



Effects of tea consumption and the interactions with lipids on breast cancer survival

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Abstract

Purpose The effect of tea consumption on breast cancer survival remained to be explored. Meanwhile, green tea favorably facilitates lipid metabolisms in breast cancer survivors. This study aimed to examine the effect of tea consumption and the interactions with lipids on breast cancer survival.

Methods A total of 1551 breast cancer patients were recruited between April 2008 and March 2012 and followed up until 31 December 2017 in Guangzhou. The endpoint was progression-free survival (PFS). Hazard ratios (HR) and 95% confidence intervals (CI) were calculated using multivariate Cox proportional to estimate the associations.

Results PFS was better among women who regularly drank all teas (mainly green tea) except oolong after cancer diagnosis compared with non-tea drinkers (HR 0.52; 95% CI 0.29~0.91). This association was more evident among women with normal (HR 0.38; 95% CI 0.18~0.82) than higher (HR 1.22; 95% CI 0.13~11.82) total cholesterol, though the interaction was not significant. Moreover, the more they drank (≥ 7 times/week), the better prognosis was (HR 0.30; 95% CI 0.11~0.84). In contrast, oolong tea was observed to have a potential impaired effect on PFS.

Conclusions Our findings suggested that regularly drinking all teas (mainly green tea) except oolong after diagnosis was beneficial to breast cancer survival, particularly for women with normal lipids, while oolong tea may have an impaired effect.

Keywords Tea consumption · Lipids · Breast cancer progression-free survival

Jia-Yi Zhang and Yu-Huang Liao contributed equally to this work.

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Introduction

Breast cancer is the most prevalent malignancy among females worldwide [1]. It is also the most common cancer in Chinese females and the incidence rate has increased significantly in the past several years [2]. Compared with most of other cancers, the prognosis of breast cancer is relatively better, with estimated 5-year survival rates of 90.2% and 83.2% in US and China, respectively [3], resulting in a large number of breast cancer survivors. Therefore, it is of great concern to identify potential prognostic factors of breast cancer to improve the survival.

Tea is one of the most popular beverages in the world and has been studied for the potential effects on a wide range of diseases, such as cancers, diabetes, and cardiovascular disease [4]. For breast cancer, accumulating evidences from the studies of experimental animal models have consistently demonstrated an inhibitory effect of green tea (non-fermentation) extracts and tea polyphenols on the proliferation of breast cancer cells [5, 6]. However, results from human studies were limited. Only three studies have

investigated the effect of green tea consumption on breast cancer survival, among which two studies focused on pre-diagnostic tea consumption [7, 8]. The diagnosis of cancer may motivate survivors to alter their lifestyle habits [9], and post-diagnostic tea consumption characteristics might be more important for breast cancer prognosis. To date, only one study has examined the association of post-diagnostic tea consumption with breast cancer survival, finding that post-diagnostic tea consumption was associated with better outcomes [10]. Moreover, this previous study just included patients with the triple-negative breast cancer and involved in limited measures of tea consumption. In addition, some studies have suggested inconsistent effects of tea. For example, it was found that pre-diagnostic consumption of black tea (full fermentation) was not associated with breast cancer survival [11], while oolong tea (semi-fermentation) had impaired impacts on health [12, 13], suggesting that different types of tea may have various biological effects. To date, no study has compared the effects of various types of tea on breast cancer prognosis, particularly for post-diagnostic consumption of teas.

Furthermore, it was found that green tea favorably modified lipid metabolisms in breast cancer survivors [14, 15], while lipids were considered to be closely related to the prognosis of breast cancer [16, 17], suggesting that tea may affect the outcomes of breast cancer through regulating lipid metabolism. However, there is no relevant study to examine the effect of tea consumption on the prognosis of breast cancer in combination with lipids.

In the current study, we firstly evaluated the associations between pre- and post-diagnostic consumption of different types of tea (as well as the change from pre-diagnosis to post-diagnosis) and breast cancer survival, and further investigated whether the associations were modified by blood lipids in the Guangzhou Breast Cancer Study (GZBCS).

Methods

Study population

A total of 1551 female patients, who were newly pathologically diagnosed with primary breast cancer between October 2008 and March 2012, were recruited in the GZBCS, as described previously [18]. Those with a history of other cancers were excluded. This study was approved by the Ethics Committee of the School of Public Health at Sun Yat-sen University. Informed consent was obtained from each participant before the interviews and the blood samples collection.

Data collection and variable definitions

Participants were interviewed in-person at baseline by trained investigators using a structured questionnaire. The questionnaire contains menstrual and reproductive history, life styles (physical exercise, smoking, alcohol consumption, tea consumption, etc.), family history of cancer, height and weight, and demographic characteristics. Information on tea consumption was collected by questions whether they regularly drank tea (drank tea at least twice a week for more than half a year in lifetime) and at what age they started regularly drinking, followed by questions on duration, frequency, brew strength, type, and amount of tea consumption per month [19].

The blood lipid metabolism measures and clinical characteristics of the breast cancer patients were collected from medical records and pathological reports. The measures were classified into two categories: normal (within the reference range) and abnormal (above the upper limit of reference value). The range of reference values in different hospitals were as follows: 0.33 ~ 1.70 mmol/L, 0.31 ~ 2.30 mmol/L, 0.20 ~ 1.70 mmol/L for triglyceride (TG), 3.10 ~ 5.70 mmol/L, 2.90 ~ 6.00 mmol/L, 2.10 ~ 6.47 mmol/L for total cholesterol (TC), 1.94 ~ 3.61 mmol/L, 1.30 ~ 3.60 mmol/L, 2.20 ~ 3.40 mmol/L for low-density lipoprotein cholesterol (LDL-C) in the First Affiliated Hospital, the Second Affiliated Hospital, and the Cancer Center of Sun Yat-sen University, respectively. The status of estrogen receptor (ER), progesterone receptor (PR), and human epidermal growth factor receptor 2 (HER2) of breast cancer tissues was determined by pathologists using immunohistochemical tests. Detailed definitions of ER, PR, and HER2 status were previously described in detail [20].

Follow-up

The patients were followed up at least every 3 months during the first year, and every 6 months during the second and the third year; thereafter, patients were followed up once every year until death or January 31, 2016; some of those who were lost were followed up again in 2017. A total of 1422 (91.7%) breast cancer patients were successfully obtained with a median follow-up time of 58.58 months. The means of follow-up included phone call, correspondence, and outpatient visit. The follow-up information included survival statuses (recurrence, metastasis, death, or newly diagnosed diseases), updated contact information, post-diagnostic life style (physical exercise, sleep, tea consumption, etc.), and treatment information. The endpoint for this study was progression-free survival

(PFS), calculated from diagnosis to the date of recurrence, metastasis, or death; the patients still alive without progression have been censored at the latest date of their follow-up.

Statistical analysis

Student *t* test and Chi square test were used to analyze the difference of demographic factors and clinical characteristics between tea consumption and non-tea consumption groups at baseline. We also evaluated the associations of demographic and clinical characteristics with breast cancer PFS (Supplementary Table 1), so as to determine the potential confounders. Then, Cox proportional hazards regression models were used to estimate the association between pre- and post-diagnostic tea consumption and the risk of PFS with hazard ratio (HR) and 95% CI, adjusting for age at diagnosis, education, menopausal status, ER and HER2 statuses, and clinical stage. We also evaluated the change from pre-diagnostic to post-diagnostic tea consumption behavior and the effect of such change on breast cancer PFS, using McNemar test and adjusted Cox proportional hazards models, respectively. Stratified analyses were further performed to assess whether the associations between post-diagnostic tea consumption and breast cancer PFS were modified by lipids. Interactions between these studied factors on the survivals were estimated by the product terms in the Cox regression models. All statistical tests were two-tailed with

$P < 0.05$ considered to be significant. Statistical analyses above were conducted by SPSS, version 23.0.

Results

Demographic characteristics and the associations with tea consumption at baseline

A total of 1551 patients were included in this analysis. The mean age at diagnosis was 48.25 (SD = 11.38) years old. Baseline characteristics of tea drinkers and non-tea drinkers were shown in Supplementary Table 2. Tea consumption patients were more likely to have normal BMI, later age at menarche, and lower clinical stage, while other characteristics were shown no significantly associations with tea consumption.

Association of tea consumption with breast cancer PFS

Pre-diagnostic tea consumption

Overall, 40% of women (575 cases) reported tea drinking regularly at the baseline survey, with a median of 15 years tea consumption duration. Compared with non-tea drinkers, regular tea consumption at baseline was not associated with breast cancer PFS (HR 1.13; 95% CI 0.78 ~ 1.31); neither were other characteristics of tea drinking (Table 1).

Table 1 Univariate and multivariate COX regression analyses for tea consumption with breast cancer PFS

Variables	Baseline				Post-diagnosis			
	Total	Events	HR (95% CI) ^a	HR (95% CI) ^b	Total	Events	HR (95% CI) ^a	HR (95% CI) ^b
Tea consumption								
No	852	165	1.00 (reference)	1.00 (reference)	592	77	1.00 (reference)	1.00 (reference)
Yes	575	108	1.13 (0.86 ~ 1.48)	1.13 (0.86 ~ 1.48)	317	23	0.53 (0.33 ~ 0.85)	0.64 (0.40 ~ 1.05)
Type of tea consumed								
Non-tea drinkers	852	165	1.00 (reference)	1.00 (reference)	592	77	1.00 (reference)	1.00 (reference)
Green tea	172	33	1.01 (0.69 ~ 1.46)	1.17 (0.78 ~ 1.76)	77	3	0.27 (0.09 ~ 0.86)	0.33 (0.10 ~ 1.05)
Black tea	54	13	1.24 (0.70 ~ 2.17)	1.00 (0.51 ~ 1.97)	25	1	0.29 (0.04 ~ 2.08)	0.32 (0.05 ~ 2.35)
Oolong tea	135	27	1.07 (0.71 ~ 1.62)	1.41 (0.91 ~ 2.18)	50	7	1.07 (0.49 ~ 2.32)	1.32 (0.60 ~ 2.90)
Green tea and black tea	59	8	0.68 (0.33 ~ 1.38)	0.66 (0.27 ~ 1.61)	43	3	0.52 (0.16 ~ 1.64)	0.72 (0.22 ~ 2.32)
Pu-erh	60	10	1.00 (0.53 ~ 1.89)	1.08 (0.55 ~ 2.13)	39	2	0.35 (0.09 ~ 1.41)	0.45 (0.11 ~ 1.85)
Other types of tea	90	17	0.95 (0.58 ~ 1.57)	1.11 (0.66 ~ 1.88)	63	4	0.49 (0.18 ~ 1.33)	0.61 (0.22 ~ 1.68)
Type of tea consumed (reclassified)								
Non-tea drinkers	852	165	1.00 (reference)	1.00 (reference)	592	77	1.00 (reference)	1.00 (reference)
Green tea and others	440	81	0.96 (0.74 ~ 1.26)	1.05 (0.79 ~ 1.42)	267	16	0.44 (0.25 ~ 0.75)	0.52 (0.29 ~ 0.91)
Oolong tea	135	27	1.07 (0.71 ~ 1.61)	1.41 (0.91 ~ 2.19)	50	7	1.07 (0.49 ~ 2.32)	1.32 (0.60 ~ 2.90)

^aThe univariate COX model

^bThe multivariate COX model, adjusted for age at diagnosis, education, menopausal, clinical stage, ER status, HER2 status; Bold character indicate statistically significant result

Post-diagnostic tea consumption

The proportion of post-diagnostic tea drinking was 35% (317 patients), with a median of 45 months tea consumption duration. Over a median of 58.58 months of follow-up, a total of 100 patients experienced breast cancer progression. As shown in Table 1, the regular tea drinkers had a marginal significant reduced risk of progression (HR 0.64; 95% CI 0.40~1.05) compared with non-tea drinkers. As for the types of tea drinking, non-significant reduced risks of progression were observed among the patients who drank green tea or other types of tea excluding oolong. The association became significant with adjusted HR of 0.52 (95% CI 0.29~0.91) when all teas (mainly green tea) except oolong were combined, while oolong tea was associated with a non-significant increased risk of progression (HR 1.32; 95% CI 0.60~2.90). Thus, patients who drank oolong tea were excluded from subsequent analyses.

A higher frequency (≥ 7 times/week) of tea drinking was associated with a better breast cancer prognosis compared

with non-tea drinkers (HR 0.30; 95% CI 0.11~0.84), while the tea strength seemed not associated with the progression, as shown in Table 2. For green tea only, the results were similar (Supplementary Table 3). We further conducted stratified analyses by menopausal status and clinical-pathological characteristics but no significant interaction between tea consumption and these factors on the progression was found (Supplementary Table 4); similar results occurred for green tea only (Supplementary Table 5).

We subsequently evaluated the association between changing patterns from pre-diagnostic to post-diagnostic tea consumption and breast cancer PFS (Table 3). In this study, 34.1% breast cancer patients altered tea consumption behavior following their diagnosis (Supplementary Table 6). Compared with those who never drink tea, there was a decreased risk for progression among those who kept all teas except oolong drinking before and after diagnosis (HR 0.31; 95% CI 0.11~0.87), whereas women who ever drank oolong tea were associated with a potential increased risk of progression (HR 2.04; 95% CI 0.79~5.25 and HR 1.69; 95% CI

Table 2 Associations between green tea and other types of tea consumption characteristics and breast cancer PFS

Variables	Baseline			Post-diagnosis		
	Total	Events	HR (95% CI) ^a	Total	Events	HR (95% CI) ^a
Strength of prepared tea						
Non-tea drinkers	852	165	1.00 (reference)	592	77	1.00 (reference)
Weak	134	24	0.99 (0.63~1.58)	100	5	0.43 (0.17~1.07)
Medium	224	42	1.04 (0.71~1.51)	103	5	0.47 (0.19~1.18)
Strong	68	13	1.27 (0.68~2.37)	18	2	0.87 (0.21~3.60)
<i>P</i> for trend			0.788			0.015
Tea consumption frequency						
Non-tea drinkers	852	165	1.00 (reference)	592	77	1.00 (reference)
<7 times per week	146	26	0.97 (0.61~1.54)	114	8	0.64 (0.30~1.34)
≥ 7 times per week	282	53	1.11 (0.79~1.56)	110	4	0.30 (0.11~0.84)
<i>P</i> for trend			0.471			0.021

^aThe multivariate COX model, adjusted for age at diagnosis, education, menopausal, clinical stage, ER status, HER2 status; Bold character indicate statistically significant result is missing

Table 3 Associations between the change of tea consumption over diagnosis and breast cancer PFS

Baseline tea consumption	Post-diagnostic tea consumption ^a	No. of patients	Progression-free survival		
			No.	HR (95% CI) ^b	HR (95% CI) ^b
Non-tea drinkers	Non-tea drinkers	432	53	1.00 (reference)	1.00 (reference)
Green tea and others	Non-tea drinkers	106	15	1.19 (0.67~2.11)	1.77 (0.97~3.23)
Oolong tea	Non-tea drinkers	31	5	1.43 (0.57~3.58)	2.04 (0.79~5.25)
Non-tea drinkers	Green tea and others	91	7	0.58 (0.27~1.28)	0.70 (0.30~1.65)
Green tea and others	Green tea and others	132	4	0.23 (0.08~0.64)	0.31 (0.11~0.87)
Oolong tea	Green tea and others	38	5	1.16 (0.46~2.90)	1.69 (0.67~4.30)

^aGreen tea and other types of tea consumption excluding oolong tea

^bThe multivariate COX model, adjusted for age at diagnosis, education, menopausal, clinical stage, ER status, HER2 status; Bold character indicate statistically significant result

0.67~4.30 for those from pre-diagnostic oolong tea drinking to either no tea drinking or all teas except oolong drinking, respectively).

Joint effects of lipids and post-diagnostic tea consumption on breast cancer PFS

The association of lipids with breast cancer PFS were shown in Table 4. A higher blood TC was associated with a worse PFS of breast cancer (HR 1.72; 95% CI 1.14~2.60). There was no significant association for TG or LDL-C with the outcome.

Given that tea consumption may affect the metabolism of lipids, we assessed the joint effects of post-diagnostic tea consumption and lipids on breast cancer PFS. It turned out that the effect of tea drinking looked opposite among those with normal (HR 0.38; 95% CI 0.18~0.82) and higher (HR 1.22; 95% CI 0.13~11.82) blood TC (Table 5), though no significant interaction was observed. Similarly, the protective effect was limited to patients with normal blood lipids for green tea only (Supplementary Table 7). In addition, mediation analysis did not demonstrate any effect of the lipid factors on the association between tea drinking and the progression (Supplementary Table 8).

Discussion

In the present study, we found that women who regularly drank all teas (mainly green tea) except oolong after cancer diagnosis had a better prognosis compared with non-tea drinkers. The more tea they drank (≥ 7 times/week), the better prognosis of breast cancer they got; women who maintained all teas except oolong drinking before and after diagnosis had a lower risk of progression, whereas women who drank oolong tea might have a poor prognosis. In addition, a

higher blood TC was associated with a worse PFS of breast cancer and there was a possible differential effect of tea drinking on the progression between the women with normal and higher TC.

Epidemiological data regarding the relation between green tea consumption and breast cancer survival are limited. Two Japanese studies and a meta-analysis for these two studies suggested that an increased consumption of green tea before diagnosis was associated with a reduced risk of recurrence for early stage breast cancer [7, 8, 21]. Meanwhile, in a Chinese cohort with triple-negative breast cancer, a reduced risk of mortality was observed for post-diagnostic green tea consumption [10]. In the present study, we confirmed this previous finding and further found that there was a dose–effect relationship of breast cancer prognosis with the frequency of tea consumption. This dose–effect relationship of green tea had been observed for breast cancer incidence [22, 23]. In addition, the result that maintenance of green tea intake behavior after diagnosis of breast cancer was beneficial to the survival also supported the protective effect of green tea on the prognosis (Table 3). It should be noted that although the association of green tea consumption as a dichotomous variable (yes vs no) with breast cancer prognosis was not significant after adjusting for potential confounders, the effect was towards a better prognosis (HR 0.33; 95% CI 0.10~1.05), implicating that the semiquantitative analysis, from which the results were significant, was more sensitive.

We observed a harmful effect of higher TC on breast cancer PFS, which was consistent with the results from most previous studies [24–27]. For example, Tartter et al. found that in breast cancer patients with higher serum TC levels, disease-free survival decreased [26]; Liu et al. showed that higher serum level of TC was an independent risk factor for distant metastasis of breast cancer [25]; Bahl et al. also indicated an adverse effect of TC on breast cancer recurrence,

Table 4 Associations of lipids with breast cancer PFS

Variables	No. of patients	Progression-free survival		
		No.	HR (95% CI) ^a	HR (95% CI) ^b
Blood triglyceride				
Normal	900	182	1.00 (reference)	1.00 (reference)
Higher than normal value	140	33	1.29 (0.89~1.88)	1.27 (0.83~1.93)
Blood total cholesterol				
Normal	902	177	1.00 (reference)	1.00 (reference)
Higher than normal value	139	39	1.63 (1.15~2.30)	1.72 (1.14~2.60)
Blood LDL-C				
Normal	745	147	1.00 (reference)	1.00 (reference)
Higher than normal value	297	69	1.21 (0.91~1.61)	1.25 (0.88~1.78)

^aThe univariate COX model

^bThe multivariate COX model, adjusted for age at diagnosis, education, menopausal, clinical stage, ER status, HER2 status; Bold character indicate statistically significant result

Table 5 Joint associations between tea consumption after diagnosis and lipids with breast cancer PFS

Characteristics	Tea consumption ^a	No. of patients	Progression-free survival	
			No.	HR (95% CI) ^b
Blood triglyceride				
Normal	No	342	50	1.00 (reference)
	Yes	176	11	0.50 (0.25 ~ 1.00)
Higher than normal value	No	55	8	1.00 (reference)
	Yes	13	0	...
<i>P</i> for multiplicative interaction				0.962
Blood total cholesterol				
Normal	No	353	53	1.00 (reference)
	Yes	161	8	0.38 (0.18 ~ 0.82)
Higher than normal value	No	45	6	1.00 (reference)
	Yes	28	3	1.22 (0.13 ~ 11.82)
<i>P</i> for multiplicative interaction				0.634
Blood LDL-C				
Normal	No	301	48	1.00 (reference)
	Yes	128	7	0.38 (0.17 ~ 0.88)
Higher than normal value	No	98	11	1.00 (reference)
	Yes	61	6	0.44 (0.11 ~ 1.81)
<i>P</i> for multiplicative interaction				0.880
Lipid metabolism				
Normal	No	262	42	1.00 (reference)
	Yes	116	7	0.47 (0.21 ~ 1.09)
One of indexes is high	No	137	17	1.00 (reference)
	Yes	72	4	0.41 (0.12 ~ 1.45)
<i>P</i> for multiplicative interaction				0.758

^aGreen tea and other types of tea consumption excluding oolong tea

^bAdjusted for age at diagnosis, education, menopausal, clinical stage, ER status, HER2 status; Bold character indicate statistically significant result

but TG was not associated with outcome [24]. We further found that the associations of green tea consumption and breast cancer prognosis were more evident among women with normal TC level than higher TC level. It was observed that green tea induced hypolipidemic and antiproliferative effects by regulating PI3 K/Akt/Sp-1 signal transduction pathway in MCF-7 breast cancer cells [28] and affected lipid rafts-associated signaling pathways in cancer cells [29, 30]. Meanwhile, cholesterol is a major component of lipid rafts, which can serve in human cancer development as platforms for several signaling cascades, including Ras, Akt, and Src signaling [31, 32]. Therefore, green tea components and cholesterol may interact to inhibit the signaling events involved in breast cancer development; elevated cholesterol could partially inhibit the tea effects on signaling [29], which might offset the protective effect of tea. However, the exact mechanisms remained to be explored.

It is worth noting that oolong tea was observed to have a potential impaired effect on breast cancer prognosis. Oolong tea was also found to have adverse effect on health in early reports: a case–control study conducted in

southern Taiwan suggested that oolong tea consumption was associated with an increased risk of bladder cancer [13]; John et al. suggested that concentrated oolong tea may associate with Transient Ischemic Attack-Like effects [12]. The possible different impacts of green and oolong tea may be due to the variety of components. Compared with green tea, oolong tea contains less catechins and flavonoids [33] which contribute to the anticarcinogenic properties of tea [34, 35], and more caffeine which may produce negative effects such as nervousness, restlessness, sleep disorders, and headaches [4]. About 30% catechins and 20% proanthocyanidins were oxidized in the manufacture of oolong tea from fresh tea shoots, and 20% of total flavonoids were decomposed in a follow-up drying process [36]. Besides, oolong tea may contain several unique components resulting from the fermentation protocol, such as oolongtheanine, oolonghomobisflavans, and 8-ascorbyl epigallocatechin gallate [37], which may have adverse effects on health. However, some studies indicated that oolong tea was beneficial to health. For example, oolong was found to have protective effect on the risk of lung cancer [38];

Mineharu et al. found that oolong tea could reduce risk of mortality from cardiovascular disease [39]. Nevertheless, the health impact of oolong tea was controversial and further studies with larger sample size are warranted.

There were some limitations in this study. First, tea consumption behaviors were self-reported, which inevitably resulted in recall bias. However, women in this study were not likely to know the study hypothesis, and misclassification due to recall bias occurred equally in patients with better and worse outcomes. This non-differential exposure misclassification was likely to reduce test power and bias study estimators towards the null [40]. Second, the longitudinal study method was hard to avoid loss to follow-up. However, we tried various ways to reduce the missing rate and the characteristics were no difference between the follow-up group and the lost group. Third, the prevalence of tea consumption stratified by types was low and some of the potential relationships may not be found. Fourth, the exclusion of patients who drank oolong tea was decided post hoc based on a review of the primary results, potentially resulting in a selection bias. However, this bias may be neglected because the distributions of the demographic and clinicopathological characteristics were not significantly different between the original entire population and the excluded subgroup (data not shown). Finally, although breast cancer specific mortality or overall mortality is also suitable endpoint for prognostic study, the number of death was too few to make so many comparisons while the progressed cases were relatively more and only PFS was applied in the present study.

In conclusion, our data qualitatively and quantitatively confirmed the beneficial effect of post-diagnostic green tea consumption on breast cancer survival. Moreover, it was suggested that green tea consumption would confer more benefit to the breast cancer patients with normal lipids. More studies on the possible adverse impact of oolong tea are warranted.

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Compliance with ethical standards

Conflict of interest All the authors declared that they have no conflict of interest.

Ethical approval This study was approved by the Ethics Committee of the School of Public Health at Sun Yat-sen University. All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

References

1. Ferlay J, Soerjomataram I, Dikshit R, Eser S, Mathers C, Rebelo M, Parkin DM, Forman D, Bray F (2015) Cancer incidence and mortality worldwide: sources, methods and major patterns in GLOBOCAN 2012. *Int J Cancer* 136(5):E359–E386. <https://doi.org/10.1002/ijc.29210>
2. Chen W, Zheng R, Baade PD, Zhang S, Zeng H, Bray F, Jemal A, Yu XQ, He J (2016) Cancer statistics in China, 2015. *CA Cancer J Clin* 66(2):115–132. <https://doi.org/10.3322/caac.21338>
3. Allemani C, Matsuda T, Di Carlo V, Harewood R, Matz M, Niksic M, Bonaventure A, Valkov M, Johnson CJ, Esteve J, Ogunbiyi OJ, Azevedo ESG, Chen WQ, Eser S, Engholm G, Stiller CA, Monnereau A, Woods RR, Visser O, Lim GH, Aitken J, Weir HK, Coleman MP (2018) Global surveillance of trends in cancer survival 2000–14 (CONCORD-3): analysis of individual records for 37 513 025 patients diagnosed with one of 18 cancers from 322 population-based registries in 71 countries. *Lancet (London, England)* 391(10125):1023–1075. [https://doi.org/10.1016/s0140-6736\(17\)33326-3](https://doi.org/10.1016/s0140-6736(17)33326-3)
4. Hayat K, Iqbal H, Malik U, Bilal U, Mushtaq S (2015) Tea and its consumption: benefits and risks. *Crit Rev Food Sci Nutr* 55(7):939–954. <https://doi.org/10.1080/10408398.2012.678949>
5. Li MJ, Yin YC, Wang J, Jiang YF (2014) Green tea compounds in breast cancer prevention and treatment. *World J Clin Oncol* 5(3):520–528. <https://doi.org/10.5306/wjco.v5.i3.520>
6. Yiannakopoulou E (2014) Green tea catechins: proposed mechanisms of action in breast cancer focusing on the interplay between survival and apoptosis. *Anti-Cancer Agents Med Chem* 14(2):290–295
7. Nakachi K, Suemasu K, Suga K, Takeo T, Imai K, Higashi Y (1998) Influence of drinking green tea on breast cancer malignancy among Japanese patients. *Jpn J Cancer Res* 89(3):254–261
8. Inoue M, Tajima K, Mizutani M, Iwata H, Iwase T, Miura S, Hirose K, Hamajima N, Tominaga S (2001) Regular consumption of green tea and the risk of breast cancer recurrence: follow-up study from the Hospital-based Epidemiologic Research Program at Aichi Cancer Center (HERPACC), Japan. *Cancer Lett* 167(2):175–182
9. Velentzis LS, Keshtgar MR, Woodside JV, Leathem AJ, Titcomb A, Perkins KA, Mazurowska M, Anderson V, Wardell K, Cantwell MM (2011) Significant changes in dietary intake and supplement use after breast cancer diagnosis in a UK multicentre study. *Breast Cancer Res Treat* 128(2):473–482. <https://doi.org/10.1007/s10549-010-1238-8>
10. Bao PP, Zhao GM, Shu XO, Peng P, Cai H, Lu W, Zheng Y (2015) Modifiable lifestyle factors and triple-negative breast cancer survival: a population-based prospective study. *Epidemiology (Cambridge, Mass)* 26(6):909–916. <https://doi.org/10.1097/ede.0000000000000373>
11. Harris HR, Bergkvist L, Wolk A (2012) Coffee and black tea consumption and breast cancer mortality in a cohort of Swedish women. *Br J Cancer* 107(5):874–878. <https://doi.org/10.1038/bjc.2012.337>
12. Layher JW Jr, Poling JS, Ishihara M, Azadi P, Alvarez-Manilla G, Puett D (2013) A possible effect of concentrated oolong tea causing transient ischemic attack-like symptoms. *Br J Med Med Res* 3(4):2157–2172. <https://doi.org/10.9734/bjmmr/2013/4703>
13. Lu CM, Lan SJ, Lee YH, Huang JK, Huang CH, Hsieh CC (1999) Tea consumption: fluid intake and bladder cancer risk in Southern Taiwan. *Urology* 54(5):823–828
14. Stendell-Hollis NR, Thomson CA, Thompson PA, Bea JW, Cussler EC, Hakim IA (2010) Green tea improves metabolic

- biomarkers, not weight or body composition: a pilot study in overweight breast cancer survivors. *J Hum Nutr Diet* 23(6):590–600. <https://doi.org/10.1111/j.1365-277X.2010.01078.x>
15. Crew KD, Ho KA, Brown P, Greenlee H, Bevers TB, Arun B, Sneige N, Hudis C, McArthur HL, Chang J, Rimawi M, Cornelison TL, Cardelli J, Santella RM, Wang A, Lippman SM, Hershman DL (2015) Effects of a green tea extract, Polyphenon E, on systemic biomarkers of growth factor signalling in women with hormone receptor-negative breast cancer. *J Hum Nutr Diet* 28(3):272–282. <https://doi.org/10.1111/jhn.12229>
 16. Peairs KS, Barone BB, Snyder CF, Yeh HC, Stein KB, Derr RL, Brancati FL, Wolff AC (2011) Diabetes mellitus and breast cancer outcomes: a systematic review and meta-analysis. *J Clin Oncol* 29(1):40–46. <https://doi.org/10.1200/jco.2009.27.3011>
 17. Tornberg S, Carstensen J (1993) Serum beta-lipoprotein, serum cholesterol and Quetelet's index as predictors for survival of breast cancer patients. *Eur J Cancer (Oxford, England: 1990)* 29a(14):2025–2030
 18. Liao YH, Ren JT, Zhang W, Zhang ZZ, Lin Y, Su FX, Jia WH, Tang LY, Ren ZF (2017) Polymorphisms in homologous recombination repair genes and the risk and survival of breast cancer. *J Gene Med* 19:9–10. <https://doi.org/10.1002/jgm.2988>
 19. Chen X, Lu W, Zheng Y, Gu K, Chen Z, Zheng W, Shu XO (2010) Exercise, tea consumption, and depression among breast cancer survivors. *J Clin Oncol* 28(6):991–998. <https://doi.org/10.1200/JCO.2009.23.0565>
 20. He JR, Tang LY, Yu DD, Su FX, Song EW, Lin Y, Wang SM, Lai GC, Chen WQ, Ren ZF (2011) Epstein-Barr virus and breast cancer: serological study in a high-incidence area of nasopharyngeal carcinoma. *Cancer Lett* 309(2):128–136. <https://doi.org/10.1016/j.canlet.2011.05.012>
 21. Seely D, Mills EJ, Wu P, Verma S, Guyatt GH (2005) The effects of green tea consumption on incidence of breast cancer and recurrence of breast cancer: a systematic review and meta-analysis. *Integr Cancer Ther* 4(2):144–155. <https://doi.org/10.1177/1534735405276420>
 22. Zhang M, Holman CD, Huang JP, Xie X (2007) Green tea and the prevention of breast cancer: a case-control study in Southeast China. *Carcinogenesis* 28(5):1074–1078. <https://doi.org/10.1093/carcin/bg1252>
 23. Shrubsole MJ, Lu W, Chen Z, Shu XO, Zheng Y, Dai Q, Cai Q, Gu K, Ruan ZX, Gao YT, Zheng W (2009) Drinking green tea modestly reduces breast cancer risk. *J Nutr* 139(2):310–316. <https://doi.org/10.3945/jn.108.098699>
 24. Bahl M, Ennis M, Tannock IF, Hux JE, Pritchard KI, Koo J, Goodwin PJ (2005) Serum lipids and outcome of early-stage breast cancer: results of a prospective cohort study. *Breast Cancer Res Treat* 94(2):135–144. <https://doi.org/10.1007/s10549-005-6654-9>
 25. Liu YL, Qian HX, Qin L, Zhou XJ, Zhang B, Chen X (2012) Association of serum lipid profile with distant metastasis in breast cancer patients. *Zhonghua zhong liu za zhi [Chin J Oncol]* 34(2):129–131. <https://doi.org/10.3760/cma.j.issn.0253-3766.2012.02.010>
 26. Tartter PI, Papatestas AE, Ioannovich J, Mulvihill MN, Lesnick G, Aufses AH Jr (1981) Cholesterol and obesity as prognostic factors in breast cancer. *Cancer* 47(9):2222–2227
 27. Zhou P, Li B, Liu B, Chen T, Xiao J (2018) Prognostic role of serum total cholesterol and high-density lipoprotein cholesterol in cancer survivors: a systematic review and meta-analysis. *Clin Chim Acta* 477:94–104. <https://doi.org/10.1016/j.cca.2017.11.039ca.2017.11.039>
 28. Yeh CW, Chen WJ, Chiang CT, Lin-Shiau SY, Lin JK (2003) Suppression of fatty acid synthase in MCF-7 breast cancer cells by tea and tea polyphenols: a possible mechanism for their hypolipidemic effects. *Pharmacogenomics J* 3(5):267–276. <https://doi.org/10.1038/sj.tpj.6500192>
 29. Duhon D, Bigelow RL, Coleman DT, Steffan JJ, Yu C, Langston W, Kevil CG, Cardelli JA (2010) The polyphenol epigallocatechin-3-gallate affects lipid rafts to block activation of the c-Met receptor in prostate cancer cells. *Mol Carcinog* 49(8):739–749. <https://doi.org/10.1002/mc.20649>
 30. Adachi S, Nagao T, Ingolfsson HI, Maxfield FR, Andersen OS, Kopelovich L, Weinstein IB (2007) The inhibitory effect of (-)-epigallocatechin gallate on activation of the epidermal growth factor receptor is associated with altered lipid order in HT29 colon cancer cells. *Cancer Res* 67(13):6493–6501. <https://doi.org/10.1158/0008-5472.can-07-0411>
 31. George KS, Wu S (2012) Lipid raft: a floating island of death or survival. *Toxicol Appl Pharmacol* 259(3):311–319. <https://doi.org/10.1016/j.taap.2012.01.007>
 32. Danilo C, Frank PG (2012) Cholesterol and breast cancer development. *Curr Opin Pharmacol* 12(6):677–682. <https://doi.org/10.1016/j.coph.2012.07.009>
 33. Tao W, Zhou Z, Zhao B, Wei T (2016) Simultaneous determination of eight catechins and four theaflavins in green, black and oolong tea using new HPLC-MS-MS method. *J Pharm Biomed Anal* 131:140–145. <https://doi.org/10.1016/j.jpba.2016.08.020>
 34. Xiang LP, Wang A, Ye JH, Zheng XQ, Polito CA, Lu JL, Li QS, Liang YR (2016) Suppressive effects of tea catechins on breast cancer. *Nutrients* 8(8):458. <https://doi.org/10.3390/nu8080458>
 35. Qadir MI (2017) Role of green tea flavonoids and other related contents in cancer prevention. *Crit Rev Eukaryot Gene Exp* 27(2):163–171. <https://doi.org/10.1615/CritRevEukaryotGeneExp.2017019493>
 36. Dou J, Lee VS, Tzen JT, Lee MR (2007) Identification and comparison of phenolic compounds in the preparation of oolong tea manufactured by semifermentation and drying processes. *J Agric Food Chem* 55(18):7462–7468. <https://doi.org/10.1021/jf0718603>
 37. Harbowy ME, Balentine DA, Davies AP, Cai Y (1997) Tea chemistry. *Crit Rev Plant Sci* 16(5):415–480. <https://doi.org/10.1080/07352689709701956>
 38. Xu X, Cai L (2013) A case-control study on tea consumption and the risk of lung cancer. *Wei sheng yan jiu = J Hyg Res* 42(2):211–216
 39. Mineharu Y, Koizumi A, Wada Y, Iso H, Watanabe Y, Date C, Yamamoto A, Kikuchi S, Inaba Y, Toyoshima H, Kondo T, Tamakoshi A (2011) Coffee, green tea, black tea and oolong tea consumption and risk of mortality from cardiovascular disease in Japanese men and women. *J Epidemiol Community Health* 65(3):230–240. <https://doi.org/10.1136/jech.2009.097311>
 40. Jurek AM, Greenland S, Maldonado G, Church TR (2005) Proper interpretation of non-differential misclassification effects: expectations vs observations. *Int J Epidemiol* 34(3):680–687. <https://doi.org/10.1093/ije/dyi060>

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