Original Article

Association Between Body Mass Index and Risk of Formation of Breast Cancer in Chinese Women

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OBJECTIVE: To analyse the association between body mass index (BMI) and breast cancer risk among Chinese women in Hong Kong.
METHODS: We conducted a population-based case control study of breast cancer in June 2002. Standardized questionnaires concerning BMI and other anthropometric data were completed by patients at the Queen Mary Hospital (QMH). The cases were 198 women aged 24–85 years who had documented breast cancer in 1995–2000 by triple assessment criteria, and the controls were 353 women who were followed up at QMH for benign breast disease after breast cancer had been excluded by triple assessment. The controls were frequency-matched to the cases by age.
RESULTS: BMI at diagnosis was positively correlated with the risk of breast cancer among postmenopausal women ($p < 0.001$ for trend). Also, when compared with women with a low BMI (< 19), women with a BMI of 23–27 and 27–31 had a 1.73-fold (95% confidence interval, CI, 1.04–2.86) and 2.06-fold (95% CI, 1.08–3.93) increased risk of breast cancer, respectively, after adjustment for non-anthropometric risk factors. BMI at diagnosis, however, was not related to the risk of breast cancer among premenopausal women. The odds ratios for premenopausal women with a BMI of 23–27 and 27–31 were 1.5 (95% CI, 0.82–2.71) and 1.32 (95% CI, 0.39–4.43), respectively. Furthermore, present BMI and BMI 5 years before diagnosis were poorly associated with breast cancer risk among both pre- and postmenopausal women.
CONCLUSION: Weight control in obese women may be an effective measure for breast cancer prevention in postmenopausal women. [*Asian J Surg* 2005;28(3):179–84]

Key Words: body mass index, breast cancer, Chinese, obesity

Introduction

The incidence of breast cancer in Hong Kong is increasing.[1] As reported by the Cancer Registry, in 1999, the crude incidence and crude death rates were 53.5 and 11.8 in 100,000, respectively. Breast cancer is now the second most common cause of cancer deaths among women in our city. If modifiable risk factors were corrected, the situation would probably improve and fewer women would suffer from the detrimental emotional impact brought by the disease. High body weight (measured in terms of body mass index, BMI) has been recognized as an important risk factor for breast cancer among postmenopausal women in many previous epidemiological studies in Western countries.[2–19] These investigations report a positive relationship between breast cancer risk and high body weight in postmenopausal women, while premenopausal women were protected by higher BMI. The increased risk in overweight postmenopausal women is chiefly due to higher

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levels of free oestrogen produced by excess aromatase activity in peripheral adipose tissue.[2] Conversely, the protective mechanism among premenopausal women is not well understood.[2] In other studies, weight at certain life points was reported to be more important than just the current weight.[4,6–8,13,20] Instead of using weight alone, we used a height-adjusted weight index, the BMI, to observe the potential association with breast cancer. In addition to BMI at the time of diagnosis, we also took into account the BMI 5 years before the diagnosis of breast cancer.

Although the association between high BMI and breast cancer risk is well established, the vast majority of studies were conducted in Western countries. Only a very few have been carried out among Asian women,[3,6,13,18] in particular, Chinese.[13] The aim of our study was to further elucidate this correlation in Chinese women, and our main focus was on BMI and its relationship to breast cancer risk.

Materials and methods

We performed a case control study to determine the relationship between BMI and breast cancer risk among Chinese women in Hong Kong. All subjects were selected from the Breast Clinic at Queen Mary Hospital in June 2002. Eligible cases included all females aged 24–85 years who had been diagnosed with primary breast cancer by triple assessment between 1995 and 2002. Triple assessment included clinical examination by specialist surgeons, radiological assessment and histological confirmation by senior pathologists. During the study period, 247 eligible cases were identified from medical records and 198 (80%) participated in our study. The major reasons for non-participation included refusal (10%), default (5%) and being too ill to answer questions (5%). We excluded subjects who had documented malignancy in other sites. Only Chinese women were recruited. All patients had undergone either mastectomy or breast-conserving surgery and adjuvant chemotherapy, hormonal therapy or radiotherapy, as indicated. Controls (n = 353) had a diagnosis of benign breast diseases between 1995 and 2002 and primary breast cancer had been excluded by triple assessment. They were aged 18–85 years. The response rate was again 80%, with similar reasons for non-participation: refusal (8.5%), default (6%) and being too ill to answer questions (5.5%). Again, only Chinese women were recruited.

A structured questionnaire was used to elicit detailed information. Subjects were asked to complete the questionnaire under the guidance of medical students or medical staff. Questions asked about body weight and height at present, at the time of diagnosis, and at 5 years before the diagnosis, and about other risk factors for breast cancer, including family history of breast cancer, menopausal status, exercise habit, smoking and drinking habit, pregnancy history and oral contraceptives use. Demographic data were also collected. Present weight and height were objectively measured in both case and control groups using standardized equipment.

Quartile distributions were used to categorize BMI to facilitate comparisons: BMI below 23, 23–27, 27–31 and above 31. Odds ratios (ORs) were used to measure the association between breast cancer risk and BMI. Logistic regression models gave the maximum likelihood estimates of OR with 95% confidence interval (CI). According to Campbell and Monga,[21] the worldwide mean age at menopause is 51 and, therefore, we defined 51 at the time of diagnosis as the cut-off point for the menopause, giving pre- and postmenopausal groups. Comparisons were drawn within each group concerning ORs for BMI at the time of diagnosis, BMI 5 years before diagnosis, and BMI at present. Tests for trends were performed by entering categorical variables as continuous parameters in the model. We performed data analysis using SPSS version 10.0 (SPSS Inc, Chicago, IL, USA), and all tests of statistical significance were two-sided.

Results

Table 1 compares demographic and traditional breast cancer risk factors in cases and controls. Cases were slightly older than controls (mean, 47.3 vs 43.6 years). The following analysis was adjusted for age but not for other factors, because there were no significant differences in education level, monthly family income, number of pregnancies, family history of breast cancer (especially first-degree relatives), alcohol consumption and smoking.

Among postmenopausal women, the BMI at diagnosis was positively associated with the risk of breast cancer ($p < 0.001$ for trend). The ORs for breast cancer increased with increasing BMI (> 23, 1.73; > 27, 2.06; > 31, 3.82 after adjusting for non-anthropometric risk factors) (Table 2), demonstrating a dose-response relationship (Figure). BMI at diagnosis, however, was not related to the risk of breast cancer among premenopausal women (> 23, 1.5; > 27, 1.32 after adjusting for non-anthropometric risk factors) (Table 2).

Present BMI was poorly associated with breast cancer among both pre- and postmenopausal women (Table 3), as was BMI 5 years before diagnosis (Table 4).

Table 1. Demographics and selected breast cancer risk factors in cases and controls

	Cases (n = 198)	Controls (n = 358)	p
Mean age, yr	55.4	44.5	< 0.001
Mean number of pregnancies	1.98	1.75	0.22
Family history of breast cancer before age 40 yr	15.7%	14.6%	0.88
Monthly income, US$	2,230	2,647	0.07
Ever smoking	5.6%	6.6%	0.89
Regular alcohol user (drink every day)	5.1%	3.0%	0.05
Previous oral contraceptive pill use	32.3%	21.5%	0.36
Tertiary education	15.2%	19.2%	0.17

Table 2. Association between body mass index (BMI) at diagnosis and breast cancer risk

BMI	Postmenopausal*			Premenopausal†		
	Cases, n (%)	Controls, n (%)	Odds ratio (95% CI)	Cases, n (%)	Controls, n (%)	Odds ratio (95% CI)
< 19	10 (8.3)	18 (13.7)		14 (19.7)	48 (22.6)	
19–23	38 (31.4)	51 (38.9)	1.78 (0.79–4.04); p = 0.17	35 (49.3)	115 (54.2)	1.19 (0.61–2.32); p = 0.61
23–27	42 (34.7)	42 (32.1)	1.73 (1.04–2.86); p = 0.03	14 (19.7)	41 (19.3)	1.49 (0.82– 2.71); p = 0.19
27–31	20 (16.5)	15 (11.5)	2.06 (1.08–3.93); p = 0.03	5 (7.0)	8 (3.8)	1.32 (0.39–4.43); p = 0.63
> 31	10 (8.3)	3 (2.3)	3.82 (1.03–14.27); p = 0.05	0	0	
Missing	1 (0.8)	2 (1.5)		3 (4.2)		

*Trend: p < 0.001; †trend: p = 0.39. Cases and controls in each group were adjusted for age. CI = confidence interval.

Discussion

This population-based case control study found that the risk of developing breast cancer increased with BMI at the time of diagnosis in postmenopausal women (p < 0.001 for trend). BMI at diagnosis, however, was not related to the risk of breast cancer among premenopausal women. Furthermore, present BMI and BMI 5 years before diagnosis were poorly associated with breast cancer risk among both pre- and postmenopausal women.

The poor association between present BMI and breast cancer may be due to multiple factors, including the effect of chemotherapy, radiotherapy and surgery on appetite and changes in lifestyle after diagnosis. Appetite changes from psychological effects on discovery of the disease may also contribute. We could not assess the effect of different factors on BMI for cases and controls, but the association between BMI at diagnosis for pre- and postmenopausal women had already fulfilled our requirement.

Our results are consistent with many previous studies, which state that there is a positive correlation between BMI and risk of breast cancer in postmenopausal women. They are similar to results from a recent case control study in Chinese women[13] as well as previous studies in Western populations. A large-scale meta-analysis involving 300,000 subjects in 1995 also gave similar results to ours among postmenopausal women. Table 5 summarizes the risks of breast cancer with a BMI cut-off of 27 in different studies.[13,16,22]

Our results among premenopausal women were also consistent with some earlier studies.[4,5,9,21,22] However, other stud-

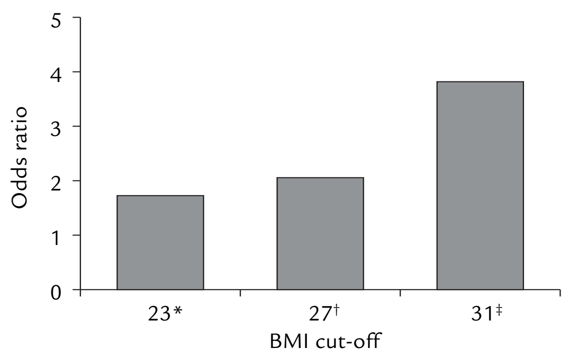

Figure. Age-adjusted odds ratio of body mass index (BMI) at the time of diagnosis in postmenopausal women at different cut-off BMIs. *p = 0.165; †p = 0.029; ‡p = 0.046.

Table 3. Association between present body mass index (BMI) and breast cancer risk

BMI	Postmenopausal*			Premenopausal†		
	Cases, *n* (%)	Controls, *n* (%)	Odds ratio (95% CI)	Cases, *n* (%)	Controls, *n* (%)	Odds ratio (95% CI)
< 19	6 (5.3)	7 (10.1)		17 (21.3)	59 (21.6)	
19–23	37 (32.5)	26 (37.7)	2.03 (0.65–6.32), p = 0.220	24 (30.0)	142 (52.0)	1.02 (0.56–1.88), p = 0.945
23–27	45 (39.5)	24 (34.8)	1.51 (0.83–2.77), p = 0.181	31 (38.8)	58 (21.2)	2.26 (0.59–4.44), p = 0.06
27–31	20 (17.5)	9 (13.0)	1.47 (0.66–3.00), p = 0.383	5 (6.3)	14 (5.1)	2.06 (0.83–5.09), p = 0.119
> 31	6 (5.3)	3 (4.3)	1.22 (0.30–5.05), p =0.782	3 (3.8)	3 (4.3)	
Missing	0	0		0	0	

*Trend: p = 0.06; †trend: p = 0.20. Cases and controls in each group were adjusted for age. CI = confidence interval.

Table 4. Association between body mass index (BMI) 5 years before diagnosis and breast cancer risk

BMI	Postmenopausal*			Premenopausal†		
	Cases, *n* (%)	Controls, *n* (%)	Odds ratio (95% CI)	Cases, *n* (%)	Controls, *n* (%)	Odds ratio (95% CI)
< 19	5 (7.1)	7 (9.5)		23 (19.2)	59 (21.8)	
19–23	21 (30.0)	27 (36.5)	0.97 (0.34–2.74), p = 0.954	53 (44.2)	140 (51.7)	1.17 (0.69–2.01), p = 0.560
23–27	24 (34.3)	26 (35.1)	1.33 (0.69–2.55), p = 0.395	31 (25.8)	58 (21.4)	1.12 (1.01–2.53), p = 0.045
27–31	12 (17.1)	10 (13.5)	1.64 (0.76–3.57), p = 0.209	9 (7.5)	14 (5.2)	2.23 (1.01–4.09), p = 0.046
> 31	8 (11.4)	4 (5.4)	2.18 (0.63–7.60), p = 0.219	4 (3.3)	0	N/A
Missing	5 (7.1)	7 (9.5)		23 (19.2)	59 (21.8)	

*Trend: p = 0.12; †trend: p = 0.32. Cases and controls in each group were adjusted for age. CI = confidence interval.

Table 5. Results in different studies when a body mass index (BMI) of 27 was used as the cut-off point in postmenopausal women

Study	Odds ratio (95% CI)	p for trend*
Present study	2.06 (1.08–3.93)	< 0.001
Xiao et al, 2001[13]	2.00 (1.20–3.20)	0.003
Taioli et al, 1995[16]	1.50 (1.00–2.30)	
van den Brandt et al,† 2000[22]	1.43 (1.21–1.67)‡	0.001

*p for trend represents the dose-response relationship between BMI and breast cancer risk; †meta-analysis of 7 cohort studies, including 337,819 women and 4,385 breast cancer cases; ‡relative risk instead of odds ratio. All odds ratios and relative risk were calculated using BMI at diagnosis. CI = confidence interval.

Table 6. Results in different studies when a body mass index (BMI) of 27 was used as the cut-off point in premenopausal women

Study	Odds ratio (95% CI)	p for trend
Present study	1.32 (0.39–1.43)	0.382
Xiao et al, 2001[13]	1.10 (0.7–1.7)	0.340
Taioli et al, 1995[16]	0.40 (0.20–0.60)	
van den Brandt et al,* 2000[22]	0.97 (0.66–1.44)†	0.007‡

*Meta-analysis of 7 cohort studies, including 337,819 women and 4,385 breast cancer cases; †relative risk instead of odds ratio; ‡the higher the BMI, the smaller the risk of formation of breast cancer. All odds ratios and relative risk were calculated using BMI at diagnosis. CI = confidence interval.

ies found that a greater BMI is protective in premenopausal women. The risks of breast cancer with a BMI cut-off of 27 in different studies are shown in Table 6.[13,16,22]

Some researchers proposed that the incidence of breast cancer might be related to the number of years of obesity instead of only pre- or postmenopausal status. One study found that the risk of breast cancer in postmenopausal women increased with maximal lifetime BMI.[23] However, in premenopausal women, the result was exactly opposite. Therefore, it seems that the duration of obesity does not correlate well with the risk of breast cancer in all women but in a subgroup of postmenopausal women. The authors did not explain their results, but they might indicate that there are two types of breast cancer with two separate pathogeneses.

The association between BMI and risk of breast cancer in premenopausal women is still unclear, and this controversial issue should be subjected to further investigation.

Some questions about the use of BMI have been raised. Some researchers suggest that BMI is simply a reflection of high fat intake and, therefore, BMI is a surrogate measure. BMI is certainly associated with an increased risk of breast cancer in postmenopausal women. The association between high fat intake and risk of breast cancer is unclear in epidemiological studies.[23–28] Some authors suggest that this may be because high fat intake is very difficult to quantify in such studies and claim that the best indicator for high fat intake is BMI. However, because of the controversy around this question, it must be answered by a separate and specific study.

Our study has a number of strengths. All subjects in this case control study were Chinese women from Hong Kong and all were born and raised in Hong Kong or nearby cities in China. Present weight and height were measured in the clinic by medical students after interview, using the same protocol and instruments in order to minimize potential recall bias. Lastly, the prevalence of obesity in the study population was low compared with that in Western countries, allowing an assessment of association of BMI with breast cancer risk in a weight range closer to an ideal normal, according to the standards in Western populations.

Our study, however, may suffer from the inherent limitations of the case control design. In addition, recall inaccuracy in parameters measuring BMI 5 years before diagnosis may contribute to the insignificant result. However, we believe the effect of recall inaccuracy was not significant in the parameters measuring BMI at diagnosis as all cases were diagnosed in recent years (1995–2002).

We believe that the recalled data on weight and height are reliable because most studies find that in both young and elderly women, ability to recall weight is excellent. The correlation between memory and actual weight 1 year ago, 5 years ago, 10 years ago and even at the time of menarche are very good, with correlation coefficients around 0.80–0.99.[29–36] These studies clearly showed that recall data on weight can be used in epidemiological analysis and have been quoted widely in many other studies.[37–48] In our study, BMI at diagnosis was obtained by recall of an event 3–5 years earlier. This generally contributes to a certain amount of inaccuracy. However, people have better memory for specific events, such as diagnosis of breast cancer, and this inaccuracy is therefore minimal for these events.[19,49,50] The inaccuracy of memory recall of data at that moment is therefore minimized.

Survivor bias is another potential pitfall in our study since the cases we selected were follow-up cases rather than newly diagnosed cases. However, we believe that the effect of survivor bias is minimal in our study because many previous studies showed no relationship between BMI and prognosis of breast cancer.[51–53]

In summary, our study found that high BMI at diagnosis was positively correlated with increased risk of breast cancer in postmenopausal Chinese women in Hong Kong. A significant dose-response relationship between BMI at diagnosis and breast cancer was also demonstrated. This indicates that weight control may be an effective measure for breast cancer prevention in postmenopausal women. The results also enhance our understanding of the pathogenesis of breast cancer in postmenopausal women and emphasize the need for research to clearly define the underlying mechanisms.

The incidence of breast cancer is rising in Hong Kong.[54] The reason is not well understood but we think that it may be related to better nutrition and increased weight (in terms of BMI) in the female population in Hong Kong.[17] This postulation is preliminary and needs further study.

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