

## Chapter 26

# Japanese Perspectives on Dietary Patterns and Risk of Dementia

Toshiharu Ninomiya, MD, PhD and Mio Ozawa, PhD

*Kyushu University, Higashi-ku, Fukuoka City, Japan*

### LIST OF ABBREVIATIONS

**AD** Alzheimer's disease  
**CI** confidence interval  
**DP1** dietary pattern 1  
**HR** hazard ratio  
**OR** odds ratio  
**VaD** vascular dementia

### INTRODUCTION

Dementia is a syndrome that affects memory, thinking, behavior, and ability to perform everyday activities. The number of individuals with dementia worldwide has been growing rapidly as a consequence of the aging population. According to the report “Dementia: a public health priority,” which was jointly published by the World Health Organization and Alzheimer's Disease International in 2012, the number of people with dementia worldwide is currently estimated at 35.6 million and will double to 65.7 million by 2030 and more than triple to 115.4 million by 2050 [1]. Therefore, the identification and development of population- and individual-based preventative strategies aimed at reducing the incidence of dementia should be an important health and economic priority for countries around the world.

Alzheimer's disease (AD) is the most common. AD has traditionally been considered a primarily neurodegenerative disorder characterized by neuritic plaques and neurofibrillary tangles, which are respectively formed by an accumulation of amyloid beta protein and the abnormal phosphorylation of tau protein in neurons. Vascular dementia (VaD) is the second most common type of dementia, and develops as a consequence of strokes or chronic brain ischemia generated by small vessel disease. In consideration of the diverse etiology of these dementia subtypes, dementia can be influenced by a number of factors, and the potential effect of nutrients has become a topic of scientific and public interest.

Since nutrients are usually consumed in combination with foods, and the two may have interactive or synergistic effects, certain dietary patterns may have a greater association with the risk of disease than single foods or nutrients. In Western countries, several epidemiological studies have reported that a higher adherence to a Mediterranean dietary pattern, which is generally characterized by proportionally high consumption of olive oil, legumes, unrefined cereals, fruits, and vegetables, moderate to high consumption of fish, moderate consumption of dairy products, moderate wine consumption, and low consumption of meat and meat products, is associated with a reduced risk of the incidence of dementia [2–5]. On the other hand, a Mediterranean diet is very different from a traditional Asian diet, and it is possible that another dietary pattern would have an equally or more preventive effect on dementia in Asian people. Particularly, Japan has one of the oldest life-spans in the world; 23.3% of individuals were 65 or older in 2011 and the life expectancy at birth was 79.6 years for men and 86.4 years for women in 2010 [6]. Therefore, it is important to determine whether there are dietary patterns that could help to reduce the burden of dementia specifically in this population. The objective of chapter is to review the Japanese perspectives on dietary patterns and risk of dementia based on epidemiological findings, which may be useful from a clinical and public health perspective.

## THE BURDEN OF DEMENTIA IN JAPAN

A recent report from the Ministry of Health, Labour and Welfare of Japan estimated that approximately 4.6 million people in Japan had dementia in 2012, which is equivalent to 15% of people aged 65 years or older [7]. The Hisayama study, which is a prospective cohort study of cerebro-cardiovascular diseases ongoing in a Japanese suburban community, has conducted four cross-sectional examinations among residents of a Japanese community aged 65 years or over in 1985, 1992, 1998, and 2005 to investigate trends in the prevalence of dementia [8]. The unadjusted prevalence of total dementia significantly increased with time (6.7%, 5.7%, 7.1%, and 12.5%, respectively;  $P$  for trend = 0.002). A similar trend was observed for AD (1.4%, 1.8%, 3.4%, and 6.1%, respectively;  $P$  for trend < 0.001), while the prevalence of VaD and other/unclassified dementia showed a decreasing trend between 1985 and 1998 and then an increasing trend in 2005 (for VaD, 2.4%, 1.9%, 1.7%, and 3.3%,  $P$  for trend = 0.82; for other/unclassified dementia: 2.9%, 2.1%, 1.9%, and 3.1%,  $P$  for trend = 0.26). These findings suggest that the burden of dementia, especially AD, has increased rapidly over the past two decades in Japan. Aging of the population is a major cause of the increase in the prevalence of total dementia and AD [9,10]. However, the upward trend in the prevalence of total dementia and AD remained significant after controlling for the confounding effects of age and sex in this study. Another possible cause would be the recent increase in the prevalence of metabolic disorders, such as diabetes, which have been associated with the risk of AD [11,12].

Additionally, a recent ecological study evaluated whether dietary changes might explain the rising trend of AD prevalence in Japan [13]. According to the data for dietary supply from the Food and Agriculture Organization of the United Nations, the largest changes between 1961 and 1985 included alcohol (from 29.6 to 57.4 kg/capita/year), animal fat (from 5 to 35 kg/capita/year), meat (from 7.6 to 33.7 kg/capita/year), energy from animal products (from 249 to 580 kcal/capita/day), and rice (from 113 to 69 kg/capita/year) (Figure 26.1). This study found that the increasing consumption of alcohol, animal products, and meat and decreasing rice supply were highly correlated with data on the prevalence of AD for 25 years, with correlation coefficients of about 90%. This finding raises the possibility that the nutrition changes in Japan, i.e., the switch from a traditional Japanese diet toward a more Western diet, has been at least partially responsible for the rapid increase in dementia in Japan.

## EPIDEMIOLOGICAL FINDINGS OF DIETARY PATTERNS AND RISK OF DEMENTIA IN JAPANESE COMMUNITIES

Only a few epidemiological studies have attempted to investigate the association between diet and the development of dementia in Japanese populations so far. The Iwaki Health Promotion Project 2011 investigated the association between dietary pattern and cognitive function in a cross-sectional sample of 388 individuals from a Japanese community [15]. Three dietary patterns were identified by principal component analysis. Although the “Healthy” dietary pattern, which depended heavily on vegetables, seaweed, tofu, fruits, and fish, was hypothesized to be associated with a lower risk of cognitive impairment, this study failed to substantiate this hypothesis. However, the study had some methodological

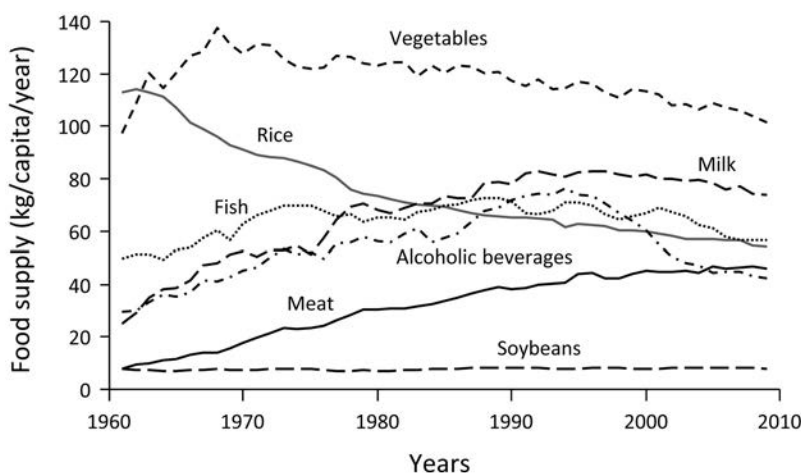


FIGURE 26.1 Trend in the food supply from 1961 to 2009 in Japan: Data from the Food and Agriculture Organization of the United Nations [14]. The graph shows the trend in the annual amount per capita of each food over time in Japan. Based on [14].

limitations, such as the study design and sample size, which could have limited its ability to address the effect of diet on the risk of cognitive impairment. In particular, the cross-sectional nature of dietary research is vulnerable to reverse causality, since dietary habits are likely affected by various disease conditions.

A prospective longitudinal study was performed to address the association between diet and the risk of dementia in a Japanese population. The Hisayama study demonstrated that higher self-reported dietary intakes of potassium, calcium, and magnesium reduced the risk of total dementia and VaD, but not of AD, in 1,081 community-dwelling Japanese individuals without dementia aged 60 years and older during a 17-year follow-up [16]. The intakes of minerals were calculated by using a 70-item semiquantitative food frequency questionnaire and were divided into quartiles. The multivariable-adjusted hazard ratios (HRs) for the development of total dementia were 0.52 (95% confidence interval [CI] 0.30–0.91), 0.64 (95% CI 0.41–1.00), and 0.63 (95% CI 0.40–1.01) for the highest quartiles of potassium, calcium, and magnesium intake, respectively, as compared with the lowest quartiles. Similarly, the subjects with the highest quartiles of potassium, calcium, and magnesium intakes had 80% (HR 0.20, 95% CI 0.07–0.56), 76% (HR 0.24, 95% CI 0.11–0.53), and 74% (HR 0.26, 95% CI 0.11–0.61) lower risk of VaD than those with the lowest quartiles. No evidence of a linear association between these mineral intakes and the risk of AD was detected. Supportively, some epidemiological evidence has indicated that these minerals have some favorable effects against cerebrovascular disease [17,18], possibly through an improvement of hypertension, dyslipidemia, and insulin resistance, antioxidative effects, and the inhibition of platelet aggregation [19–21]. Participants in the highest quartiles of these minerals tended to eat more potatoes, soybeans and soybean products, vegetables, fruits and fruit juices, algae, fish, eggs, and milk and dairy products and had less rice, meat, sugar, and alcoholic beverages.

This study also evaluated the relation between dietary patterns and the risk of dementia in 1,006 community-dwelling Japanese individuals without dementia aged 60–79 years during a 17-year follow-up [22]. Dietary patterns associated with the risk of dementia were determined by using a reduced rank regression analysis [23], for which seven nutrients were selected as risk or preventive factors for dementia—namely, saturated fatty acid, monounsaturated fatty acid, polyunsaturated fatty acid, vitamin C, potassium, calcium, and magnesium [16,24–26]—and dietary patterns related to the intakes of these seven nutrients were derived on the basis of 19 food groups. By this analysis, seven dietary patterns were extracted and the scores for dietary pattern 1 (DP1) accounted for 54.8% of total variation of all responsible variables, while the scores for dietary patterns 2–7 explained very few variations. A higher score of DP1 was characterized by a high intake of soybeans and soybean products, green vegetables, other vegetables, algae, and milk and dairy products, and a low intake of rice (Table 26.1). Individuals with higher adherence to DP1 were also likely to eat potatoes, fruits and fruit juices and fish, and were unlikely to drink alcohol. The age- and sex-adjusted risk of total dementia decreased by two-thirds (HR 0.66, 95% CI 0.47–0.94) in individuals with the highest quartile of scores for DP1 as compared with those with the lowest quartile. With regard to subtypes of dementia, individuals with the highest quartile of scores for DP1 had a significantly lower risk of either AD (HR 0.62, 95% CI 0.39–0.99) or VaD (HR 0.48, 95% CI 0.24–0.93) (Figure 26.1). These associations were not substantially altered after adjusting for potentially confounding factors.

A number of previous epidemiological studies addressed effects of the Mediterranean dietary pattern on risk of dementia and showed that higher intakes of vegetables, fruits, and fish were linked to lower risk of dementia [5]. Gu et al. assessed the dietary pattern associated with the incidence of dementia in a US population by using a reduced rank regression analysis in a similar manner to the Hisayama Study, with the result that the extracted dietary pattern was positively correlated with high intake of salad dressing, nuts, tomatoes, poultry, cruciferous vegetables, fruits, and dark-green leafy vegetables, and negatively correlated with high-fat dairy, red meat, organ meat, and butter, and a greater adherence to this dietary pattern was associated with a lower risk of dementia [27]. Despite the different dietary customs among various populations, the dietary patterns and food groups detected in these studies are substantially similar. Meanwhile, the major food groups in the Japanese dietary pattern that appear to contribute to the prevention of dementia are high intakes of dairy products and soybean products (Figure 26.2).

## DAIRY CONSTITUENTS AND RISK OF DEMENTIA

In the Hisayama study, consumption of milk and dairy products was positively correlated with adherence to a dietary pattern favorable for the prevention of dementia. Recently, this study also presented some additional findings that the age- and sex-adjusted incidence of total dementia, AD, and VaD significantly decreased with an increased intake of milk and dairy products ( $P$  for trend = 0.03 for total dementia, = 0.04 for AD, and = 0.01 for VaD) [28]. In support of these findings, the Adult Health Study of atomic bomb survivors in Japan retrospectively evaluated the relationship of milk intake that was assessed 25 to 30 years earlier with the prevalence of AD and VaD, and concluded that subjects who consumed milk every day had significantly lower prevalence of VaD (odds ratio [OR] 0.26,  $P$  = 0.002), but not AD, compared with those who consumed milk twice a week or less (Table 26.2) [29]. Several epidemiological studies have suggested that

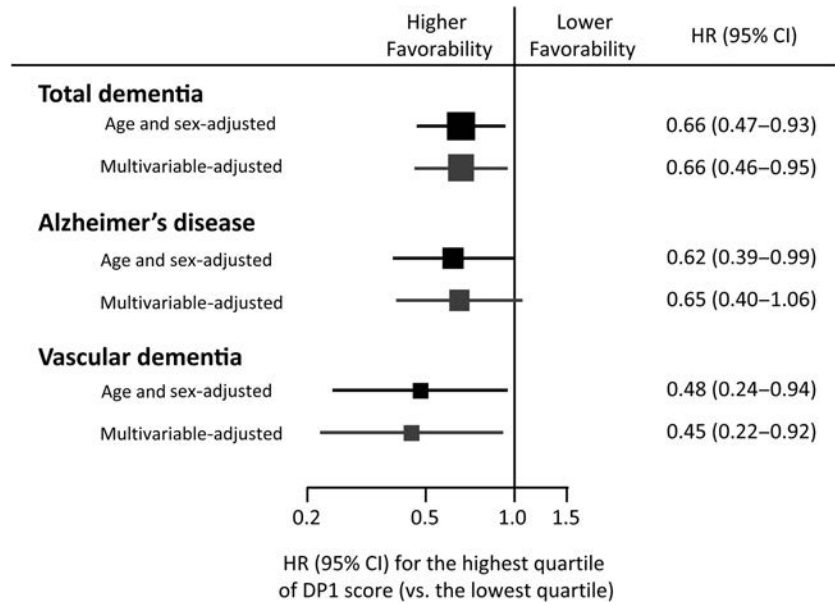
**TABLE 26.1** Factor Loadings of Good Groups Associated with a Dietary Pattern Favorable for the Prevention of Dementia: Results from the Hisayama Study [22]

Food Groups	Factor Loadings (Dietary Pattern 1)
<b>Rice</b>	<b>-0.45</b>
Breads	0.10
Noodles and other cereals	0.01
Potatoes	0.16
<b>Soybeans and soybean products</b>	<b>0.37</b>
Miso	0.01
Pickles	0.04
<b>Green vegetables</b>	<b>0.40</b>
<b>Other vegetables</b>	<b>0.36</b>
Fruits and fruit juices	0.19
<b>Algae</b>	<b>0.24</b>
Fish	0.17
Meat	0
Egg	0.15
<b>Milk and dairy products</b>	<b>0.37</b>
Fats and oils	0.12
Sugar and confection	-0.10
Alcoholic drinks	-0.17
Salt	-0.008

Factor loadings represent the magnitude and direction of the contribution of each food group to a dietary pattern 1 score. A positive value of factor loading indicates an increased intake of the food group. A negative value of factor loading indicates a reduced intake of the food group. The food groups with factor loadings of  $< -0.20$  and  $> 0.20$  are shown in bold. Source: Based on [22].

consumption of dairy products, especially low-fat dairy products, may be associated with beneficial health outcomes, including a reduction in the incidence of hypertension and diabetes, an improvement of insulin resistance, lower levels of inflammatory markers, and a decreased risk of cardiovascular disease [30–34]. While much of this data was obtained from longitudinal observational studies rather than from intervention trials, it provides encouraging evidence that dairy products may help to prevent dementia.

A Mediterranean dietary pattern, which has shown the significant association with the reduced risk of dementia in Western countries [5], is characterized by a low to moderate consumption of milk and dairy products. However, this finding is not consistent with the results of studies conducted in Japanese communities. According to the data from the Food and Agriculture Organization of the United Nations, there has been a clear difference in the amount of milk and dairy consumption between Japan and Western countries: the amount of milk and dairy consumption in the Japanese population was about half that of Western populations [14]. This evidence suggests that the difference in the amount of milk and dairy consumption between Japan and Western countries could be the reason for the discrepancy in the influence of milk and dairy consumption on the risk of dementia between these populations. In populations with relatively low intake of milk and dairy, a high intake of these foods is considered to reduce the risk of dementia. Further investigations will be required to clarify this issue in other ethnic populations.



**FIGURE 26.2 Risk of incident dementia associated with the score for dietary pattern favorable for the prevention of dementia: Results from the Hisayama Study [22].** HRs of < 1.0 suggest that people with higher adherence to dietary pattern identified in the Hisayama Study have a lower risk of the indicated subtype of dementia than those with lower adherence. In the multivariable-adjusted analyses, the HRs were adjusted for age, sex, education, hypertension, diabetes, serum total cholesterol, body mass index, history of stroke, smoking habits, regular exercise, and energy intake. Abbreviations: HR, hazard ratio; CI, confidence interval; DP1, dietary pattern 1. Based on [22].

**TABLE 26.2 Risk Factors for Vascular Dementia and AD in the Multivariable-Adjusted Logistic Regression Analysis: Results from the Adult Health Study [29]**

Risk Factors	Odds Ratio (95% Confidence Interval)
<b>For vascular dementia</b>	
Age (per 5-year increments)	1.29 (1.05 – 1.59)
Systolic blood pressure in midlife (per 10-mmHg increments)	1.33 (1.14 – 1.56)
Milk intake almost daily in midlife (versus <4 times a week)	0.35 (0.14 – 0.77)
<b>For AD</b>	
Age (per 5-year increments)	2.48 (2.00 – 3.12)
Education (per 3-year increments)	0.41 (0.25 – 0.67)

Higher milk intake in midlife was significantly associated with lower risk of vascular dementia. Odds ratios of <1.0 or >1.0 suggest that people with the indicated factor have a lower or higher risk of the indicated subtype of dementia, respectively.  
Source: Based on [29].

## SOYBEAN PRODUCTS AND RISK OF DEMENTIA

There is growing interest in the physiological functions of soy isoflavones, particularly in terms of whether they affect cognitive function and have beneficial effects on neurodegenerative diseases. Soybeans are one of the richest sources of isoflavones, which are phytoestrogens and can bind estrogen receptors [35]. Since soy isoflavones may mimic the actions and functions of estrogens on the brain, they have a possible role in the prevention of the cognitive decline in females [36]. The data from the Hisayama Study suggested that higher intakes of soybeans and soybean products were correlated with higher adherence to dietary patterns favorable for the prevention of dementia. However, the effect of soybeans and soybean products on cognitive function has been an area of some controversy. The Honolulu-Asia Aging Study, which is a longitudinal

**TABLE 26.3** The Effect of Soy Protein on the Standardized Changes in Cognitive Scores Over 2.5 Years: Results from the Women’s Isoflavone Soy Health Trial [40]

Outcomes	Isoflavone-Rich Soy Protein Group ( <i>n</i> = 154)	Placebo Group ( <i>n</i> = 159)	<i>P</i> Value
<b>Cognitive composite score</b>	0.42 (0.09)	0.31 (0.08)	0.36
<b>Individual cognitive test scores</b>			
Executive/expressive/visuospatial factor	0.08 (0.20)	0.45 (0.20)	0.20
Verbal episodic memory (list learning) factor	0.22 (0.12)	0.3 (0.11)	0.61
Verbal episodic memory (logical memory) factor	0.15 (0.14)	−0.12 (0.14)	0.19
Visual episodic memory factor	0.74 (0.10)	0.41 (0.10)	0.018

Cognitive performance of visual episodic memory improved more in isoflavone-rich soy protein intake group than placebo group.

For all scores, a positive change represents improved cognitive performance. Values are the least squares mean change from baseline (standard error).

Source: Based on [40].

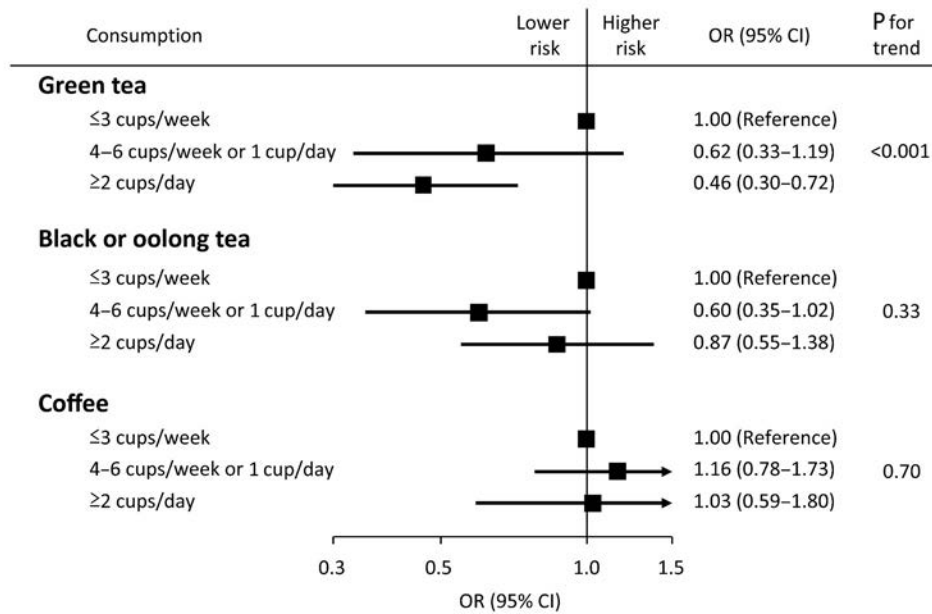
study of aging and dementia conducted in 3,734 Japanese-American men aged 71–93 years, reported that higher midlife tofu consumption was independently associated with poor cognitive test performance, enlargement of ventricles, and low brain weight in late life [37].

The findings from randomized control trials refute concerns that soybean-derived foods or supplements could be harmful for cognitive function, although they do not provide definitive evidence of protective effects on cognitive impairment. A systematic review of the evidence from randomized control trials examining the efficacy and safety of soy foods, soy supplements, or soy isoflavone supplements for health outcomes revealed that soy isoflavones appeared to have a modest but positive effect on cognitive abilities, without serious safety concerns, among postmenopausal women [38]. Three of the four trials selected in this review indicated that soy or soy isoflavones improved short-term memory, frontal lobe function, mental flexibility, planning ability, category fluency, and sustained attention in postmenopausal women. However, these three trials were small (<100 participants) and had short follow-up periods (<6 months). The remaining double-blind randomized trial with 202 healthy postmenopausal women aged 60–75 years, who were randomly assigned to receive 25.6 g of soy protein containing 99 mg of isoflavones or total milk protein, found that cognitive function did not differ significantly between the groups after a year [39]. Additionally, the recent Women’s Isoflavone Soy Health trial examined the change from baseline on the global cognitive composite score from 14 neuropsychological tests over 2.5 years in 313 healthy postmenopausal women aged 45–92 years who were randomly allocated to receive daily 25 g of isoflavone-rich soy protein or milk protein-matched placebo [40]. The results showed that women allocated to the soy isoflavone group showed a greater improvement in visual memory than those allocated to the placebo group (mean standardized difference 0.33, 95% CI 0.06–0.60). However, there was no significant difference in the change in global cognition function between groups (mean standardized difference 0.11, 95% CI 0.13–0.35) (Table 26.3).

Taken together, these studies on the effect of soybeans and soybean products on cognitive function have been inconclusive. Nevertheless, at least it may be said that the evidence from the double-blind randomized trials does not support the hypothesis that the soy protein increases the risk of cognitive impairment, but it allows us to expect a possible benefit of soy protein on cognition function in postmenopausal women. An expert panel organized by the North American Menopause Society suggests soy could favorably impact cognition in women younger than 65. Meanwhile, the panel also emphasized that more research is needed to understand the risk and benefits of soy products [41].

## RICE AND RISK OF DEMENTIA

The favorable dietary pattern detected in the Hisayama Study showed a negative correlation with rice consumption. Rice constitutes a large part of the Japanese daily diet. Given the negative correlation between rice consumption and the prevalence of dementia [13], this association may arise from an imbalance in food intake (i.e., a high intake of rice may result in



**FIGURE 26.3 Association between beverage consumption and cognitive impairment: Results from the Tsurugaya Project [43].** Odds ratios of <1.0 suggest that people consuming the indicated amount of the beverage have a lower risk of the presence of cognitive impairment defined as a Mini-Mental State Examination score of <26 than those consuming the lowest amount (i.e., reference group). The odds ratios were adjusted for age, sex, education, hypertension, diabetes, history of stroke, depressive symptoms, visiting friends, energy intake, intake of nondietary vitamin C or E, fish consumption, consumption of green tea, consumption of Black or oolong tea, and consumption of coffee. Abbreviations: OR, odds ratio; CI, confidence interval. *Based on [43].*

lower intake of foods favorable for the prevention of dementia) rather than any harmful effects of rice itself, and may simply underscore that a well-balanced meal with many nutritional foods is recommended for a reduction in risk of dementia. On the other hand, excess intake of white rice may increase the incidence of type 2 diabetes, which is being recognized as a risk factor for dementia [11]. A recent meta-analysis of prospective cohort studies with 352,384 participants and 13,284 incident cases of type 2 diabetes demonstrated that a higher consumption of white rice is associated with a significantly increased risk of type 2 diabetes, especially in Asian (Chinese and Japanese) populations: the dose–response meta-analysis indicated that for each serving per day increment of white rice intake, the relative risk of type 2 diabetes was 1.11 (1.08–1.14) (P for linear trend <0.001) [42]. The effect of rice consumption remains inconclusive.

## OTHER DIETARY FACTORS ASSOCIATED WITH DEMENTIA RISK

A cross-sectional study from the Tsurugaya Project indicated the inverse dose–response relationship between consumption of green tea and the prevalence of cognitive impairments defined as the Mini-Mental State Examination of <26 scores in 1,003 community-dwelling Japanese individuals aged 70 years or older (Figure 26.3) [43]. Subjects who drank 2 cups or more of green tea a day had significantly lower prevalence of cognitive impairments (OR 0.46, 95% CI 0.30–0.72) than those who drank 3 cups or less a week. Nutrients such as polyphenols, catechins, and vitamin C, in which green tea is rich, may have some beneficial effect on cognitive function in the elderly. As another explanation, more consumption of green tea could mean higher adherence to the traditional Japanese diet. However, we cannot infer a causal relationship from the findings of this cross-sectional study, and the results may be affected by residual confounding.

## CONCLUSION

The possible effect of diet on the prevention of the onset of dementia is of tremendous scientific and general interest in Japan, since there is no definitive evidence of any effective pharmacological treatment for dementia [44]. The studies available in the literature provide plausible evidence that high adherence to a traditional Japanese diet, which is characterized by a high intake of soybean products, vegetables, algae, fruit, fish, and green tea, and low consumption of alcoholic beverages, in addition to a high intake of milk and dairy products and a balanced intake of rice, is associated with a decreased risk

of dementia. However, it should be noted that there have been only a few studies examining the relationship between diet and dementia in Japan, and most of those were performed in the same cohort population. In addition, since these findings were derived from observational studies, the efficacy of these diets on cognitive function has not been proven in intervention trials. Nevertheless, the trend in the food supply in Japan is shifting from a traditional Japanese diet toward a Western diet with a high percentage of energy derived from meat and animal products. This shift may be related to the rapid rise in the prevalence of dementia in Japan. Therefore, the studies performed to date suggest that it is important to pay attention to dietary habits, including the traditional Japanese diet, as well as the prevention and amelioration of risk factors such as hypertension and diabetes in order to reduce the societal burden of dementia in the future. Further researches, especially well-planned intervention trials, are warranted to establish a causative role for specific nutrients, foods, and dietary patterns on the development of dementia.

## APPLICATION TO OTHER SUBTYPES OF DEMENTIA

The current evidence from the Japanese observational studies regarding dietary patterns associated with a reduced risk of dementia is mainly based on data regarding the onset of VaD and AD. The dietary patterns detected in these Japanese studies appear to have some favorable effects against stroke and cerebral vascular lesions, possibly through the improvement of hypertension, dyslipidemia, and insulin resistance, the antioxidative effect, and the inhibition of platelet aggregation. However, since the etiology of other minor dementias (e.g., dementia with Lewy bodies and frontotemporal dementia, Huntington's disease, progressive supranuclear palsy) has not been clarified, it is unclear whether or not the detected dietary pattern can be applied to prevent the development of these other subtypes of dementia. At the same time, it is very hard to plan studies on other subtypes of dementia than VaD and AD, because the prevalence of these other dementias is too small to perform epidemiological research. Thus, an international collaborative investigation would be necessary to clarify the etiology of other subtypes of dementia. Nevertheless, as the dietary pattern detected did not show any harmful effects on the healthy outcomes, this favorable diet can be applied safely to general populations. In addition, a favorable diet may suppress the deterioration of cognitive function in patients with other subtypes of dementia by preventing concomitant cerebral vascular injury. Hence, we believe that a favorable diet could also have a modest but positive effect on cognitive function without serious adverse effects among people with dementias other than VaD and AD.

## PRACTICAL ISSUES

Dementia, especially AD, is an extremely complex and still poorly understood disorder. There is still no definitive evidence of any effective pharmacological treatment for dementia, and it would be quite unrealistic to expect a single medication to prevent cognitive impairments and to remarkably ameliorate existing dementia. Therefore, the combination of an appropriate pharmacological treatment, a favorable diet, and lifestyle modifications will be needed for the effective prevention and amelioration of dementia. Primary prevention with dietary modification may be most appropriate strategy, and could be applied for healthy people before symptoms of cognitive impairment manifest, since it is safe and cost-effective. Dietary modification would have the dual effect of slowing the onset of cognitive impairment and subsequent dementia, as well as decreasing the risk of stroke. It would also be expected to have some benefits on overall health. For the prevention of cognitive impairment, a traditional Japanese diet characterized by a high intake of soybean products, vegetables, algae, fruit, and fish and a low consumption of alcoholic beverages; the consumption of milk and dairy products and green tea; the avoidance of excess calories from rice and animal products; the regular practice of aerobic exercise; and the prevention and amelioration of obesity, diabetes, and hypertension would be recommended. It is hoped that new and effective drugs will be made available for the treatment of dementia within the next few years, but dementia appears to be a disorder that is more readily prevented or at least markedly postponed than treated. In the meantime, therefore, it is crucial to begin protecting the brain before any mild cognitive impairment becomes manifest.

## SUMMARY POINTS

- The prevalence of dementia, especially AD, is increasing rapidly in Japan, accounting for approximately 15% of people aged 65 years or older in 2012.
- The trend in the food supply in Japan is shifting from a traditional Japanese diet toward a Western diet with high intake of meat and animal products.
- The epidemiological evidence suggests that high adherence to a traditional Japanese diet in addition to a high intake of milk and dairy products and a balanced intake of rice is associated with a decreased risk of dementia.



- The influence of milk and dairy consumption on the risk of dementia appears to be different between Japan and Western countries, probably because the amount of milk and dairy consumption is lower in Japanese than in Western populations.
- Soy appears to have a modest but positive effect on cognitive abilities, without serious safety concerns, among postmenopausal women, although the effect has been inconclusive so far.
- Studies examining the relationship between diet and cognitive function are very few in Japan, and the efficacy of a traditional Japanese diet in protecting cognitive function has not been established by the intervention trials.

## REFERENCES

- [1] World Health Organization and Alzheimer's Disease International. Dementia: a public health priority. <[http://www.who.int/mental\\_health/publications/dementia\\_report\\_2012/en/](http://www.who.int/mental_health/publications/dementia_report_2012/en/)> ; 2012.
- [2] Scarmeas N, Stern Y, Tang MX, Mayeux R, Luchsinger JA. Mediterranean diet and risk for Alzheimer's disease. *Ann Neurol* 2006;59:912–21.
- [3] Feart C, Samieri C, Rondeau V, Amieva H, Portet F, Dartigues JF, et al. Adherence to a Mediterranean diet, cognitive decline, and risk of dementia. *JAMA* 2009;302:638–48.
- [4] Scarmeas N, Luchsinger JA, Schupf N, Brickman AM, Cosentino S, Tang MX, et al. Physical activity, diet, and risk of Alzheimer disease. *JAMA* 2009;302:627–37.
- [5] Psaltopoulou T, Sergentanis TN, Panagiotakos DB, Sergentanis IN, Kosti R, Scarmeas N. Mediterranean diet, stroke, cognitive impairment, and depression: a meta-analysis. *Ann Neurol* 2013;74:580–91.
- [6] Cabinet Office Government of Japan. Annual Report on the Aging Society <<http://www8.cao.go.jp/kourei/english/annualreport/2012/pdf/1-1.pdf>>; 2012.
- [7] Working report from the Ministry of Health, Labour and Welfare of Japan [Japanese]. <[http://www.tsukuba-psychiatry.com/wp-content/uploads/2013/06/H24Report\\_Part1.pdf](http://www.tsukuba-psychiatry.com/wp-content/uploads/2013/06/H24Report_Part1.pdf)>; 2012.
- [8] Sekita A, Ninomiya T, Tanizaki Y, Doi Y, Hata J, Yonemoto K, et al. Trends in prevalence of Alzheimer's disease and vascular dementia in a Japanese community: the Hisayama Study. *Acta Psychiatr Scand* 2010;122:319–25.
- [9] Yoshitake T, Kiyohara Y, Kato I, Ohmura T, Iwamoto H, Nakayama K, et al. Incidence and risk factors of vascular dementia and Alzheimer's disease in a defined elderly Japanese population: the Hisayama Study. *Neurology* 1995;45:1161–8.
- [10] Luck T, Riedel-Heller SG, Lupp M, Wiese B, Wollny A, Wagner M, et al. Risk factors for incident mild cognitive impairment—results from the German Study on Ageing, Cognition and Dementia in Primary Care Patients (AgeCoDe). *Acta Psychiatr Scand* 2010;121:260–72.
- [11] Biessels GJ, Staekenborg S, Brunner E, Brayne C, Scheltens P. Risk of dementia in diabetes mellitus: a systematic review. *Lancet Neurol* 2006;5:64–74.
- [12] Ohara T, Doi Y, Ninomiya T, Hirakawa Y, Hata J, Iwaki T, et al. Glucose tolerance status and risk of dementia in the community: the Hisayama study. *Neurology* 2011;77:1126–34.
- [13] Grant WB. Trends in diet and Alzheimer's disease during the nutrition transition in Japan and developing countries. *J Alzheimers Dis* 2014;38:611–20.
- [14] Food and Agriculture Organization of the United Nations. FAOSTAT data. <<http://faostat3.fao.org/faostat-gateway/go/to/home/E>>.
- [15] Sugawara N, Yasui-Furukori N, Umeda T, Tsuchimine S, Kaneda A, Tsuruga K, et al. Relationship between dietary patterns and cognitive function in a community-dwelling population in Japan. *Asia Pac J Public Health* 2013 (in press).
- [16] Ozawa M, Ninomiya T, Ohara T, Hirakawa Y, Doi Y, Hata J, et al. Self-reported dietary intake of potassium, calcium, and magnesium and risk of dementia in the Japanese: the Hisayama Study. *J Am Geriatr Soc* 2012;60:1515–20.
- [17] Larsson SC, Virtanen MJ, Mars M, Mannisto S, Pietinen P, Albanes D, et al. Magnesium, calcium, potassium, and sodium intakes and risk of stroke in male smokers. *Arch Intern Med* 2008;168:459–65.
- [18] Iso H, Stampfer MJ, Manson JE, Rexrode K, Hennekens CH, Colditz GA, et al. Prospective study of calcium, potassium, and magnesium intake and risk of stroke in women. *Stroke* 1999;30:1772–9.
- [19] Young DB, Lin H, McCabe RD. Potassium's cardiovascular protective mechanisms. *Am J Physiol* 1995;268:R825–837.
- [20] Karanja N, Morris CD, Illingworth DR, McCarron DA. Plasma lipids and hypertension: response to calcium supplementation. *Am J Clin Nutr* 1987;45:60–5.
- [21] Mooren FC, Kruger K, Volker K, Golf SW, Wadepuhl M, Kraus A. Oral magnesium supplementation reduces insulin resistance in non-diabetic subjects—a double-blind, placebo-controlled, randomized trial. *Diabetes Obes Metab* 2011;13:281–4.
- [22] Ozawa M, Ninomiya T, Ohara T, Doi Y, Uchida K, Shirota T, et al. Dietary patterns and risk of dementia in an elderly Japanese population: the Hisayama Study. *Am J Clin Nutr* 2013;97:1076–82.
- [23] Hoffmann K, Schulze MB, Schienkiewitz A, Nothlings U, Boeing H. Application of a new statistical method to derive dietary patterns in nutritional epidemiology. *Am J Epidemiol* 2004;159:935–44.
- [24] Solfrizzi V, Colacicco AM, D'Introno A, Capurso C, Torres F, Rizzo C, et al. Dietary intake of unsaturated fatty acids and age-related cognitive decline: a 8.5-year follow-up of the Italian longitudinal study on aging. *Neurobiol Aging* 2006;27:1694–704.
- [25] Morris MC, Evans DA, Bienias JL, Tangney CC, Bennett DA, Wilson RS, et al. Consumption of fish and n-3 fatty acids and risk of incident Alzheimer disease. *Arch Neurol* 2003;60:940–6.
- [26] Harrison FE. A critical review of vitamin C for the prevention of age-related cognitive decline and Alzheimer's disease. *J Alzheimers Dis* 2012;29:711–26.
- [27] Gu Y, Nieves JW, Stern Y, Luchsinger JA, Scarmeas N. Food combination and Alzheimer disease risk: a protective diet. *Arch Neurol* 2010;67:699–706.

- [28] Ozawa M, Ohara T, Ninomiya T, Hata J, Yoshida D, Mukai N, et al. Milk and dairy consumption and risk of dementia in an elderly Japanese population: the Hisayama study. *J Am Geriatr Soc* 2014;62:1224–30.
- [29] Yamada M, Kasagi F, Sasaki H, Masunari N, Mimori Y, Suzuki G. Association between dementia and midlife risk factors: the Radiation Effects Research Foundation Adult Health Study. *J Am Geriatr Soc* 2003;51:410–4.
- [30] Toledo E, Delgado-Rodriguez M, Estruch R, Salas-Salvado J, Corella D, Gomez-Gracia E, et al. Low-fat dairy products and blood pressure: follow-up of 2290 older persons at high cardiovascular risk participating in the PREDIMED study. *Br J Nutr* 2009;101:59–67.
- [31] Engberink MF, Hendriksen MA, Schouten EG, van Rooij FJ, Hofman A, Witteman JC, et al. Inverse association between dairy intake and hypertension: the Rotterdam Study. *Am J Clin Nutr* 2009;89:1877–83.
- [32] Elwood PC, Pickering JE, Fehily AM. Milk and dairy consumption, diabetes and the metabolic syndrome: the Caerphilly prospective study. *J Epidemiol Community Health* 2007;61:695–8.
- [33] Elwood PC, Pickering JE, Givens DI, Gallacher JE. The consumption of milk and dairy foods and the incidence of vascular disease and diabetes: an overview of the evidence. *Lipids* 2010;45:925–39.
- [34] Esmailzadeh A, Azadbakht L. Dairy consumption and circulating levels of inflammatory markers among Iranian women. *Public Health Nutr* 2010;13:1395–402.
- [35] Vitale DC, Piazza C, Melilli B, Drago F, Salomone S. Isoflavones: estrogenic activity, biological effect and bioavailability. *Eur J Drug Metab Pharmacokinet* 2013;38:15–25.
- [36] Lee YB, Lee HJ, Sohn HS. Soy isoflavones and cognitive function. *J Nutr Biochem* 2005;16:641–9.
- [37] White LR, Petrovitch H, Ross GW, Masaki K, Hardman J, Nelson J, et al. Brain aging and midlife tofu consumption. *J Am Coll Nutr* 2000;19:242–55.
- [38] Geller SE, Studee L. Soy and red clover for mid-life and aging. *Climacteric* 2006;9:245–63.
- [39] Kreijkamp-Kaspers S, Kok L, Grobbee DE, de Haan EH, Aleman A, Lampe JW, et al. Effect of soy protein containing isoflavones on cognitive function, bone mineral density, and plasma lipids in postmenopausal women: a randomized controlled trial. *JAMA* 2004;292:65–74.
- [40] St Henderson VW, John JA, Hodis HN, Kono N, McCleary CA, Franke AA, et al. Long-term soy isoflavone supplementation and cognition in women: a randomized, controlled trial. *Neurology* 2012;78:1841–8.
- [41] North American Menopause Society. The role of soy isoflavones in menopausal health: report of The North American Menopause Society/Wulf H. Utian Translational Science Symposium in Chicago, IL (October 2010). *Menopause* 2011;18:732–53.
- [42] Hu EA, Pan A, Malik V, Sun Q. White rice consumption and risk of type 2 diabetes: meta-analysis and systematic review. *Br Med J* 2012;344:e1454.
- [43] Kuriyama S, Hozawa A, Ohmori K, Shimazu T, Matsui T, Ebihara S, et al. Green tea consumption and cognitive function: a cross-sectional study from the Tsurugaya Project 1. *Am J Clin Nutr* 2006;83:355–61.
- [44] Cooper C, Li R, Lyketsos C, Livingston G. Treatment for mild cognitive impairment: systematic review. *Br J Psychiatry* 2013;203:255–64.