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Short communication

Evidence for a programing effect of early menarche on the rise of breast cancer incidence in Hong Kong

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Abstract

Background: Younger age at menarche and older age at first live birth are implicated as risk factors for breast cancer, but the extent to which these factors contribute to the sharply rising incidence of this disease in developing countries has received little study. *Methods*: We conducted a retrospective analysis of 702 consecutive breast cancer patients diagnosed at a single hospital in Hong Kong during 2003–2006. Comparisons were made between patients with different ages at cancer diagnosis (hence, belonging to different birth cohorts) and their respective ages at menarche and at first live birth. We then correlated these age-dependent differences with overall breast cancer incidence data from the Hong Kong Cancer Registry. *Results*: When patients diagnosed before age 40 are compared with those after 60, the age of menarche is lower in the former subgroup (12.7 vs. 14.2; $p < 10^{-6}$) while the age of first live birth is greater (28.2 vs. 25.5; $p < 0.01$). However, registry data suggest that the progressive rise in breast cancer incidence has not affected those over 65, nor very young (20–39 years) patients. *Conclusion*: Lifestyle variables that reduce age at menarche may contribute to the rising risk of breast cancer diagnosed after age 40 in Hong Kong, whereas earlier-onset cancers may be characterised by a distinct pathogenesis. Although retrospective, these data raise the possibility that cancer-preventive health interventions could gainfully target reversible risk factors favoring early menarche – such as formula infant feeding, high-fat diets, and lack of exercise – in children and adolescents living in developing countries such as China.

Keywords: Breast neoplasms; Epidemiology; Menarche; Breastfeeding; Diet; Carcinogenesis; Lifestyle variables; Age distribution; Self-detected; Screen-detected

1. Introduction

The lifetime risk of breast cancer in European and American females is approximately three times higher than in females in East Asia [1]. Early menarche, older age at first live birth, increased caloric intake and reduced physical activity are established risk factors for breast cancer in Caucasians [2], and are generally believed to act via secondary upregulation of endogenous estrogen metabolism [3]. Studies in China have supported the relevance of these risk factors to Chinese breast cancer patients [4–8].

Rising breast cancer incidences are now recognized in modernizing Asian countries such as Japan and Singapore [9,10], and similar trends have been confirmed in Hong Kong Chinese female breast cancer patients [11]. Exogenous ''Western'' risk factors that have been implicated in this rise include weight gain [12], alcohol [13], hormonal medications [14] and xenobiotic pollutants [15], whereas ''Eastern'' exposures may include phytoestrogens in soy and tofu dietary constituents [16]. In Hong Kong the lifetime risk of breast cancer is approximately half that of the 10.6% lifetime risk for American women; this level of risk in Hong Kong has itself doubled over the previous two decades [17],

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and remains about twice the lifetime risk level of mainland Chinese females.

To clarify the contribution to breast cancer risk of two well-recognized risk factors – age at menarche and age at first live birth – the present study analyzed the age distributions of these variables in Hong Kong patients, and compared these with changing population incidence data.

2. Materials and methods

2.1. Hong Kong breast cancer patients

Records of 702 patients referred to the Hong Kong Sanatorium & Hospital with newly diagnosed breast cancer were examined. More than 90% of these patients were ethnic Chinese. Age of diagnosis, age of menarche and age of first live birth were analysed. Patients with a diagnosis of benign or pre-malignant breast conditions, secondary breast cancers and male breast cancers were excluded.

The age distribution at diagnosis of the study population was assessed using the cut-offs: <45 years, 45–54 years, 55–64 years, 65–74 years, and >75 years. To compare the patterns of age at menarche and age at first live birth within the study population as a function of birth cohort, the sample was arbitrarily subclassified into those younger than 40 years ($n = 132$), those aged 40–60 ($n = 459$), and those aged more than 60 ($n = 113$). A control analysis to determine whether the method of breast cancer detection affected the distribution of age at menarche or age at first live birth was performed by comparing these latter endpoints in the youngest and oldest quintiles of the cohort, subdivided into either self-detected or screen-detected patient subsets.

2.2. Hong Kong Cancer Registry data

Access to Hong Kong Cancer Registry breast cancer incidence data was obtained via the organization's web portal (www3.ha.org.hk/cancereg/). Crude incidence rates of new female breast cancer diagnosed between the years 1990 to 2001 were analysed. The age-specific incidence rates of female breast cancers in patients arbitrarily classified as being under 40, between the ages of 40 and 60, and those over 60, were then compared.

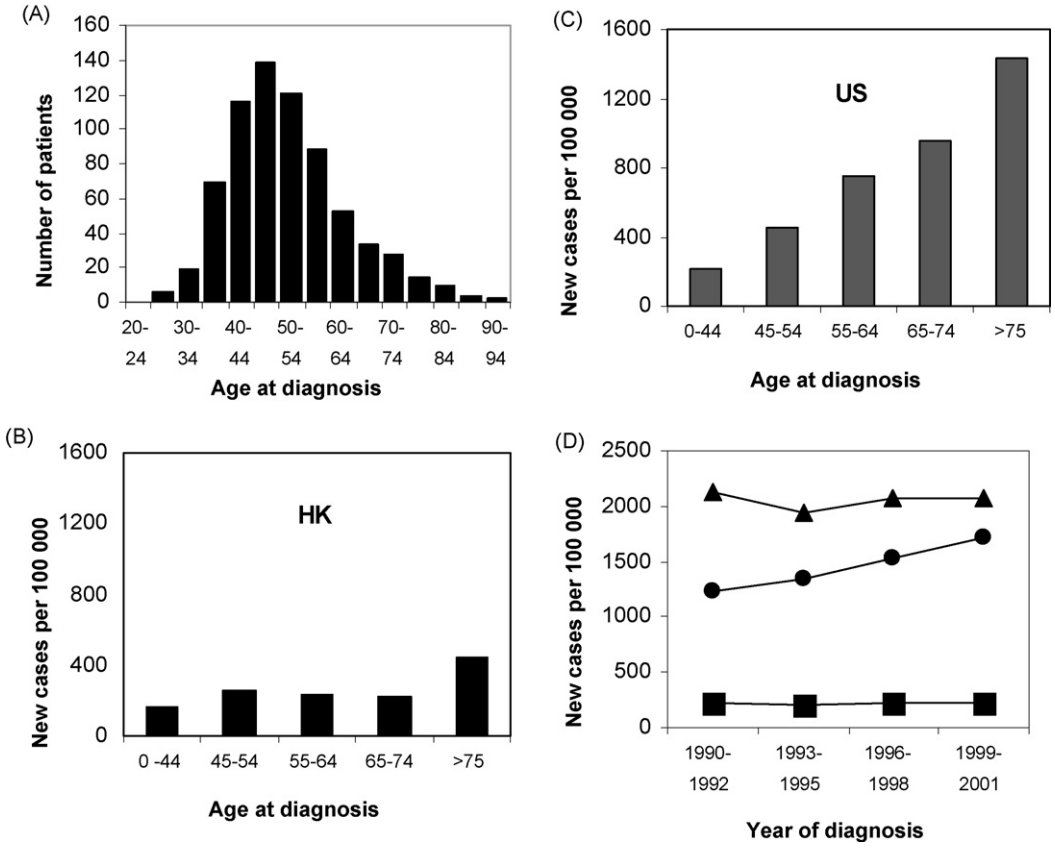

Fig. 1. Breast cancer incidence trends in Hong Kong. (A) Age frequency distribution of 702 consecutive Hong Kong breast cancer patients. (B) Age-specific incidence rate per 100,000 women of breast cancer in Hong Kong in year 2002 (source: Hong Kong Cancer Registry). (C) Age-specific incidence rate per 100,000 women of breast cancer in the United States from year 1998 to 2002 (source: Surveillance, Epidemiology and End Results Database of the National Cancer Institute of the United States). (D) Incidence rates of breast cancer per 100,000 females in the years 1990 to 2002 (y-axis) correlated with age of diagnosis (x-axis). Square labels, patients diagnosed before 40 years; round labels, patients diagnosed between ages 40–60; triangular labels, patients diagnosed after 60 years of age. *Source*: Hong Kong Cancer Registry.