Impact of reproductive factors on breast cancer incidence: pooled analysis of nine cohort studies in Japan

Prior studies reported the association of reproductive factors with breast cancer (BC), but the evidence is inconsistent.

We conducted a pooled analysis of nine cohort studies in Japan to evaluate the impact of six reproductive factors: 1) age at menarche; 2) age at first birth; 3) number of births; 4) age at menopause; 5) use of female hormones; 6) breastfeeding on BC incidence. Population-based cohort studies including the Japan Public Health Center-based Prospective Study, Cohort I (JPHC-I), Cohort II (JPHC-II), the Japan Collaborative Cohort Study (JACC), the Miyagi Cohort Study (MIYAGI-I), the Three-Prefecture Cohort Study in Miyagi (MIYAGI-II), the Three-Prefecture Cohort Study in Aichi (AICHI), the Takayama Study (TAKAYAMA), the Ohsaki National Health Insurance Cohort Study (OHSAKI), the Life Span Study (LSS) were included in this pooled analysis. We conducted analyses according to menopausal status at the baseline or at the diagnosis. Hazard ratio (HR) and 95% confidence interval (CI) were estimated by applying the Cox proportional-hazards model in each study. These hazard ratios were integrated using a random-effects model.

187,999 women (premenopausal: 61,113, postmenopausal: 126,886) were included in the present pooled analysis. 1) Age at menarche was not associated with BC incidence among both premenopausal and postmenopausal women. 2) Although P value for trend was not significant for age at first birth, women giving first birth at ages ≥ 36 and at ages 26-35 years experienced significantly higher BC incidence than at ages 21-25 years among premenopausal and postmenopausal women, respectively (**Figure 1**, in the next page). 3) Among premenopausal women, although P value for trend was not significant for number of births (P for trend: 0.30), women who had ≥ 2 births experienced significantly lower BC incidence than nulliparous women. Among postmenopausal women, more births significantly decreased BC incidence (P for trend: 0.03) (**Figure 2**, in the next page). 4) Although P value for trend was not significant for age at menopause (P for trend: 0.37), women with age at menopause: ≥ 50 years experienced significantly higher BC incidence than age at menopause: ≤ 44 years (**Figure 3**, in the next page). 5) Use of female hormones significantly increased BC incidence (HR: 1.53, 95%CI: 1.04-2.25) among premenopausal women, whereas it was not associated with BC incidence among postmenopausal women. 6) BC incidence was similar according to breastfeeding history among both premenopausal and postmenopausal women.

In conclusion, among Japanese women, use of female hormones increased BC incidence in premenopausal women, and more births decreased BC incidence in postmenopausal women. In the present study, we did not have information on types of female hormones. Further studies would be needed to elucidate which type of female hormones is associated with BC incidence among Japanese women.

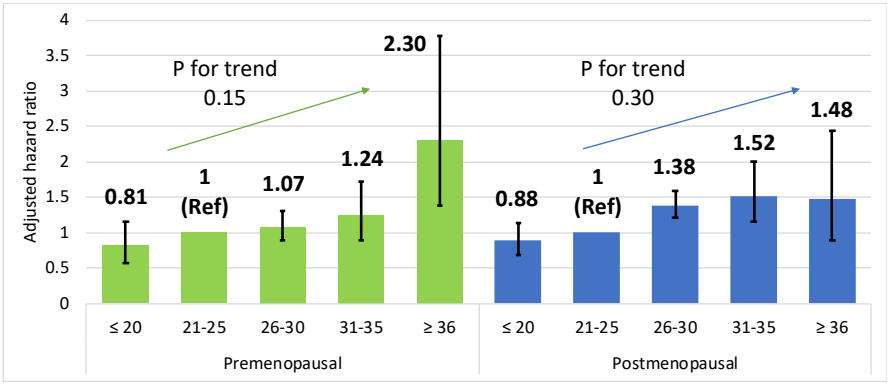

Figure 1. Age at first birth

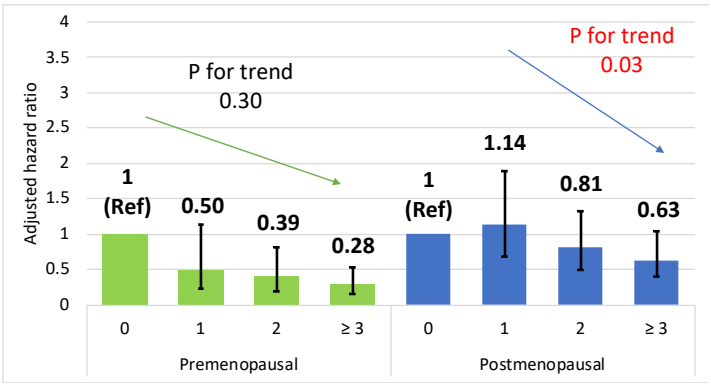

Figure 2. Number of births

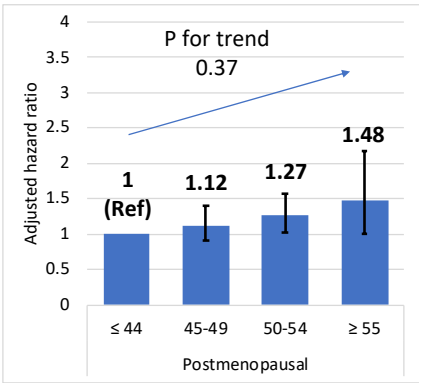

Figure 3. Age at menopause

Summary on other papers

○ **Mortality of Japanese Olympic athletes: 1952-2017 cohort study**

We compared the mortality of Japanese Olympic athletes with that of the Japanese population.

○ **Factors associated with population trends in Japan**

I analyzed factors associated with population increase or decrease in Japan by using the Japanese government statistics which is available at e-Stat, the portal site of Japanese official statistics.

○ **Profile of Patients with Novel Coronavirus Disease 2019 (COVID-19) in Osaka Prefecture, Japan: A Population-Based Descriptive Study**

○ **Characteristics of patients with novel coronavirus disease (COVID-19) during the first surge versus the second surge of infections in Osaka Prefecture, Japan**

We described the characteristics and outcomes of COVID-19 patients in Osaka Prefecture, Japan.

○ **The effect of a cancer history on patients with acute myocardial infarction after percutaneous coronary intervention: insights from the OACIS registry**

We evaluated the effect of a cancer history on outcomes of patients with acute myocardial infarction.

○ **Mortality of Japanese Olympic athletes in 1964 Tokyo Olympic Games**

Among Japanese Olympic athletes in 1964 Tokyo Olympic Games, we evaluated the association of body mass index (BMI), history of smoking, or handgrip strength at baseline with their mortality.