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A potential association between recent increased incidence of breast and uterine body cancers in Japanese women and changes in dietary saturated fat and folate intake: A meta-analysis

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Abstract

Recent increases in breast and uterine body cancers among Japanese women suggest the involvement of some modifiable factors in cancer development, including drinking and smoking habits, which are generally associated with Westernized lifestyles. Using national data on annual cancer incidence, this study examines the associations between recent changes in cancer incident rates and dietary habits. Data on age-specific incidence and mortality rates of breast, uterine body, colon, and lung cancers from 2004 to 2019, as well as annual changes in the intake of animal protein, plant protein, saturated fatty acids, and folate from 2001 to 2019 among Japanese women, were obtained from e-Stat, a portal site of Japanese Government Statistics. The analysis indicates that the incidence rates of breast and uterine body cancers among Japanese women increased from 2004 to 2019, displaying distinct distribution patterns with two peaks for breast cancer and one peak for uterine body cancer. The rising incidence rates of both cancers were positively correlated with annual changes in animal protein and saturated fat intake and inversely correlated with changes in plant protein and folate intake. Health-care professionals should be aware of the notable and characteristic increase in breast and uterine body cancer incidence among Japanese women and emphasize the importance of lifestyle modifications to counteract Westernized dietary habits.

Keywords: Breast cancer; Uterine body cancer; Animal protein; Plant protein; Saturated fat; Folate

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1. Introduction

We previously reported that age-specific incidence rates of breast cancer among Japanese women increased from 2005 to 2015 in a bimodal distribution pattern, with two peaks in the age groups of 45 – 49 and 60 – 64 years (pre- and post-menopausal groups).[1] It was presumed that the low prevalence of obesity and high intake of soy products or isoflavones among Japanese women may contribute to this bimodal distribution pattern by suppressing the extent of the increase in breast cancer incidence rates among post-menopausal women. Furthermore, we reported that the increasing breast cancer incidence was positively correlated with drinking prevalence during the same period or smoking prevalence during the period 10 years before the cancer incidence. These correlations were compared with those of uterine body, colon, and lung cancer incidence.[2] The incidence of uterine body cancer, which is also an estrogen-related cancer like breast cancer,[3,4] increased in a bell-shaped distribution pattern and was similarly correlated with drinking and smoking prevalence.

Recent increases in breast and uterine body cancers among Japanese women have highlighted some modifiable factors for cancer development, including drinking and smoking habits, which are generally associated with Westernized lifestyles.[5-7] It has been demonstrated that the Japanese diet continued to Westernize from 2003 to 2015.[8] The impact of these modifiable factors on breast and uterine body cancer risk has been evidenced by studies on immigrants, where an increased risk was observed among Asian women migrating to the United States.[9,10] In the present study, using national annual data on cancer incidence rates up to 2019, we examined the associations between recent changes in cancer incident rates and dietary habits.

2. Data and methods

Data pertaining to age-specific incidence rates (per 100,000 population in each 5-year age group) of breast, uterine body, colon, and lung cancers among Japanese women from 2004 to 2019 were retrieved from the e-Stat portal (a portal site of Japanese Government Statistics: https://www.e-stat.go.jp/en/node). In 2016, the age-specific breast cancer incidence rates transitioned from national estimates to data based on the National Cancer Registry. Annual changes in the intake of animal protein, plant protein, saturated fatty acid, and folate from 2001 to 2019 among Japanese women, stratified by 10-year age groups (with 70 years and over as one group), are also available on the e-Stat site. Note that national surveys on plant protein and saturated fatty acid intake were not conducted in 2001 and 2003.

The cancer incidence rates were recalculated from per 100,000 population in each 5-year age group to per 100,000 population in each 10-year age group to match the nutrient intake data. Linear correlations of cancer incidence rates in 10-year age groups (30s, 40s, 50s, 60s, and ≥70s) from 2011 to 2019 with annual changes in nutrient intake among the same 10-year age groups during the same period (30s, 40s, 50s, 60s, and ≥70s from 2011 to 2019) or 10 years before cancer incidence (20s, 30s, 40s, 50s, and 60s from 2001 to 2009) were assessed using Pearson's correlation coefficients. Nine pairs of data (n=9) were used for this assessment, except for plant protein and saturated fat intake from 2001 to 2009, which used seven pairs of data (n=7). All tests were two tailed, and statistical significance was set at $P < 0.05$.

3. Results

Figure 1 shows the 5-year age-specific incidence and mortality rates of breast, uterine body, colon, and lung cancers among Japanese women in 2004, 2009, 2014, and 2019. The age-specific incidence rates of breast cancer increased markedly over the 15-year period, displaying a bimodal distribution pattern. The pre- and post-menopausal peaks were observed in the age groups of 45 – 49 years and 60 – 64 years in 2004, 2009, and 2014. However, by 2019, the post-menopausal peak had shifted to the age group of 70 – 74 years. The mortality rates of breast cancer, which rise with age, increased in the age groups above 60 years, while slightly decreasing in the age groups between 40 and 54 years.

The incidence rates of uterine body cancer were lower than those of breast cancer but still showed an increase from 2004 to 2019, following a bell-shaped distribution pattern that peaked in the age group of 55 – 59 years. The mortality rates of uterine body cancer, also rising with age, increased during the same period in the age groups above 40 years.

The incidence rates of both colon and lung cancers, which also rise with age, gradually increased from 2004 to 2019 in the age groups above 60 years, except for the lung cancer incidence rate in the age group of 85 years and older. The mortality rates of colon cancer, which rise with age, slightly decreased from 2004 to 2019 in the age groups of 70 – 84 years, while those of lung cancer remained unchanged during the same period.

Re-calculating the incidence rates of breast, uterine body, colon, and lung cancers from per 100,000 population in each 5-year age group to per 100,000 population in each 10-year age group, the annual changes in their cancer incidence rates from the 20s to 70s age groups from 2004 to 2019 are shown in Figure 2. Breast cancer incidence rates were higher and rising in individuals in their 40s and older compared to other cancer incidence rates. The incidence rates of uterine body cancer were low but more than doubled from 2004 to 2019. This increase was also observed in the breast cancer incidence rate in individuals in their 70s. The colon and lung cancer incidence rates were similar and rose slowly during the period in individuals in their 60s and 70s. From 2016 to 2019, the previously increasing trends in breast, lung, and colon cancer incidence rates became stagnant, except for breast cancer in individuals in their 70s.

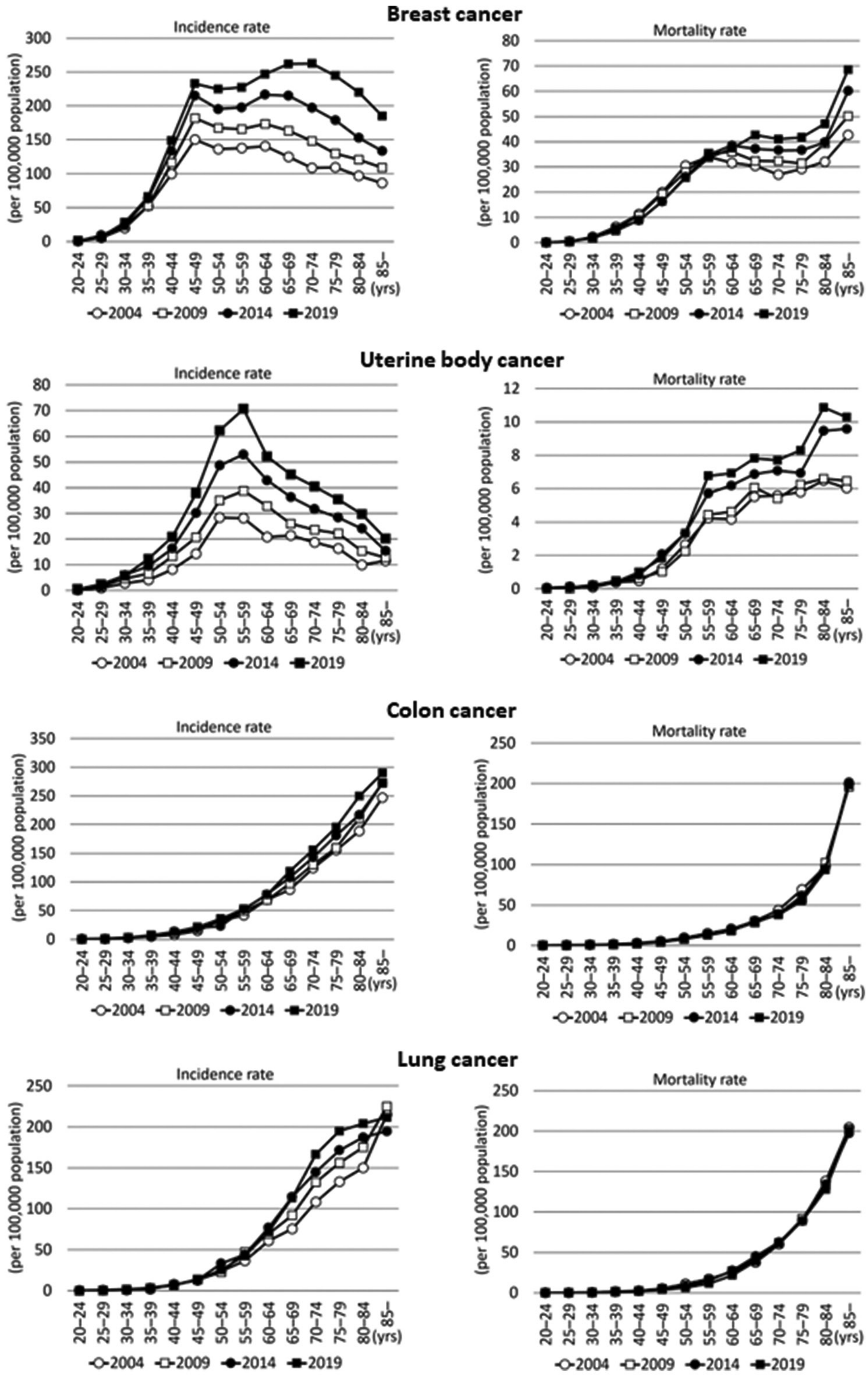

Figure 1. Age-specific incidence and mortality rates of breast, uterine body, colon, and lung cancers among Japanese women in 2004, 2009, 2014, and 2019

Figure 3 shows annual changes in animal protein, plant protein, saturated fatty acid, and folate intakes from 2001 to 2019 among Japanese women stratified by 10-year age groups. Trends of annual changes during this period

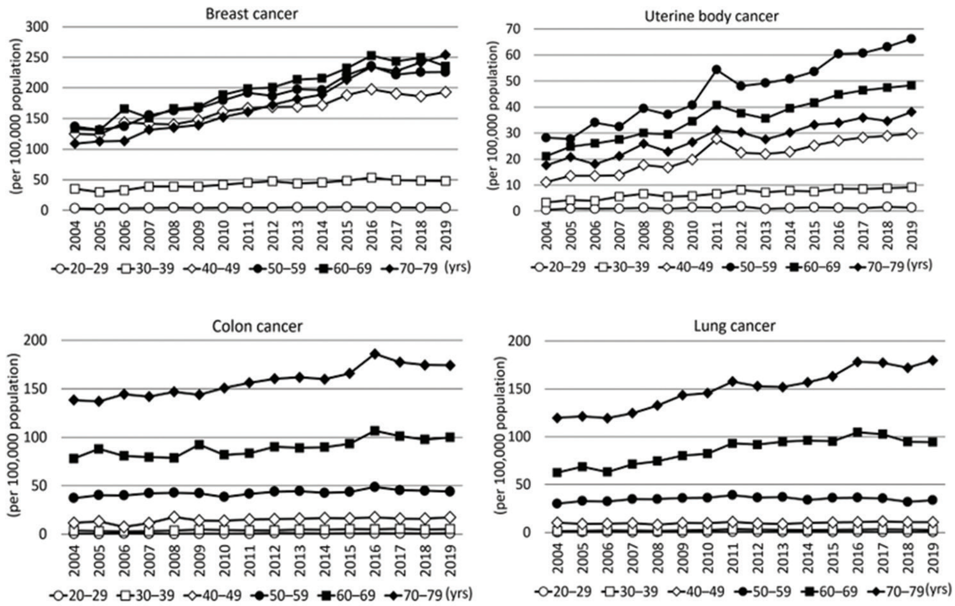

Figure 2. Annual changes in the incidence rates of breast, uterine body, colon, and lung cancers from 2004 to 2019 among Japanese women, stratified by 10-year age groups (20s – 70s)

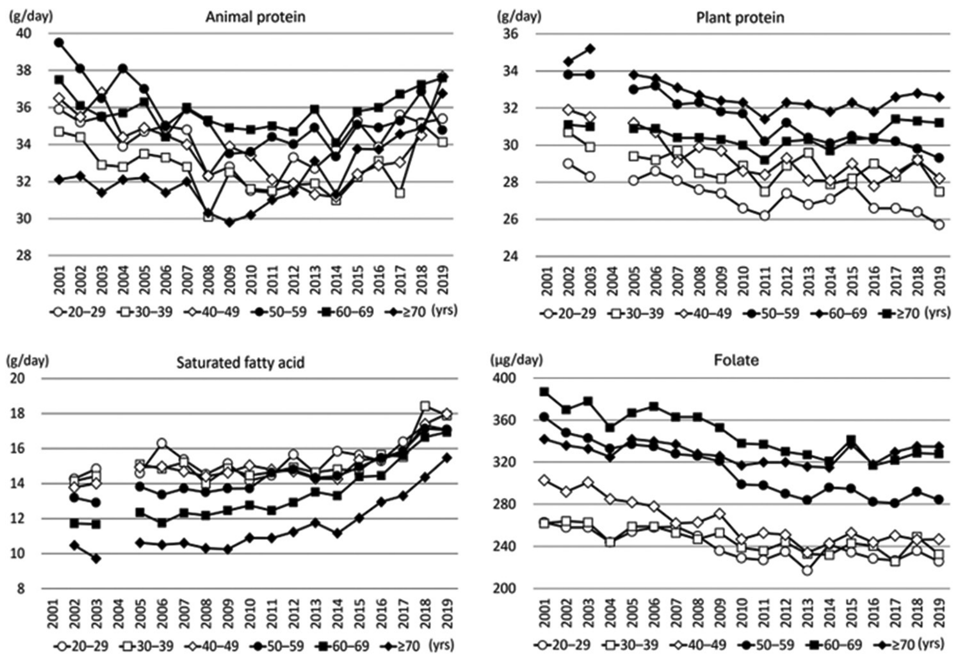

Figure 3. Annual changes in animal protein, plant protein, saturated fatty acid, and folate intakes from 2001 to 2019 among Japanese women, stratified by 10-year age groups

exhibited a U-shaped pattern in animal protein intake, an increasing pattern in saturated fatty acid intake, and a decreasing pattern in plant protein and folate intake. The intake of plant protein and folate was clearly lower in younger generations (20s, 30s, and 40s) compared to older generations, whereas the intake of saturated fatty acids was higher in younger generations. For animal protein intake, such generation gaps were not observed.

Table 1 presents the correlations between changes in cancer incidence rate (2011 to 2019) and changes in nutrient intake during the same period or 10 years before cancer incidence. Comparing Figures 2 and 3, it is evident

Table 1. Correlations between changes in cancer incidence rates (2011 – 2019) and changes in nutrient intake during the same period or 10 years before cancer incidence

Cancer type	Nutrient	The same period (2011 – 2019)					10 years prior (2001 – 2009)				
		30s	40s	50s	60s	70 s	30s	40s	50s	60s	70s
Breast cancer	Animal protein	r=0.41; P=0.27	r=0.62; P=0.07	r=0.63; P=0.07	r=0.72; P=0.03*	r=0.92; P<0.01*	r=−0.19#; P=0.63	r=−0.41#; P=0.28	r=−0.68#; P=0.04*	r=−0.81#; P<0.01*	r=−0.71#; P=0.03*
	Plant Protein	r=0.14; P=0.72	r=−0.16#; P=0.69	r=−0.53#; P=0.14	r=0.52; P=0.16	r=0.84; P<0.01*	r=0.10; P=0.83	r=−0.70#; P=0.08	r=−0.68#; P=0.09	r=−0.67#; P=0.10	r=−0.93#; P<0.01*
	Saturated fatty acid	r=0.33; P=0.39	r=0.67; P=0.049*	r=0.71; P=0.03*	r=0.80; P=0.01*	r=0.93; P<0.01*	r=0.72; P=0.07	r=0.62; P=0.14	r=0.90; P<0.01*	r=0.56; P=0.19	r=0.69; P=0.09
	Folate	r=0.24; P=0.53	r=0.14; P=0.72	r=−0.48#; P=0.19	r=−0.40#; P=0.28	r=0.67; P=0.047*	r=0.02; P=0.96	r=−0.28#; P=0.47	r=−0.78#; P=0.01*	r=−0.79#; P=0.01*	r=−0.60#; P=0.09
Uterine body cancer	Animal Protein	r=0.64; P=0.06	r=0.78; P=0.01*	r=0.60; P=0.09	r=0.78; P=0.01*	r=0.81; P<0.01*	r=−0.72#; P=0.03*	r=−0.38#; P=0.31	r=−0.72#; P=0.03*	r=−0.72#; P=0.03*	r=−0.35#; P=0.35
	Plant Protein	r=0.09; P=0.82	r=−0.02#; P=0.95	r=−0.79#; P=0.01*	r=0.49; P=0.19	r=0.71; P=0.03*	r=−0.43#; P=0.34	r=−0.84#; P=0.02*	r=−0.88#; P=0.01*	r=−0.93#; P<0.01*	r=−0.97#; P<0.01*
	Saturated fatty acid	r=0.77; P=0.02*	r=0.82; P<0.01*	r=−0.69#; P=0.04*	r=0.87; P<0.01*	r=0.86; P<0.01*	r=0.37; P=0.41	r=0.31; P=0.50	r=0.61; P=0.15	r=0.74; P=0.06	r=0.81; P=0.03*
	Folate	r=0.07; P=0.86	r=0.41; P=0.28	r=−0.40#; P=0.29	r=−0.19#; P=0.62	r=0.75; P=0.02*	r=0.57; P=0.11	r=−0.30#; P=0.43	r=−0.79#; P=0.01*	r=−0.69#; P=0.04*	r=−0.52#; P=0.16
Colon cancer	Animal Protein	r=0.30; P=0.44	r=0.59; P=0.10	r=0.38; P=0.31	r=0.64; P=0.06	r=0.71; P=0.03*	r=−0.34#; P=0.37	r=−0.32#; P=0.41	r=−0.33#; P=0.38	r=−0.84#; P<0.01*	r=−0.74#; P=0.02*
	Plant Protein	r=0.01; P=0.99	r=−0.53#; P=0.14	r=−0.01#; P=0.99	r=0.45; P=0.22	r=0.71; P=0.03*	r=−0.57#; P=0.18	r=−0.70#; P=0.08	r=−0.21#; P=0.66	r=−0.57#; P=0.18	r=−0.64#; P=0.12
	Saturated fatty acid	r=0.34; P=0.37	r=0.49; P=0.18	r=0.32; P=0.40	r=0.71; P=0.03*	r=0.72; P=0.03*	r=0.60; P=0.16	r=0.47: P=0.29	r=0.45; P=0.31	r=0.46; P=0.30	r=0.22; P=0.63
	Folate	r=−0.34#; P=0.37	r=−0.28#; P=0.47	r=−0.75#; P=0.02*	r=−0.57#; P=0.11	r=0.35; P=0.35	r=−0.32; P=0.40	r=−0.37#; P=0.33	r=−0.47#; P=0.21	r=−0.74#; P=0.02*	r=−0.29#; P=0.45
Lung cancer	Animal Protein	r=−0.01#; P=0.98	r=0.39; P=0.30	r=−0.42#; P=0.26	r=0.22; P=056	r=0.81; P<0.01*	r=0.34; P=0.37	r=−0.09#; P=0.83	r=0.90; P<0.01*	r=−0.40#; P=0.29	r=−0.55#; P=0.12
	Plant Protein	r=−0.14#; P=0.73	r=−0.01#; P=0.98	r=0.54; P=0.13	r=−0.04#; P=0.93	r=0.72; P=0.03*	r=0.24; P=0.61	r=−0.48#; P=0.27	r=0.62; P=0.14	r=−0.19#; P=0.68	r=−0.88#; P<0.01*
	Saturated fatty acid	r=0.02; P=0.96	r=0.45; P=0.22	r=−0.72#; P=0.03*	r=0.25; P=0.53	r=0.85; P<0.01*	r=0.27; P=0.56	r=0.57; P=0.18	r=−0.14#; P=0.76	r=0.20; P=0.66	r=0.59; P=0.16
	Folate	r=0.03; P=0.94	r=0.66; P=0.06	r=−0.09#; P=0.83	r=−0.67#; P=0.047*	r=0.56; P=0.11	r=0.61; P=0.08	r=−0.32#; P=0.41	r=0.76; P=0.02*	r=−0.37#; P=0.32	r=−0.42#; P=0.27

Notes: *Denotes $P<0.05$ ($n=9$, except for plant protein or saturated fatty acid intake 10 years prior [$n=7$]); #denotes inverse correlation.

that breast cancer incidence from 2011 to 2019 was positively and significantly correlated with animal protein intake in individuals in their 60s and 70s. Similarly, it was significantly correlated with saturated fatty acid intake in individuals in their 40s, 50s, 60s, and 70s during the same period. Conversely, breast cancer incidence was inversely and significantly correlated with animal protein intake in individuals in their 50s, 60s, and 70s, as well as with folate intake in individuals in their 50s and 60s from 10 years prior. Uterine body cancer incidence was positively and significantly correlated with animal protein intake in individuals in their 40s, 60s, and 70s and with saturated fatty acid intake in individuals in their 30s, 40s, 60s, and 70s during the same period. It was inversely and significantly correlated with animal protein intake in individuals in their 30s, 50s, and 60s and with folate intake in individuals in their 50s and 60s from 10 years prior. Unlike breast cancer incidence, uterine body cancer incidence also showed an inverse and significant correlation with plant protein intake in individuals in their 40s, 50s, 60s, and 70s from 10 years prior. For colon and lung cancer incidence, significant correlations were found in a much smaller number of 10-year age groups.

4. Discussion

The updated data on age-specific breast and uterine body cancer incidence rates among Japanese women show an increase until 2019, with the incidence rates exhibiting bimodal and single peak distribution patterns, respectively. The mortality rates of both cancers increased among post-menopausal women from 2004 to 2019, likely due to early cancer detection and advanced cancer treatments.[11] However, these measures appear less effective for uterine body cancer than breast cancer, especially among pre-menopausal women. In Japan, mammography for breast cancer screening was introduced in 2000.[12] For colon and lung cancers, which are generally regarded as age-related cancers,[13] the age-specific incidence rates mostly increased after 60 years from 2004 to 2019. However, the mortality rates did not show a corresponding increase, suggesting that early detection and improved treatments contributed to these trends. In contrast, the mortality rates of breast and uterine body cancers increased, especially among post-menopausal women, indicating actual increases in their incident rates.

An interesting finding is the shift in the post-menopausal peak of breast cancer incidence from the 60 to 64 age group to the 70 to 74 age group in 2019. The latter peak resembles that observed among Asian/Pacific Islander women in the United States from 2015 to 2019, where the incidence rates were highest among White women.[14] Breast cancer incidence rates increased among all racial and ethnic groups in the United States from 2015 to 2019, with a faster pace among Asian/Pacific Islander women (2.1%/year) compared to White women (0.5%/year). In Japan, according to the report on age-standardized rates of cancer incidence up to 2015 by Katanoda *et al*.,[15] the increasing trend of breast cancer incidence slowed down after 2010. Interestingly, the present study, using the same national data, showed that 10-year age-stratified breast cancer incidence became stagnant after 2016. However, the increasing trend continued from 2016 to 2019 in the age group of 70 to 79 years. The increasing trend in age-specific uterine body cancer incidence was more pronounced than that of breast cancer. In North America, from 1995 to 2018, early-onset endometrial (uterine body) cancer incidence (diagnosed before 50 years) rose faster than late-onset endometrial cancer (diagnosed at 50 years or older) among non-white women.[16] The single peak at the age group of 55 – 59 years was lower and younger than the peak at 75 – 79 years in the United Kingdom from 2016 to 2018.[17] From the perspective of two-component mixture models comprising pre- and post-menopausal components,[18] it is inferred that the post-menopausal component was smaller in uterine body cancer but becoming larger in breast cancer. The recent increase in breast cancer incidence among Japanese post-menopausal women might be attributable to age-related carcinogenicity,[13] in addition to estrogen-related carcinogenicity.[3]

This ecological study, using national data among Japanese women stratified by 10-year age group, demonstrated that recent breast and uterine body cancer incidence rates from 2011 to 2019 exhibited stronger correlations with annual changes in animal protein, saturated fat, plant protein, and folate intake compared to those of colon and lung cancers. Notably, recent uterine body cancer incidence, which appeared to be more affected by estrogen than breast cancer, was inversely correlated with past intake trends (10 years prior) of plant protein, presumably reflecting soy products containing isoflavones (phytoestrogens).[19] Similarly, uterine body cancer incidence was positively correlated with current animal protein and saturated fat intake trends and inversely correlated with past folate intake trends. Meat intake increased while fish and shellfish intake decreased among Japanese women from 2001 to 2019, with meat intake being higher and fish and shellfish intake being lower in younger generations compared to older generations.[20] Changes in dietary habits likely contributed to the U-shaped annual change in animal protein intake observed during this period, as shown in the present study. Similar decreasing trends were observed in the intakes of vegetables, fruits, and algae,[20] of which are dietary sources of folate. These foods may have anti- or pro-inflammatory potential, influencing cancer development.[21,22] The effect of folate on cancer development might persist long term by acting as methyl-group donors to DNA methylation.[23,24] Algae, a typical food in the Japanese diet, has been shown to decrease endogenous estrogen levels.[25]

Breast cancer is well researched for its estrogen etiology, with clinical and experimental studies showing estrogen's role in carcinogenesis through estrogen metabolism and receptor pathways.[3] Elevated blood estrogen levels in post-menopausal women with obesity, due to the conversion of androgen to estrogen by aromatase in adipose tissue,[26] are linked to the development of estrogen receptor-positive breast cancer.[27] Although the prevalence of drinking habits and obesity is low in Japan, alcohol consumption contributes to breast cancer incidence[28] by elevating blood estrogen levels in pre- and post-menopausal women.[29,30] Globally, increasing breast cancer incidence rates in East and Southeast Asia are associated with the Westernization of reproductive and lifestyle patterns, leading to cumulative exposure of breast tissue to endogenous and exogenous estrogen.[31,32] Similar factors likely influence uterine body cancer. However, the use of oral contraceptives or hormone replacement therapy is low in Japan.[33]

Regarding breast cancer risk, another scenario may be inferred from the association between non-alcoholic fatty liver disease and extrahepatic cancers, including breast cancer.[34,35] Non-alcoholic fatty liver disease, closely associated with increased visceral adipose tissue, the main component of central obesity, can induce low-grade chronic inflammation and insulin resistance, creating a favorable microenvironment for cancer development.[36] Although obesity is known to be associated with endometrial and breast cancer risk,[37] Kim *et al*.[34] reported that the association between non-alcoholic fatty liver disease and the development of breast cancer was found in non-obese women but not in obese women in Korea. In Japan, it was observed that non-alcoholic fatty liver disease continued to increase in both men and women from 2008 to 2019, regardless of body mass index and age, and its prevalence was correlated with the dietary intake of saturated fatty acids as well as total fat.[38] Interestingly, in a Japanese cohort, it was predicted that an isocaloric substitution of 3% of energy from fish protein or plant protein for animal or processed meat protein significantly reduced cancer-related mortality.[39]

One of the limitations of the present ecological study is the lack of a direct correlation between cancer incidences or mortality and dietary nutrition intake, as the data were not obtained from the same individuals. However, the data stratified by sex and age were considered to be representative averages for the respective stratified groups across Japan. Another limitation is that the present analysis was purely descriptive and did not categorize cancers into clinically relevant or specific histological subtypes. Further studies are needed to clarify the factors underlying the observed association trends between cancer incidence and dietary intake.

5. Conclusion

The present ecological study, using national data, demonstrated that the incidence rates of estrogen-related breast and uterine body cancers among Japanese women increased from 2004 to 2019, exhibiting distinct bimodal and single peak distribution patterns, respectively. Rising incidence rates of these cancers were positively correlated with annual changes in animal protein and saturated fat intake and inversely correlated with changes in plant protein and folate intake. Health-care professionals should be aware of the notable and characteristic increase in breast and uterine body cancer incidence among Japanese women and emphasize the importance of lifestyle modifications to counteract Westernized dietary habits.

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Conflict of interest

The author declares that he has no competing interests.

Author contributions

This is a single-authored article.

Ethics approval and consent to participate

Not applicable.

Consent for publication

Not applicable.

Availability of data

Data are available on the e-Stat portal (a portal site of Japanese Government Statistics: https://www.e-stat.go.jp/en/node).

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