafter DHA) from fish and shellfish were consumed more by Japanese than Mediterranean people, and in both cases much more than by American people. Cholesterol was universally supplied by eggs and milk, then by marine foods in the Japanese diet; by animal meat and fish and shellfish in the Mediterranean diet; and by meat in the American diet.

Discussion

The low risks of FRCs in Japanese may be partly attributable to a limited intake of total fat but this is not the case in Mediterranean people. These latter do not appreciably differ from the Americans in this respect; however, the risks of FRCs in the former were much lower than in the latter (La Vecchia et al., 1995; Trichopoulou et

al., 1995). Thus, the link between intake of total fat, SFAs and MUFAs, with the risks of FRCs must remain debatable (Prentice and Sheppard, 1990; Wynder et al., 1992; Giovannucci et al., 1994; WCRF/AICR, 1997). In this context, the type/composition of fatty acids and the ratio of n-6 PUFAs to n-3 PUFAs, in particular, need specific attention with regard to carcinogenesis (Lands et al., 1990; Okuyama et al., 1997).

Linoleic acid is an essential fatty acid; however, if taken in excess of physiological requirements, it acts as a tumor promoter and an immunosuppressor (Reddy et al., 1992; Yam et al., 1996; Zock and Katan, 1998). PUFAs, especially n-3 PUFAs, have been reported to be not so labile to oxidation under physiological milieu, if oxygen- and lipid peroxy-scavengers, including glutathione-peroxidase and antioxidants (such as vitamin E and C) ordinarily exist. n-3 PUFAs (α-linolenic acid, EPA and DHA), like NSAIDs, compete with n-6 PUFAs, which are precursors for the arachidonic acid cascade, and have been demonstrated to suppress cell proliferation (Greenberg and Baron, 1996; Latham et al., 1999), promote apoptosis, inhibit gene expression of cyclooxygenase (COX) (Oshima et al., 1995, 1996), suppress synthesis of prostaglandin E_2, and accordingly act as anti-promoters in the carcinogenesis (Hirose et al., 1990; Reddy, 1992, Takahashi et al., 1993; Okuyama et al., 1997). Epidemiological and intervention studies have reported beneficial effects of intake of fish and shellfish and n-3 PUFAs on the risk of colorectal cancer (Bartram et al., 1993; Anti et al., 1994; Huang et al., 1996; de Lorgeril et al., 1998; Caderni et al., 1999; de Deckere, 1999; Fernandez et al., 1999) as well as CHD (Kromhout et al., 1985; Burr et al., 1989; Dolecek and Grandits, 1991; de Lorgeril et al., 1994).

Accordingly, the low risks of FRCs in Japanese appeared to be explainable by low consumption of fats and oils as a whole, and particularly the low ratio of n-6 PUFAs versus n-3PUFAs due to consumption of the latter from marine foods, together with beneficial dietary habits and lifestyle, such as moderate consumption of vegetables and fruit, soy and soy products and green tea, and relatively limited consumption of energy providing an appropriate BMI, determined not only by genetic predisposition but also by relatively high physical activity. In contrast, Mediterranean people consume moderate amount of fats and oils abundantly from olive oil, containing not only oleic acid but also polyphenols (including flavonoids), α-tocopherol and carotenoids (including β-carotene), which are antioxidants and anti-carcinogenic as in red wine, vegetables (including herbs) and fruit, being frequently consumed by Mediterranean people (Ferro-Luzzi et al., 1994; Martin-Moreno et al.,1994; La Vecchia et al., 1995; Trichopoulou et al., 1995; Visioli et al., 1998) . Their diet features moderate intake of fish and shellfish,

presumably yielding a medium value of n-6 PUFAs/n-3 PUFAs between the Japanese and American diets, along with cereals/pasta/bread containing dietary fiber. From the standpoint of total intake of fats and oils, the low risk of FRCs in Japanese seems "plausible," while the low risk in Mediterranean people may be termed "paradoxical"(Martin-Moreno et al.,1994; La Vecchia et al., 1995; Trichopoulou et al., 1995).

Finally, less consumption of fats and oils, moderate intake of marine foods, and vegetables and fruit, modest intake of energy in combination of moderate physical exercise may be advocated for promoting health, prolonging life and prevention of lifestyle-related diseases including FRCs, in this new millennium.

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He was once a keen angler, but now is addicted to LSD (not **lys**ergic acid **d**iethylamide but **L**ong, **S**low and **D**istance jog) in order to survive as a tortoise-paced triathlete as well as a five-hour marathon runner. He enjoys classical music as a background when working at his beloved IBM compatible computer.