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Association between average daily television viewing time and the incidence of ovarian cancer: Findings
from the Japan Collaborative Cohort Study

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Abstract

PURPOSE: Seventy-five percent of epidemiological studies have reported that sedentary behavior is associated with ovarian cancer incidence. Although Japan has one of the most sedentary populations, with median sitting times of 7 hours/day, this association has not been investigated. This study aimed to elucidate the association between average daily television (TV) viewing time, which is a major sedentary behavior, and the incidence of ovarian cancer in a large-scale nationwide cohort study in Japan.

METHODS: A total of 34,758 female participants aged 40–79 years without a history of cancer at baseline were included in the study. The inverse probability weighted competing risk model was used to calculate the hazard ratio (HR) and 95% confidence interval (CI) for the incidence of ovarian cancer.

RESULTS: During a median follow-up of 19.4 years, 59 participants developed ovarian cancer (ICD-10: C56), 2,706 participants developed other types of cancer, and 4,318 participants died. Participants who watched TV for ≥ 5 hours/day were more likely to develop ovarian cancer than those who watched TV for < 2 hours/day (HR 2.15; 95% CI 1.54-2.99).

CONCLUSION: Our findings suggest that reducing the amount of time spent sedentarily may be beneficial for preventing ovarian cancer.

Keywords: ovarian neoplasms, sedentary behavior, cohort study, risk assessment, epidemiology

Introduction

Ovarian cancer is the seventh most common type of cancer globally and the eighth most common cancer causing death in women (globally, 239,000 new cases resulting in 152,000 deaths were recorded in 2012)[1]. The incidence of ovarian cancer has been increasing in Japan with a cumulative incidence of 14.3 per 10,000 people in 2012[2]. This incidence was higher than in the United States (11.7 per 10,000 people)[3], and China (0.6 per 10,000 people)[4]. Early menarche or late menopause[5] and genetic associations such as a family history of ovarian, breast[6], or prostate[7] cancer or with a BRCA1 or BRCA2 mutation[8] have been demonstrated to be a likely risk factors for ovarian cancer.

Previously, the Ovarian Cancer Association Consortium reported that recreational physical inactivity, which is defined by the absence of moderate-vigorous physical activity, was positively associated with epithelial ovarian cancer[9]. Sedentary behavior, distinct from the absence of moderate-vigorous physical activity[10], was also reported to be a risk factor for ovarian cancer reported in the United states [11-13] and China [14]. However, consistent results were not obtained regarding this association. The length of sitting time among Japanese people has been reported to be approximately 7 hours/day, being the longest in the world [15]. The time spent watching television (TV) is a good indicator of leisure time associated sedentary and sitting time in developed countries, including Japan[16]. In 2015, the prevalence of TV watching for at least 5 hours was 25% in Japan[17]. However, whether TV watching is associated with the incidence of ovarian cancer among Japanese women remains unclear.

Therefore, we examined the association between daily TV viewing time and the incidence of ovarian cancer in Japanese women in a large-scale national cohort study.

Material and Methods

Study population and data collection

The Japan Collaborative Cohort Study for Evaluation of Cancer Risk (JACC Study) was established in 1988-90 and has been described in detail in previous publications[18]. Briefly, 110,585 (46,395 men and 64,190 women) inhabitants aged 40 to 79 years from 45 areas throughout Japan were enrolled. Participants in this study were limited to 24 study areas where the incidence of cancer could be ascertained.

Of the 38,613 original female cohort participants, 705 were excluded because they had a history of cancer. A further 2,057 participants in two areas were also excluded because the questionnaire used did not include an item on average daily TV viewing hours. Finally, 1,093 participants with missing data on average daily TV viewing hours were excluded. Consequently, 34,758 participants were evaluated in the present study.

The data was collected using a self-administered questionnaire, and a response rate of 83% was obtained. Information on the average daily number of hours spent watching TV was obtained in the baseline questionnaire using the following question, “On average, how many hours a day do you spend

watching TV?”. We sequentially created five categories for TV viewing time (<2, 2-2.9, 3-3.9, 4-4.9, ≥ 5 hours/day) and set <2 hours/day as a reference category based on previously identified associations with ovarian cancer risk[14].

Follow-up

The incidence of cancer could be ascertained in 24 study areas where population-based cancer registries or local major hospital records were available for review and coded according to the tenth revision of the International Classification of Disease (ICD-10). The primary outcome of interest in the present study was the incidence of ovarian cancer (ICD-10: C56). The date and cause of death were confirmed by death certificates. Participants who moved away from the study area during the study period were treated as censored cases. Those records were followed up until the end of 2009, with the exception of participants in 4 areas who were followed up until 2003. Participants in one area were another exception as they were followed up until 2002. The study design was approved by the Ethical Board of Nagoya University School of Medicine.

Statistical analysis

Multivariate hazard ratios (HR) and confidence intervals (CI) for the incidence of ovarian cancer were calculated using an inverse probability weighted (IPW) [19,20] competing risk model[21] in which we

treated incidence of cancer other than ovarian cancer and death as a competing events[22]. To develop the generalized propensity score, we conducted a multinomial logistic regression analysis using variables for all demographic information[23], including age (a continuous variable), body mass index (BMI; <18.5, 18.5–24.9, or ≥ 25.0 kg/m², or missing), educational level (school up to age 15, 15–18, or ≥ 19 years, or missing), smoking status (never, former, or current smoker, or missing), alcohol drinking status (never, former, or current alcohol drinker, or missing), average daily sleeping time (<6.5, 6.5–8.4, or ≥ 8.5 hours/day, or missing), average daily walking time (<1, ≥ 1 hours/day, or missing), age at menarche (<13, 13–15, or ≥ 16 years, or missing), age at menopause (<44, 44–48, 49–52, or ≥ 52 years, or having periods/missing), parity (none, 1–2, ≥ 3 times, or missing), use of hormone therapy ever (never, user, or missing), family history of breast, ovarian, or prostate cancer (yes or no/missing) [24]. To assess the covariate balance, we showed the propensity score overlap using kernel density plots. An alpha level of 0.05 was considered to be a statistically significant. All statistical analyses were performed using SAS 9.4 (SAS Institute Inc., Cary, NC, USA). The graphs were drawn using JMP 12.2 (SAS Institute Inc., Cary, NC, USA)

Results

Table 1 shows the baseline characteristics of participants based on TV viewing hours. The mean age of participants $\pm$ standard deviation (SD) at baseline was 58.1 ± 10.1 years. Approximately 14.8% of

participants watched TV for longer than 5 hours daily. Compared to participants who viewed TV for less than 2 hours, participants who viewed TV for more than 5 hours tended to be older, more likely to be overweight/obese, current smokers, current alcohol drinkers, longer sleepers, older at menarche, and post-menopausal, and less likely to be daily walkers, and parity. The distributions of propensity scores among the five categories of TV viewing were well balanced after weighting (Figure 1 and eTable 1).

During a median follow-up of 19.4 years, 59 participants developed ovarian cancer, 2,706 participants developed other types of cancer, and 4,318 participants died. Table 2 shows the HRs for the incidence of ovarian cancer based on the average daily TV viewing hours using a competing risk model. Participants that watched TV for ≥ 5 hours/day were more likely to develop ovarian cancer than those that watched TV for < 2 hours/day (HR 2.15, 95% CI 1.54-2.99).

Discussion

In this large cohort study, we found that a prolonged average daily TV viewing time at baseline was associated with an increased risk of ovarian cancer incidence among Japanese women. Our results are consistent with the findings from 75% of other studies, including a Chinese case-control study[14] and two American cohort studies[12,11]. There was an association between an interviewer-administered exposure to sitting duration while watching TV and epithelial ovarian cancer (adjusted odds ratio 3.39, 95% CI 1.00–11.50 for > 4 vs. < 2 h/day) among 906 Chinese women (cases $n = 254$, controls $n = 652$)

who were < 75 years old[14]. Additionally, there were two cohort studies investigating similar associations; one of which evaluated the association between self-reported sitting time and the incidence of ovarian cancer (adjusted HR 1.55, 95% CI 1.08-2.22 for ≥ 6 vs. <3 h/day) among 59,695 (a mean age of 62.7 years) United States (US.) women[12], and another which evaluated the association between self-reported leisure-time sitting and the incidence of ovarian cancer (adjusted HR for total ovarian cancer 1.44, 95% CI 1.12-1.85 for ≥ 6 vs. <3 h/day) among 63,972 postmenopausal US. women aged 50-74 years[11]. In contrast, a cohort study evaluated the association between sedentary behavior and the incidence of ovarian cancer among 148,892 US. women aged 50-71 years, but there were no statistically significant association between self-reported sedentary behavior and the incidence of ovarian cancer (adjusted relative risk 1.06, 95% CI 0.81-1.39 for ≥ 7 vs. <3 h/day overall sitting time; 1.02, 95% CI 0.67-1.55 for ≥ 7 vs. <3 h/day TV watching time)[13].

Although potential mechanisms are still unclear, metabolic dysfunction may be involved in the pathogenesis of ovarian cancer. Sedentary lifestyles are associated with obesity[25,26], elevated insulin resistance[27], and type 2 diabetes mellitus[28]. These conditions lead to hyperinsulinemia which increases the rate of androgen synthesis [29]. High serum androgens may stimulate ovarian epithelial proliferation and contribute to ovarian cancer risk [30]. In addition to the effects of hyperinsulinemia, excess adipose tissue found in overweight and obese individuals can increase levels of inflammatory factors such as free fatty acids, interleukin-6, tumor necrosis factor-alpha, and leptin [31]. Each of these

factors might play an etiologic role in regulating malignant transformation or cancer progression.

A previous study showed risk factors for ovarian cancer differed by histological types of ovarian cancer[32]. Although the exact biologic pathway is unclear, the association between sedentary behavior and ovarian cancer may differ by histological types of ovarian cancer as a prospective cohort study of 63,972 postmenopausal US. women showed a different association between self-reported leisure-time sitting and the incidence of ovarian cancer based on histological type (adjusted HR for serous ovarian cancer 1.52, 95% CI 1.06-2.16; adjusted HR for non-serous ovarian cancer 1.08, 95% CI 0.57-2.04 for ≥ 6 vs. < 3 h/day) [11]. Approximately 70% of ovarian cancer cases in US are the serous type, whereas 31.4% of those cases in Japan are the serous type [33]. However, we were unable to obtain information on the histological types of ovarian cancer. Further epidemiological studies with information on histological types of ovarian cancer will be valuable to evaluate the histological-specific effect of sedentary behavior.

One major form of sedentary behavior in many industrialized countries such as Japan, the United Kingdom, and the US. is watching TV[34-36]. Thus, watching TV could be an indicator of leisure-time sedentary behavior[16]. However, data regarding the average TV viewing hours was obtained via self-report and was not validated in this study, thus there may have been misclassification of exposure to the average TV viewing hours[37]. Furthermore, Japanese women reportedly spend 4 to 5 hours/day on housework such as kitchen chores, vacuuming, laundry, ironing, and sewing and of those women spend

more than 1.3 hours/day on housework while watching TV[38]. Such cases might cause an overestimation of the sedentary time, and consequently, our results may be under-estimated. Using an objective measurement, such as an accelerometer, would ensure more robust results[39].

The strengths of the present study include its prospective cohort design, the long follow-up period, and the inclusion of participants from throughout Japan. However, the present study also includes some limitations that warrant consideration. First, several meta-analyses reported that sedentary behavior is a risk factor for all-cause mortality, and mortality due to cardiovascular disease and cancer[22,40]. Therefore, since sedentary behavior is a risk factor of mortality from cardiovascular disease and cancer, it leads to an underestimation of the incidence of ovarian cancer. However, to reduce this bias, we conducted a competing risk analysis. Second, the information on the average TV viewing hours was only collected at baseline and was not updated during the study period. The average TV viewing hours is gradually decreasing in Japan[41], thus, some non-differential reporting bias such as misclassification might have been affected our results. Third, although the incidence of ovarian cancer in this study was 0.1 per 1,000 person-years, there are many potential confounders to adjust in the statistical model. Since Cox models should be used with a minimum of 10 outcome events per covariate [42], we used an IPW method based on generalized propensity scores. This approach is not only useful for reducing the number of covariates but it also offers a statistical alternative to implementing propensity score matching to balance for confounders in non-randomized studies[19]. However, the weights may be inaccurate or unstable for

participants with a very low probability due to the nature of the logistic regression [43]. Fourth, we could not obtain information on the use of oral contraceptives. The baseline surveys of this cohort were performed in 1988-90. The first oral contraceptive was introduced in 1999; therefore, the lack of data on oral contraceptives might not have affected our data. Fifth, although we adjusted age at menopause as a potential confounder, the proportion of participants with premenopausal data missing was the largest category. However, we could not distinguish between participants with premenopausal and with data missing because we do not have any further information. Therefore, some misclassification might be included in our results. Sixth, the number of ovarian cancer cases was very small ($n = 56$); therefore, our findings may be premature to claim that the associations are evident. Further larger-scale epidemiologic studies or a larger meta-analysis are warranted to help verify our findings.

Conclusion

This nationwide cohort study provides evidence that Japanese women, aged between 40–79 years, who watched TV ≥ 5 hours/day were more likely to develop ovarian cancer than those who watched TV < 2 hours/day. Thus, reducing exposure to the hours spent watching TV may help to prevent ovarian cancer incidence among Japanese women.

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Appendix

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Conflicts of interest

The authors declare that they have no conflict of interest with respect to this research study and paper.

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Table 1. Baseline characteristics based on average daily television viewing hours

Characteristic	Category	Average daily television viewing hours (h/day)				
		<2 (n = 6,341)	2-2.9 (n = 9,525)	3-3.9 (n = 9,081)	4-4.9 (n = 4,468)	≥5 (n = 5,343)
Age, years		55.2 ± 10.4	56.6 ± 10.0	58.2 ± 9.7	59.5 ± 9.5	62.5 ± 9.3
Body mass index, kg/m ²	<18.5	6.9	5.6	6.3	5.4	6.0
	18.5–24.9	69.4	69.8	65.6	65.5	60.7
	≥25.0	18.6	20.0	23.3	23.3	26.0
	Missing	5.1	4.7	4.9	5.8	7.3
College education	Yes	0.2	0.1	0.1	0.1	0.0
	No	88.8	87.3	85.5	84.8	82.2
	Missing	10.9	12.7	14.4	15.2	17.8
Smoking status	Current	3.0	4.0	4.3	5.9	7.6
	Former	1.0	1.0	1.4	1.6	2.7
	Never	88.1	85.6	84.0	81.7	75.4
	Missing	8.0	9.4	10.4	10.8	14.2
Alcohol consumption	Current	20.8	22.1	22.0	22.9	23.8
	Former	1.2	1.4	1.6	1.7	3.4
	Never	73.1	70.2	69.7	68.5	64.7
	Missing	4.9	6.3	6.7	7.0	8.2
Daily sleeping time, h/day	<6.5	29.4	26.3	24.9	24.5	25.8
	6.5-8.4	61.4	64.5	64.1	63.7	59.4
	≥8.5	4.7	5.2	6.2	6.4	7.8
	Missing	4.5	4.0	4.8	5.5	7.1
Daily walking time, h/day	<1	42.7	42.4	42.9	46.1	50.0
	≥1	47.5	46.4	45.0	41.3	36.9
	Missing	9.8	11.2	12.1	12.6	13.1
Age at menarche, years	<13	8.1	7.0	5.6	5.9	5.6
	13-15	57.7	56.5	56.1	54.9	51.2
	≥16	28.0	30.8	31.9	32.1	34.1
	Missing	6.1	5.7	6.5	7.1	9.1
Age at menopausal, years	<44	6.6	7.5	7.8	8.5	9.3
	44-48	9.8	11.1	11.5	11.6	12.6
	49-52	24.7	27.6	30.6	32.1	33.6
	≥52	15.2	17.1	18.4	19.9	21.8
	Having periods/missing	43.7	36.7	31.8	27.8	22.7
Parity, times	None	4.1	3.5	3.9	4.8	6.1
	1-2	40.9	42.0	42.0	41.8	37.5
	≥3	49.1	47.8	46.4	45.1	45.1
	Missing	5.9	6.8	7.8	8.3	11.2
Hormone therapy	Nonuser	85.8	85.5	84.8	84.0	81.8
	User	4.5	4.4	4.2	4.7	5.0
	Missing	9.8	10.0	11.0	11.4	13.2
Family history of breast, ovarian, or prostate cancer	No	97.8	98.1	98.1	97.6	98.2
	Yes	2.2	1.9	1.9	2.4	1.8

Values are expressed as mean ± standard deviation or %.

Table 2. Hazard ratios for the incidence of ovarian cancer based on average daily television viewing hours using a competing risk model

Category	Average daily television viewing time (h/day)				
	<2	2-2.9	3-3.9	4-4.9	≥5
Person-years	107,045	159,744	147,551	70,195	75,367
Number of cases	10	14	16	6	13
HR (95% CI) ^a	ref	0.97(0.43, 2.17)	1.21(0.54, 2.71)	0.98(0.36, 2.69)	2.00(0.83, 4.83)
HR (95% CI) ^b	ref	0.98(0.44, 2.18)	1.17(0.53, 2.60)	0.90(0.33, 2.44)	1.81(0.75, 4.39)
HR (95% CI) ^c	ref	1.03(0.70, 1.50)	1.18(0.82, 1.70)	0.81(0.54, 1.21)	2.15(1.54, 2.99)*

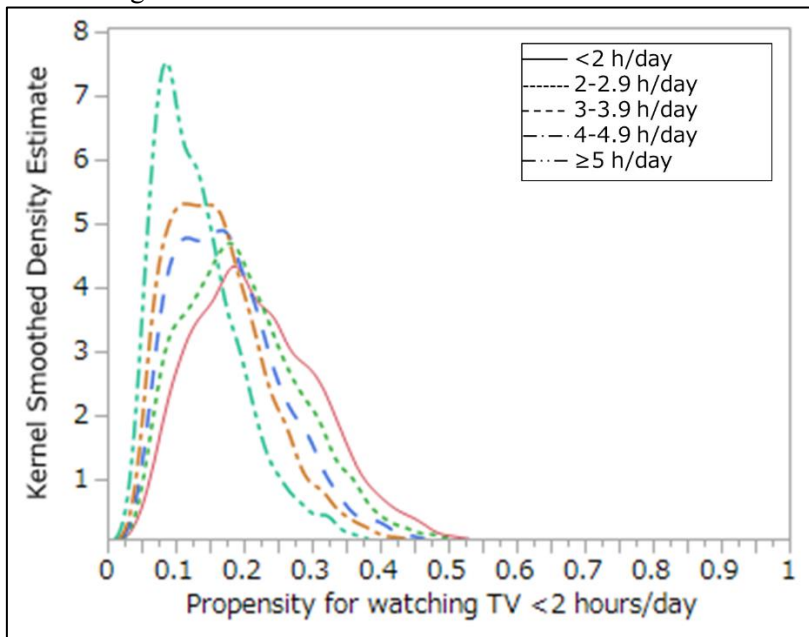
HR: hazard ratio, CI: confidence interval; ref, reference. * $P < 0.05$

^aadjusted for age.

^badjusted for all variables indicated in Table 1.

^cinverse propensity weighted competing risk model.

A. Unweighted



B. Weighted

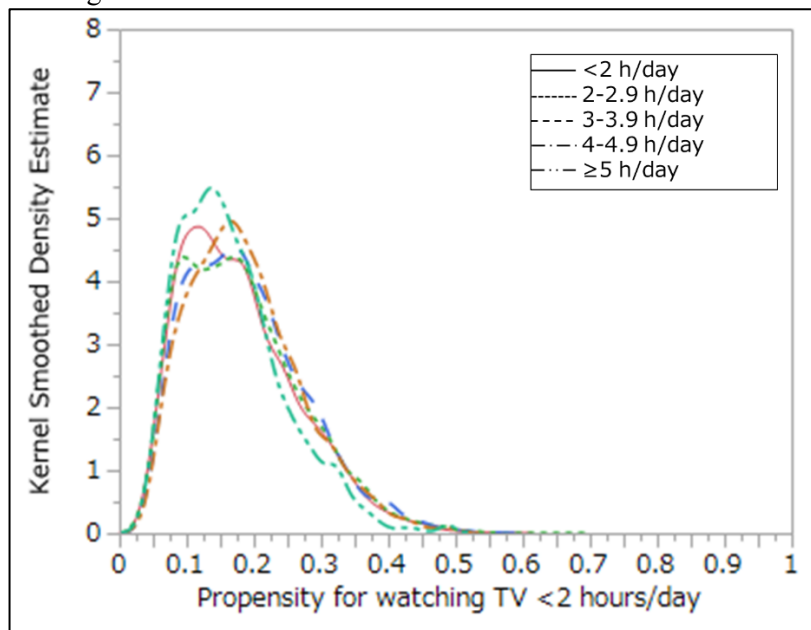


Figure 1. Kernel smoothed density estimate of propensity for watching television <2 h/day
Kernel smoothed density estimates show improved overlap of propensity for watching television <2 h/day after inverse probability weighting.