The associations of healthy lifestyle index with breast cancer incidence and mortality in a population-based study

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Abstract

Purpose To investigate how a healthy lifestyle index (HLI) is associated with breast cancer risk and survival in a population-based breast cancer study.

Methods The study included 1319 breast cancer cases and 1310 controls from the population-based Long Island Breast Cancer Study Project and its follow-up study where vital status was ascertained using the National Death Index (521 deaths, 210 from breast cancer; median follow-up 214.5 months). HLI scores were generated from body mass index, physical activity, intake of plant and animal foods, alcohol consumption, breastfeeding, and smoking, with higher values corresponding to healthier behaviors obtained from baseline questionnaire. Multivariable logistic and Cox regression models were used to estimate breast cancer odds ratios (ORs) and mortality hazards ratios (HRs), respectively.

Results Compared to women in the low HLI tertile, a significant reduction in risk of breast cancer was observed for women in the intermediate (OR = 0.78, 95% CI 0.64–0.93) and high (OR = 0.73, 95% CI 0.60–0.88) tertiles; a one-point increase in HLI score was associated with a 14% reduction in breast cancer risk (OR = 0.86, 95% CI 0.80–0.93). For survival, a significant reduction in all-cause mortality was also observed in women in the intermediate (HR = 0.68, 95% CI 0.56–0.84) and high (HR = 0.72, 95% CI 0.58–0.88) HLI tertiles with a 17% reduction in all-cause mortality (HR = 0.83, 95% CI 0.76–0.91) for one-point increase in HLI score. These inverse associations were more prominent among postmenopausal women.

Conclusion A healthy lifestyle is beneficial not only in reducing breast cancer risk but also in improving overall survival after breast cancer diagnosis, especially among postmenopausal women.

Keywords Lifestyle · Index · Breast cancer · Risk factors · Mortality

Introduction

Female breast cancer has surpassed lung cancer to become the most commonly diagnosed cancer worldwide in 2020, according to a collaborative report from the American Cancer Society and the International Agency for Research on Cancer [1]. While less than 10% of breast cancers are attributed to inherited genetic variations [2–6], many other risk factors have been identified for breast cancer, including environmental, reproductive, and lifestyle factors, some of which are potentially modifiable [7–9]. A substantial number of epidemiologic studies have shown that individual lifestyle factors, such as obesity in postmenopausal women [10, 11], moderate-to-high alcohol consumption [12], and physical inactivity [13], are associated with increased breast cancer risk. Dietary and cigarette smoking habits may also influence risk of breast cancer, but results are inconclusive.
As behavioral factors and lifestyle pattern often cluster together [19, 20], it is important to consider these factors simultaneously and to take into account possible synergistic or antagonistic health effects.

The healthy lifestyle index (HLI) is a composite measurement of multiple recognized modifiable risk factors, or patterns of behavior, and it has been applied to various chronic diseases, including cardiovascular disease [21–24], diabetes [25, 26], and various types of cancer [27–29]. Studying the joint effects of modifiable lifestyle factors on chronic diseases is not only essential to improve understanding of the etiology but also facilitate the development of prevention strategies [30]. Although several studies on the relationship between HLI and breast cancer risk have been published, different risk factor combinations and cut-off points have been used for HLI construction [28, 29, 31–35]. Most of these studies did not include breastfeeding or smoking status, which are established breast cancer risk factors [36, 37]. Some did not take into account the opposing direction in BMI association with pre- and post-menopausal breast cancer [38–40].

More importantly, a few studies have explored the association between HLI and breast cancer survivorship [41]. One study from the Third National Health and Nutrition Examination Survey (NHANES III) investigated the association between combined lifestyle behaviors and overall mortality in cancer survivors, but did not specify the cancer types [42]. To our knowledge, only one study has explored the joint effect of lifestyle factors on breast cancer survival [41], but the role of HLI in relation to breast cancer survival remains ambiguous. Therefore, based on World Cancer Research Fund/American Institute of Cancer Research (WCRF/AICR) guidelines [43], we created a comprehensive HLI score combining myriad lifestyle factors, including diet, physical activity, body mass index (BMI), smoking, alcohol consumption, and breastfeeding. The purpose of this study is to investigate the association between our newly constructed and more comprehensive HLI and breast cancer risk as well as mortality after breast cancer diagnosis in a population-based breast cancer study.

### Materials and methods

#### Study population

We utilized a population-based case–control study, i.e., Long Island Breast Cancer Study Project (LIBCSP) [44] and its follow-up study [45]. The parent study included 1,508 women diagnosed with incident invasive or breast carcinoma in situ between August 1, 1996 and July 31, 1997 and 1,556 women without breast cancer who were residents of the same two counties, frequency matched by 5-year age group. The average length of time between the referent date (day of diagnosis for cases and date of identification for controls) and interview date was 96 days for cases and 167 days for controls [44]. Potentially eligible control women were identified by Waksberg’s method of random digit dialing [46] for those under 65 years of age, and the Health Care Finance Administration (HCFA) rosters for those 65 years and older. Institutional Review Board approval was obtained from all participating institutions and written informed consent was obtained prior to study participation.

This current study included 1319 cases and 1310 controls who had complete data on the components of HLI score, including diet, alcohol consumption, physical activity, BMI, and menopausal status. The CONSORT diagram in Supplementary Fig S1 provides the details of the study population. For the 1319 women with breast cancer, vital status was ascertained through linkage with the National Death Index (NDI). They were followed from the time of diagnosis in 1996–1997 through December 31, 2014 to determine the date and cause of death, including death from breast cancer, identified using International Classification of Death codes 174.9 and C-50.9 listed on the death certificate [45]. Over a median follow-up of 214.5 months (range 2.8–224.2 months), we identified 521 deaths, including 210 deaths from breast cancer. Information on the tumor receptor status, including estrogen receptor (ER), progesterone receptor (PR), and the human epidermal growth factor receptor (HER2), was obtained from the pathology records.

### Construction of HLI

The information on demographic characteristics, pregnancy history, menstrual history, hormone use, family history of cancer, body size changes, current alcohol use, active and passive cigarette smoking, physical activity, and breastfeeding history were obtained from the main study questionnaire completed at enrollment. A detailed description of the food frequency questionnaire (FFQ) for the LIBCSP, which captured information on diet in the year prior to diagnosis among cases or prior to enrollment among controls, has been published elsewhere [47, 48].

The HLI was generated from the information of six lifestyle recommendations (i.e., body fatness, physical activity, consumption of plant foods, animal foods, alcohol, and breastfeeding) based on the new WCRF/AICR guidelines [43] with additional consideration on smoking [18, 49]. The scoring system, described in details in Table 1, was based on the assumption that each major recommendation would contribute equally to the study outcomes. In brief, each of seven HLI components was assigned the same score of “1”; thus, a maximum value of HLI is “7”. For binary variables, i.e., breastfeeding, a score of “0” or “1” was assigned to women whose response was “no”
and “yes”, respectively. For categorical components (i.e., physical activity, alcohol consumption, and BMI), each was given a score of “1” when the recommendation was met, “0.5” when it was partially met, and “0” otherwise. Because BMI was inversely associated with breast cancer risk in premenopausal women, but positively associated with breast cancer risk in postmenopausal women [38–40], a high HLI score represented high BMI in premenopausal women and low BMI among postmenopausal women. Consumptions of plants or animals foods consisted two or three subcomponents, respectively. Each subcomponent consisted of three categories, and each category was given a score of “0.5”, “0.25”, and “0” point when the recommendation was fully, partially, and not met, respectively. Consistent with the previous studies [31–33, 35, 50, 51], smoking was included in the HLI score and scored as “1” for being never smokers, “0.5” for being a former smoker who quit more than 12 months before reference date, or “0” points for being a current smokers at or within 12 months of the reference date. Therefore, the range of total HLI score was from “0” to “7”, with higher scores indicating a healthier lifestyle. Based on the distribution of HLI scores of the controls, we then categorized the study population into tertiles as low, intermediate, and high HLI groups.

Table 1 The construction of Healthy Lifestyle Index (HLI) components

| WCRF/AICR recommendations (HLI components) | HLI in LIBCSP | Categories | Scores |
|-------------------------------------------|---------------|------------|--------|
| 1. Body fatness: be a healthy weight      | Body mass index (BMI) at the interview (kg/m²) | Premenopausal |          |
|                                           |               | 18.5–24.9  | 0      |
|                                           |               | 25.0–29.9  | 0.5    |
|                                           |               | > 29.9     | 1      |
|                                           |               | Postmenopausal |        |
|                                           |               | 18.5–24.9  | 1      |
|                                           |               | 25.0–29.9  | 0.5    |
|                                           |               | > 29.9     | 0      |
| 2. Physical activity: be physically active| Physical activity (hours/week) | 0          | 0      |
|                                           |               | 0.69       | 0.5    |
|                                           |               | ≥ 0.70     | 1      |
| 3. Plant foods: eat a diet rich in wholegrains, vegetables, fruits, and beans | Total fruits and vegetables including juices in ½ cup servings per week | 0–18 ½ cup servings/week | 0 |
|                                           |               | 19–34 servings/week | 0.25 |
|                                           |               | ≥ 35+ servings/week | 0.5 |
|                                           | Beans servings per week | ≤ 2 servings | 0 |
|                                           |               | ≥ 2 to ≤ 6 servings | 0.15 |
|                                           |               | > 6 servings | 0.25 |
|                                           | Whole grains intake per week | ≤ 2 servings | 0 |
|                                           |               | ≥ 2 to ≤ 6 servings | 0.15 |
|                                           |               | > 6 servings | 0.25 |
| 4. Animal foods: limit consumption of red and processed meat | Red meat intake per week | > 6 times | 0 |
|                                           |               | > 2–6 times | 0.25 |
|                                           |               | ≤ 2 times | 0.50 |
|                                           | Processed meat intake per week | > 6 times | 0 |
|                                           |               | > 2–6 times | 0.25 |
|                                           |               | ≤ 2 times | 0.50 |
| 5. Alcoholic drinks limit alcohol consumption | Lifetime alcohol intake (gram/day) | Non-drinkers | 1 |
|                                           |               | < 15 | 0.5 |
|                                           |               | ≥ 15 | 0 |
| 6. Breastfeed: for mothers: breastfeed your baby if you can | Lactation | Ever | 1 |
|                                           |               | Never | 0 |
| 7. Smoking is not included in the WCRF/AICR guidelines | Smoking | Never smoker | 1 |
|                                           |               | Former smoker | 0.5 |
|                                           |               | Current smoker | 0 |
Statistical analyses

The general characteristics of cases and controls were compared using independent samples Student’s t test or Wilcoxon test for continuous variables and Chi-square for categorical variables. An unconditional multivariable logistic regression was used to estimate the odds ratios (ORs) and 95% confidence intervals (CIs) for associations between HLI scores and incident breast cancer. HLI scores were modeled as a continuous (1-point increment) and categorical variables (tertiles) with the low tertile of HLI score serving as the reference group in the categorical analyses. All models were adjusted for reference age (continuous in years; age at diagnosis for cases and age at study enrollment for controls). Potential confounders of the association between healthy lifestyle and breast cancer risk or mortality included: age at reference, family history of breast cancer in a first-degree relative, education, and parity. Separate models were also fitted according to the breast cancer subtypes [i.e., hormone receptor (ER + PR) and HER2 receptor status]. Cox regression models were used to estimate the hazard ratios (HRs) and 95% CIs for all-cause and breast cancer-specific mortality in association with HLI scores. The proportional hazards assumption was checked before running Cox regression model. Starting from fully adjusted models, none of these variables altered the OR estimates by more than 10%; therefore, only age-adjusted results are presented (fully adjusted models were shown in Table S1). Similar to logistic regression analyses mentioned above, only age-adjusted results reported in Cox regression model. Since the risk factors differ by menopausal and hormone receptor status, we also performed stratified analyses by these two variables. Analyses were also performed for the associations between HLI and risk of all-cause and breast cancer mortality in the invasive breast cancer cases only, and the premenopausal women with assigning low BMI to a high HLI score. Sensitivity analyses were performed with the different weights for fruits/vegetables, beans, whole grains, read meat, and processed meat in HLI food score. The analyses were carried out using glm (generalized linear model) function, and the “survival” and “forestplot” packages in R version 3.6.1 [52–54]. All tests were two-tailed, and P values < 0.05 were considered statistically significant.

Results

The distributions of the population characteristics of cases and controls are shown in Table 2. Compared to the controls, the cases were older, less educated, with lower parity, and greater family history of breast cancer. For the individual components of the HLI score, there were no significant differences between cases and controls except that cases had a lower prevalence of a history of lactation (31.9% vs 35.7%, P = 0.043). The median HLI score was significantly higher in controls than in cases (4.15 vs. 4.00, P = 0.001). When stratified by menopausal status, the difference in HLI scores between cases and controls was only statistically significant in postmenopausal (P < 0.001) but not premenopausal women (Table S2). Among the breast cancer cases, there are 84.8% with invasive breast carcinoma, 73.9% with small tumors (< 2 cm), and 22.2% with lymph-node metastasis.

Compared to women in the low HLI tertile, women with higher HLI scores had reduced risk of breast cancer (intermediate: OR = 0.78, 95% CI 0.64–0.93; high: OR = 0.73, 95% CI 0.60–0.88). Modeled as a continuous variable, a one-point increase in the HLI score was associated with a breast cancer OR of 0.86 (95% CI 0.80–0.93). As shown in Fig. 1A, these inverse associations were more pronounced and statistically significant only among postmenopausal women. In the hormone receptor-specific analyses (Fig. 1B), we included all controls (n = 1310). The high HLI tertile was associated with a reduced breast cancer risk in women with ER+/PR+ tumors (OR = 0.63, 95% CI 0.49–0.82) compared to women in the low HLI tertile. A one-point increase of HLI score was also associated with reduced risk of both HER2+ (OR = 0.82, 95% CI 0.70–0.95) and HER2- (OR = 0.85, 95% CI 0.77–0.94) tumors. There were no statistically significant associations between HLI and ER+/PR+ or triple-negative breast cancer (TNBC) tumors.

In survival analyses, we examined the HLI in relation to both overall and breast cancer-specific mortality. Among the 1319 women with breast cancer, 521 deaths were reported during the 15+ years of follow-up (median duration of follow-up = 214.5 months, range, 2.8–224.2 months); 210 (40.3%) died of breast cancer. The 5-, 10-, and 15-year survival rate were 88.9% (95% CI 87.3–90.6%), 76.7% (95% CI 74.5–79.0%), and 67.2% (95% CI 64.7–69.8%), respectively. Compared to women in the low HLI tertile, women with higher HLI tertile had lower rates of all-cause mortality (intermediate: HR = 0.68, 95% CI 0.56–0.84; high: HR = 0.72, 95% CI 0.58–0.88) (Fig. 2A). Additionally, a one-point increase of HLI score was associated with a 17% decreased all-cause mortality (HR = 0.83; 95% CI 0.76–0.91). These inverse associations were more prominent among postmenopausal women (Fig. 2A). With respect to breast cancer-specific mortality (Fig. 2B), and associations were similar to all-cause mortality where reduced mortality was observed among women with intermediate HLI tertile (HR = 0.68; 95% CI 0.49–0.95) and the postmenopausal women with high HLI tertile (HR = 0.63; 95% CI 0.42–0.96). Similarly, stronger inverse association was present among menopausal women. In addition, when we restricted our analysis to the 1119 invasive breast cancer cases, similar results were observed as with all cases (Table S3).
| Characteristics                              | Cases  | Controls | \(P\) values* |
|---------------------------------------------|--------|----------|---------------|
| Age at reference, mean (SD)                | 58.5 (12.7) | 56.9 (12.7) | <0.001        |
| Age at menarche, mean (SD)                 | 12.6 (1.6) | 12.6 (1.6) | 0.745         |
| Race (%)                                    |        |          |               |
| White                                       | 1240 (94.1) | 1214 (92.7) | 0.143         |
| Black                                       | 57 (4.3) | 61 (4.7) |               |
| Others (Asian, Native American, etc.)      | 21 (1.6) | 35 (2.7) |               |
| Missing                                     | 1      | 0        |               |
| Education level (%)                        |        |          |               |
| Less than high school                      | 160 (12.2) | 123 (9.4) | 0.027         |
| High school graduate                      | 480 (36.5) | 448 (34.3) |               |
| Some college                               | 308 (23.4) | 336 (25.7) |               |
| College graduate                           | 162 (12.3) | 199 (15.2) |               |
| Post-college                               | 206 (15.7) | 202 (15.4) |               |
| Missing                                     | 3      | 2        |               |
| Family history*, yes (%)                   | 265 (20.7) | 174 (13.6) | <0.001        |
| Menopausal status, postmenopausal (%)      | 878 (66.6) | 853 (65.1) | 0.457         |
| Parity status, mean (SD)                   | 2.4 (1.5) | 2.6 (1.7) | 0.001         |
| OC use, ever (%)                           | 579 (44.0) | 597 (45.6) | 0.419         |
| HRT use, ever (%)                          | 347 (26.3) | 319 (24.4) | 0.258         |
| Healthy lifestyle factors                  |        |          |               |
| Plant food consumption, mean (SD)          | 0.39 (0.26) | 0.41 (0.26) | 0.071         |
| Animal food consumption, mean (SD)         | 0.95 (0.11) | 0.95 (0.13) | 0.395         |
| Alcohol users, (%)                         | 805 (61.0) | 805 (61.5) | 0.857         |
| Physical activity, > 0.7 h/week, (%)       | 614 (46.6) | 645 (49.2) | 0.180         |
| BMI, mean (SD)                             | 26.59 (5.61) | 26.34 (5.71) | 0.270         |
| Smoker, (%)                                 | 723 (54.8) | 706 (53.9) | 0.664         |
| Lactation, ever (%)                        | 421 (31.9) | 468 (35.7) | 0.043         |
| HLI, median (range)                        | 4.00 (1.25–6.75) | 4.15 (0.90–7.00) | 0.001 |
| HLI                                         |        |          |               |
| Low (<3.65)                                 | 495 (37.5) | 417 (31.8) | 0.008         |
| Intermediate (3.65–4.55)                   | 437 (33.1) | 463 (35.3) |               |
| High (>4.55)                                | 387 (29.3) | 430 (32.8) |               |
| Tumor size                                  |        |          |               |
| < 2 cm                                      | 374 (73.9%) |               |               |
| 2–5 cm                                      | 210 (23.7%) |               |               |
| > 5 cm                                      | 12 (2.4%) |               |               |
| Missing                                     | 813    |           |               |
| Stage                                       |        |          |               |
| In situ                                     | 200 (15.2) |               |               |
| Invasive                                    | 1119 (84.8) |               |               |
| Lymph-node metastasis                       |        |          |               |
| No                                          | 407 (77.8%) |               |               |
| Yes                                         | 116 (22.2%) |               |               |
| Missing                                     | 796    |           |               |

*HRT* hormone replacement therapy, *OC* oral contraceptive, *HLI* healthy lifestyle index, *BMI* body mass index

*Family history of first-degree relative

*P* values are from Student’s *t* test for continuous variables and Chi-square for categorical variables
While we assigned BMI differently between pre- and post-menopausal women, driven by the opposing effect of BMI on breast cancer risk, we are aware that high BMI does not represent a healthy lifestyle. Thus we performed a sensitivity analysis using the same postmenopausal HLI (i.e., low BMI in high HLI). No substantial changes in risk of breast cancer were observed when assigning low BMI to a high HLI score compared to low BMI to a low HLI score (Table S4). For all-cause mortality, 1-point increase of the new HLI was associated with a significant decreased all-cause mortality (HR = 0.82, 95% CI 0.67–0.99, Table S4), compared to the original non-significant results (HR = 0.94, 95% CI 0.78–1.14 for all-cause mortality).

We also performed stratified analyses by family history of breast cancer. There are the 265 cases (20.7%) who had family history of breast cancer; similar results were observed, although they were not statistically significant among those with family history, possibly due to small sample size (no family history: OR = 0.86, 95% CI 0.79–0.94; with family history: OR = 0.86, 95% CI 0.71–1.05; Table S5). Finally, sensitivity analyses with the different weights for fruits/vegetables, beans, whole grains, red meat, and processed meat in HLI food score did not materially alter the results.

**Discussion**

In this population-based study with long-term follow-up, we observed that a healthy lifestyle was associated with not only a reduced risk of developing breast cancer, but also improvement of survival after breast cancer diagnosis, especially among postmenopausal women who constitute the majority of the breast cancers diagnosed.

There is accumulating evidence associating combined lifestyle factors or patterns of behavior to cardiovascular disease [21–24], diabetes [25, 26], and various types of cancer [27–29]. Several studies have reported joint effects of common modifiable risk factors on breast cancer risk [28, 29, 31–35]. However, these studies used different combination of lifestyle and/or cut-off points to construct HLI, and they employed various analytical techniques and examined populations from different geographical areas. Importantly, data are lacking on associations between HLI and breast cancer mortality.

Investigators of the European Prospective Investigation into Cancer and Nutrition (EPIC) cohort reported a lower breast cancer risk (HR = 0.84, 95% CI: 0.78–0.90) for women with a high HLI score. However, their HLI did not...
include smoking, an established risk factor of breast cancer [34]. In another study from the same cohort, McKenzie and colleagues used a breast cancer-specific HLI, and reported that women in the highest versus the lowest category had an even greater reduction in risk (HR = 0.74, 95% CI: 0.66–0.83) among postmenopausal women [33]. Similarly, the Canadian Study of Diet, Lifestyle, and Health demonstrated that postmenopausal women with a high HLI score had a 30% reduction in the risk of breast cancer (HR = 0.70, 95% CI: 0.53–0.93) and each unit increase in the HLI score was associated with a 3% reduction [51]. However, the breastfeeding was not included in HLI in these studies [33, 51].

We observed stronger inverse associations between HLI and breast cancer risk among postmenopausal women in this study. These findings are consistent with previously published studies. A case–control study conducted by McKenzie et al. reported reduced breast cancer risk with high HLI scores (OR = 0.47, 95% CI 0.23–0.94) only in postmenopausal women in New Zealand [32]. However, two other studies found significant associations between healthy lifestyle and risk of breast cancer in both pre- and postmenopausal women. A study conducted in Morocco by Khalis et al. showed that a one-point increment in HLI score was inversely associated with risk of breast cancer among all women (OR = 0.44, 95% CI 0.32–0.61), as well as premenopausal (OR = 0.51, 95% CI 0.37–0.70) and postmenopausal women (OR = 0.41, 95% CI 0.28–0.60) [31]. A case–control study in Mexican women found the highest quintile of HLI had significantly lower breast cancer risk than those in the lowest quintile (premenopausal OR = 0.5, 95% CI 0.29–0.84; postmenopausal OR = 0.20, 95% CI 0.11–0.37) [35]. Our study may be underpowered to detect an association between HLI and breast cancer risk among premenopausal women given the limited sample size. The fact that all point estimates (ORs) were less than one regardless of menopausal status suggests that a healthy lifestyle may be beneficial for both premenopausal and postmenopausal women. Another possibility is that genetics (such as BRCA1 mutations) plays a more important role in early onset breast cancer [55, 56], and the influence of lifestyle factors may be less prominent in premenopausal women.

Our findings suggest that a healthy lifestyle is associated with reduced risk of ER+/PR+ tumors (OR = 0.61, 95% CI 0.47–0.78), which constitutes approximately 70% of breast tumors [57]. This finding is in line with the previous
studies. Arthur et al. reported that women in the highest HLI score quintile had a reduced risk for ER+/PR+ tumors compared with those in the lowest quintile (HR = 0.63, 95% CI 0.57–0.69) [58]. McKenzie et al. also demonstrated an inverse association between HLI score and risk of ER+/PR+ cancers [33]. Similar to Romaguera et al. [29], we observed a non-significant inverse association between HLI score and ER+/PR− and TNBC tumor, which may be limited by small sample size. This may also be partially explained by TNBC being associated with a young age at diagnosis [59].

The association between combined lifestyle behaviors and breast cancer survivorship has not been investigated extensively. There is only one previous study from a population-based cohort in Norway that explored the joint effect of lifestyle factors on breast cancer survival and reported that an unfavorable lifestyle was associated with a higher overall mortality [41]. The combined lifestyle factors in the Norwegian study only included BMI, physical activity, alcohol use, smoking, and hypertension. Another study from NHANES III found lower all-cause mortality associated with increased HLI score for cancer survivors (HR = 0.81, 95% CI 0.72–0.90, per 1 unit increase) [42]; however, the report did not specify the cancer type. In our study, we observed significant reduction in both all-cause mortality and breast cancer-specific associated with high HLI, especially among postmenopausal women. The components of HLI in NHANES III were similar to those used in our study, i.e., being a never smoker, lifetime healthy body weight maintenance, practicing moderate-to-vigorous physical activity, moderate alcohol consumption, and high diet quality; however, breastfeeding was not included in the HLI.

BMI is an important risk factor for breast cancer risk, but it appears to have opposing effects among pre- and postmenopausal women [38–40]. In our studies, a high HLI score represents high BMI in premenopausal women and low BMI among postmenopausal women. However, we did a sensitivity analysis with low BMI presenting a high HLI among premenopausal women. There was no substantial changes in risk of breast cancer among the premenopausal women. A significant decreased all-cause mortality was associated with 1-point increase of the new HLI (assigning low BMI presenting high HLI), compared to the original non-significant results (assigning low BMI presenting low HLI). Since the changes of lifestyles should be considered in the survival analysis, it would be included in the future study to explore the relationship between BMI and survival outcome.

Our study has several strengths. All the breast cancer cases were confirmed and centrally adjudicated using medical records and pathology reports. The population-based study design enhances the ability to generalize to other populations. We also acknowledge several limitations of our study: (1) Differential recall bias between cases and controls is one inherent limitation of all case–control studies. (2) Breast cancer diagnosis or its treatments may also alter the lifestyle patterns. However, only incident cases were recruited prior to any major treatment, which may minimize such bias. We observed similar results when we restricted our analysis to those who received no treatment (Table S6). (3) We did not have sufficient information to include all recommendations in the guidelines of WCRF/AICR cancer prevention [8], such as the intake of supplements for cancer prevention. However, the findings using our modified HLI score are consistent with those from studies based on WCRF/AICR guidelines. (4) Information on certain clinical information (e.g., lymph-node metastasis and tumor size) and treatment information was incomplete in the LIBCSP population. (5) We did not have information on the post-diagnostic assessment and changes of lifestyle. Further analysis and study should examine the association between post-diagnostic factors and survival status.

Conclusion

Our results strongly support the hypothesis that a healthy lifestyle may reduce the risk of breast cancer as well as improve survival after breast cancer, especially in postmenopausal women. These findings support lifestyle-based prevention and intervention strategies to reduce the disease burden of breast cancer.

Supplementary Information The online version contains supplementary material available at https://doi.org/10.1007/s12282-022-01374-w.

Author contributions Conception and design of the study was conducted by QL, JC, and ST. Analysis and interpretation of data was conducted by QL. The draft of the manuscript was written by QL, CL, AN, RS, HP, ST, and JC reviewed the data and participated in revising the manuscript. All authors read and approved the final manuscript.

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Declarations

Conflict of interest Neugut has consulted for Otsuka, GlaxoSmithKline, Eisai, Hospira, and United Biosource Corp. He is a member of the Medical Advisory Board of EHE Intl. All other authors declare that they have no conflict of interest.
Ethical approval Institutional Review Board approval was obtained from all participating institutions. All procedures were in accordance with the ethical standards of the institutional and national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

Informed consent Informed consent was obtained from all individual participants included in the study.

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