

RESEARCH ARTICLE

Alcohol Consumption and Breast Cancer Survival: A Meta-analysis of Cohort Studies

Yun-Jiu Gou^{1,2}, Ding-Xiong Xie³, Ke-Hu Yang⁴, Ya-Li Liu⁴, Jian-Hua Zhang¹, Bin Li¹, Xiao-Dong He^{2*}

Abstract

Background and Objectives: Evidence for associations between alcohol consumption with breast cancer survival are conflicting, so we conducted the present meta-analysis. **Methods:** Comprehensive searches were conducted to find cohort studies that evaluated the relationship between alcohol consumption with breast cancer survival. Data were analyzed with meta-analysis software. **Results:** We included 25 cohort studies. The meta-analysis results showed that alcohol consumption was not associated with increased breast cancer mortality and recurrence after pooling all data from highest versus lowest comparisons. Subgroup analyses showed that pre-diagnostic or post-diagnostic consumption, and ER status did not affect the relationship with breast cancer mortality and recurrence. Although the relationships of different alcohol consumption with breast cancer mortality and recurrence were not significant, there seemed to be a dose-response relationship of alcohol consumption with breast cancer mortality and recurrence. Only alcohol consumption of >20 g/d was associated with increased breast cancer mortality, but not with increased breast cancer recurrence. **Conclusion:** Although our meta-analysis showed alcohol drinking was not associated with increased breast cancer mortality and recurrence, there seemed to be a dose-response relationship of alcohol consumption with breast cancer mortality and recurrence and alcohol consumption of >20 g/d was associated with increased breast cancer mortality.

Keywords: Alcohol - breast neoplasms - survival - meta-analysis

Asian Pac J Cancer Prev, 14 (8), 4785-4790

Introduction

Breast cancer patients are often concerned that their lifestyle might affect their survival, so they often wonder whether modifying these behavior factors would improve their prognosis (Newcomb et al., 2013). Of these lifestyle factors, alcohol consumption is a modified factor. However, the available evidence is controvertible. Both meta-analysis and pooled study showed that (Poli et al., 2012; Bagnardi et al., 2013) alcohol consumption increases risk of breast cancer. However, the information on whether alcohol consumption is related to breast cancer survival is mixed (Hebert et al., 1989; Ewertz et al., 1991; Rohan et al., 1993; Fuchs et al., 1995; Zhang et al., 1995; Thun et al., 1997; Holmes et al., 1999; Saxe et al., 1999; Jain et al., 2000; McDonald et al., 2002; Borugian et al., 2004; Barnett et al., 2008; Reding et al., 2008; Franceschi et al., 2009; Flatt et al., 2010; Hellmann et al., 2010; Kwan et al., 2010; Allemani et al., 2011; Beasley et al., 2011; Breslow et al., 2011; Harris et al., 2012; Vrieling et al., 2012; Holm et al., 2013; Kwan et al.,

2013). Some studies reported that alcohol consumption was associated with reduced breast cancer mortality (Barnett et al., 2008; Reding et al., 2008; Flatt et al., 2010), while other studies revealed that alcohol consumption was associated with increased breast cancer mortality (Hebert et al., 1989; Fuchs et al., 1995; Jain et al., 2000; McDonald et al., 2002; Allemani et al., 2011; Vrieling et al., 2012). Even though, most studies found no relationship between alcohol consumption and breast cancer mortality (Ewertz et al., 1991; Rohan et al., 1993; Zhang et al., 1995; Thun et al., 1997; Holmes et al., 1999; Saxe et al., 1999; Borugian et al., 2004; Franceschi et al., 2009; Hellmann et al., 2010; Kwan et al., 2010; Beasley et al., 2011; Breslow et al., 2011; Harris et al., 2012; Holm et al., 2013; Kwan et al., 2013; Newcomb et al., 2013). For the association of alcohol consumption with breast cancer recurrence, available evidence was also conflicted (Hebert et al., 1989; Saxe et al., 1999; Kwan et al., 2010; Holm et al., 2013; Kwan et al., 2013). So a meta-analysis is necessary to investigate the relationship of alcohol intake and breast cancer survival (mortality and recurrence).

¹Department of Thoracic Surgery, Lanzhou University, Second Hospital, ²The Second Clinical Medical College of Lanzhou University, ³First People's Hospital of Lanzhou City, Gansu Provincial Cardiovascular Institute, ⁴Evidence-Based Medicine Center, School of Basic Medical Sciences, Lanzhou University, Lanzhou, Gansu Province, China *For correspondence: hexiaodong2006@126.com

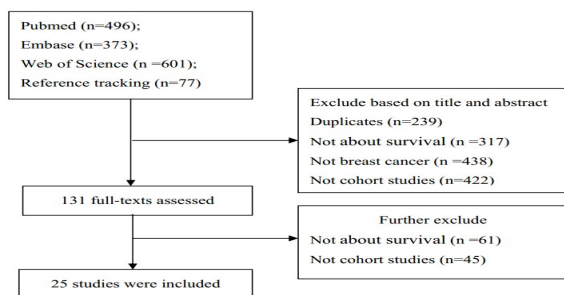


Figure 1. Flow Chart

Materials and Methods

We did this systematic review of the available literature in accordance with Guidelines for Meta-Analyses and Systematic Reviews of Observational Studies [MOOSE] (Stroup et al., 2000) for the conduct of meta-analyses of observational studies.

Search Strategy

PubMed, EMBASE, and ISI Web of Knowledge were searched using (alcohol* or ethanol) and (breast cancer* OR breast neoplasm* OR breast tumor* OR breast adenocarcinoma). Subject heading terms were added in all searches for Pubmed and EMBASE searches. Reference lists from the review articles and identified studies were reviewed to identify further relevant citations. All the searches were conducted independently by two reviewers (Yunjiu Gou and Dingxiong Xie) in February 2013 without language restrictions; differences were resolved by discussion.

Inclusion criteria and study selection

We identified all published cohort studies that evaluated whether alcohol consumption affect the survival (including mortality or recurrence) in breast cancer patients. When multiple articles for a study were published, we used the most comprehensive data. Letters, comments, editorials, practice guidelines and trials published without the outcome measures of interest were excluded. Two reviewers (Yunjiu Gou and Yali Liu) independently assessed potentially relevant citations for inclusion, disagreements were resolved involved with a third reviewer (Kehu Yang).

Data abstraction

Using a standardized data extraction form by two authors (Li Bin and Zhang Jianhua), we collected the following baseline characteristics for cases and control groups: lead author, publication year, variation in age, sample size and outcomes. Any disagreements in abstracted data were resolved by a third reviewer (Xiaodong He).

Data analysis

Meta-analysis was conducted by comprehensive meta-analysis software. And we expressed the data using hazard ratio (HR) and its 95% confidence interval (95%CI). Data was pooled using the random-effects model. The percentage of variability across trials attributable to heterogeneity was estimated with the I^2 test, which was

deemed significant when p was less than 0.05. Subgroup analyses of different ER statuses (ER positive vs. ER negative), different menopausal statuses (premenopausal vs. postmenopausal) and different doses based available data were conducted. Publication bias was assessed by visually inspecting a funnel plot. The small-study effect in terms of publication bias was also estimated using Egger's linear regression test.

Results

Search results

After systematic search, we found 1547 citations. After duplicating 239 citations, we excluded studies that were not about survival ($n=317$), not about breast cancer ($n=438$), and not cohort studies ($n=422$). After reading full-texts, we excluded studies that were not cohort studies ($n=61$) and not about survival ($n=61$). Finally, 25 cohort studies (Hebert et al., 1989; Ewertz et al., 1991; Rohan et al., 1993; Fuchs et al., 1995; Zhang et al., 1995; Thun et al., 1997; Holmes et al., 1999; Saxe et al., 1999; Jain et al., 2000; McDonald et al., 2002; Borugian et al., 2004; Barnett et al., 2008; Dal Maso et al., 2008; Reding et al., 2008; Franceschi et al., 2009; Flatt et al., 2010; Hellmann et al., 2010; Kwan et al., 2010; Allemani et al., 2011; Beasley et al., 2011; Breslow et al., 2011; Harris et al., 2012; Vrieling et al., 2012; Holm et al., 2013; Kwan et al., 2013; Newcomb et al., 2013) (patients) were included (Figure 1).

Characteristic of included studies

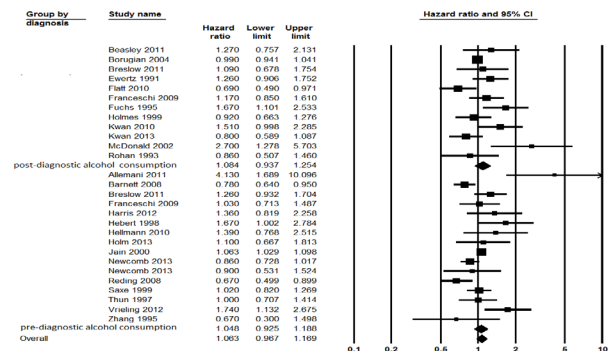
All studies focused on breast cancer mortality and only five studies (Hebert et al., 1989; Saxe et al., 1999; Kwan et al., 2010; Holm et al., 2013; Kwan et al., 2013) focused on breast cancer recurrence. Of 25 studies, 14 were from USA, three were from Denmark, two were from Germany, and the rest were from Italy, Australia, Canada, France, Sweden and UK, separately. 14 studies were about pre-diagnostic alcohol drinking, and ten were about post-diagnostic alcohol drinking, and one is about both pre- and post- diagnostic alcohol drinking. The total sample size for all included cohort studies were 719,555, the number of the breast cancer death was 10,912, and the number of the breast cancer recurrence was 2,027. The median follow-up ranged from 2.9 years to 18 years. And the other characteristics were presented in Table 1.

Results of meta-analysis

25 studies (Hebert et al., 1989; Ewertz et al., 1991; Rohan et al., 1993; Fuchs et al., 1995; Zhang et al., 1995; Thun et al., 1997; Holmes et al., 1999; Saxe et al., 1999; Jain et al., 2000; McDonald et al., 2002; Borugian et al., 2004; Barnett et al., 2008; Reding et al., 2008; Franceschi et al., 2009; Flatt et al., 2010; Hellmann et al., 2010; Kwan et al., 2010; Allemani et al., 2011; Beasley et al., 2011; Breslow et al., 2011; Harris et al., 2012; Vrieling et al., 2012; Holm et al., 2013; Kwan et al., 2013; Newcomb et al., 2013) reported mortality and five studies reported recurrence (Hebert et al., 1989; Saxe et al., 1999; Kwan et al., 2010; Holm et al., 2013; Kwan et al., 2013). Pooling all data from highest versus lowest comparisons, alcohol

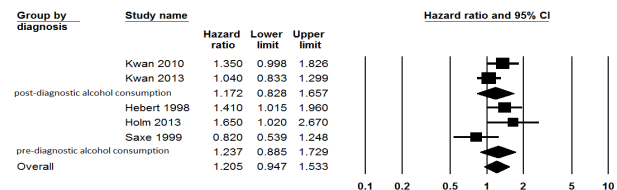
Table 1. The Characteristics of Included Studies

Study	Country	Age	Sample size	Event (death/recurrence)	Alcohol drinking	Follow-up
Allemani 2011	Italy	34-70	264	43/0	Pre-diagnosis	7.6 years
Barnett 2008	UK	<70 years	4,560	564/0	Pre-diagnosis	6.82 years
Beasley 2011	USA	20-79	4441	137/0	Post-diagnosis	7 years
Borugian 2004	Canada	19-75	603	112/0	Post-diagnosis	10 years
Breslow 2011	USA	>18	82605	677/0	Post-diagnosis	11 years
Ewertz 1991	Denmark	<70	1612	485/0	Post-diagnosis	6 years
Fuchs 1995	USA	30-55	121,700	350/0	Post-diagnosis	12 years
Flatt 2010	USA	18-70	3088	315/0	Pre-diagnosis	7.3 years
Franceschi 2009	France	23-74	1,453	503/0	Pre- and post- diagnosis	12.6 years
Harris 2012	Sweden	-	3146	385/0	Pre-diagnosis	11 years
Hebert 1998	USA	20-80	472	73/109	Pre-diagnosis	8-10 years
Hellmann 2010	Denmark	33.1-95.4	528	323/0	Pre-diagnosis	7.8 years
Holm 2013	Denmark	59-77	1,052	106/110	Pre-diagnosis	6 years
Holmes 1999	USA	54	1982	378/0	Post-diagnosis	18 years
Jain 2000	Germany	40-59	49,165	241/0	Pre-diagnosis	10.3 years
Kwan 2010	USA	18-70	2,269	273/293	Post-diagnosis	7.4 years
Kwan 2013	USA	58.8 years	9,329	911/1487	Post-diagnosis	10.3 years
McDonald 2002	USA	64.2 ± 12.2	125	33/0	Post-diagnosis	64.8 months
Newcomb 2013	USA	20-79	23,344	3,484/0	Pre-diagnosis	11.3 years
Reding 2008	USA	< 45 years	1286	335/0	Pre-diagnosis	12 years
Rohan 1993	Australia	20-74	451	112/0	Post-diagnosis	5.5 years
Saxe 1999	USA	26-95	149	26/28	Pre-diagnosis	>5 years
Thun 1997	USA	35-69	451876	691/0	Pre-diagnosis	9 years
Vrieling 2012	Germany	50-74	2,522	299	Pre-diagnosis	5.5 years
Zhang 1995	USA	55-69	698	56	Pre-diagnosis	2.9 years

**Figure 2. Meta-analysis Results of Subgroup Analysis of the Relationship of Pre- and Post- Alcohol Consumption Statuses with Breast Cancer Mortality**

consumption was not associated with increased breast cancer mortality (HR1.06, 95%CI 0.97 1.17, $I^2=31\%$) (Figure 2) and recurrence (HR1.21, 95%CI 0.95 1.53, $I^2=0\%$) (Figure 3).

15 studies (Hebert et al., 1989; Zhang et al., 1995; Thun et al., 1997; Saxe et al., 1999; Jain et al., 2000; Barnett et al., 2008; Reding et al., 2008; Franceschi et al., 2009; Hellmann et al., 2010; Allemani et al., 2011; Breslow et al., 2011; Harris et al., 2012; Vrieling et al., 2012; Holm et al., 2013; Newcomb et al., 2013) evaluated the relationship of post-diagnostic alcohol consumption with breast cancer mortality and three studies (Hebert et al., 1989; Saxe et al., 1999; Holm et al., 2013) evaluated the relationship of post-diagnostic alcohol consumption with breast cancer recurrence. And the meta-analysis results showed pre-diagnostic alcohol consumption was not associated with increased breast cancer mortality (HR1.05, 95%CI 0.93 1.19, $I^2=36\%$) (Figure 2) and recurrence (HR1.24, 95%CI 0.89 1.73, $I^2=31\%$) (Figure 3).

**Figure 3. Meta-analysis Results of Subgroup Analysis of the Relationship of Pre- and Post- Alcohol Consumption Statuses with Breast Cancer Recurrence**

12 studies (Ewertz et al., 1991; Rohan et al., 1993; Fuchs et al., 1995; Holmes et al., 1999; McDonald et al., 2002; Borugian et al., 2004; Franceschi et al., 2009; Flatt et al., 2010; Kwan et al., 2010; Beasley et al., 2011; Breslow et al., 2011; Kwan et al., 2013) evaluated the relationship of post-diagnostic alcohol consumption with breast cancer mortality and two studies (Kwan et al., 2010; Kwan et al., 2013) evaluated the relationship of post-diagnostic alcohol consumption with breast cancer recurrence. And the meta-analysis results showed post-diagnostic alcohol consumption was not associated with increased breast cancer mortality (HR1.08, 95%CI 0.94 1.25, $I^2=30\%$) (Figure 2) and recurrence (HR1.17, 95%CI 0.80 1.73, $I^2=0\%$) (Figure 3).

Subgroup analysis of different ER statuses showed the relationship of alcohol consumption with mortality and recurrence did not differ in ER positive and negative breast cancer patients. Subgroup analysis of different menopausal statuses showed the relationship of alcohol consumption with mortality did not differ in postmenopausal and premenopausal breast cancer patients. However, increased breast cancer recurrence was associated with premenopausal status, but not with postmenopausal status (Table 2).

Table 2. Summary of the Results of Subgroup Analysis of ER and Menopausal Statuses

Highest vs. lowest	Death			Recurrence		
	Study	Effect size	Heterogeneity	Study	Effect size	Heterogeneity
ER negative	(Barnett et al., 2008, Kwan et al., 2010, Kwan et al., 2013)	0.98 (0.69 1.40)	0%	(Kwan et al., 2010)	2.00 (0.96 4.15)	
ER positive	(Barnett et al., 2008, Kwan et al., 2010, Kwan et al., 2013)	1.03 (0.77 1.37)	37%	(Kwan et al., 2010)	1.23 (0.89 1.71)	
Postmenopausal	(Zhang et al., 1995, Borugian et al., 2004, Hellmann et al., 2010, Kwan et al., 2010, Vrieling et al., 2012, Kwan et al., 2013)	1.17 (0.94 1.44)	17%	(Kwan et al., 2010)	1.09 (0.78 1.52)	
premenopausal	(Hebert et al., 1989, Borugian et al., 2004, Hellmann et al., 2010, Kwan et al., 2010, Kwan et al., 2013)	1.05 (0.81 1.36)	53%	(Hebert et al., 1989, Kwan et al., 2010)	1.52 (1.21 1.90)	0%

Table 3. Summary of the Results of Dose-response Relationship Meta-analysis

Subgroups	Death			Recurrence		
	Study	Effect size	Heterogeneity	Study	Effect size	Heterogeneity
<10g/d	(Ewertz et al., 1991, Rohan et al., 1993, Fuchs et al., 1995, Zhang et al., 1995, Holmes et al., 1999, Saxe et al., 1999, Jain et al., 2000, Reding et al., 2008, Flatt et al., 2010, Hellmann et al., 2010, Kwan et al., 2010, Breslow et al., 2011, Harris et al., 2012, Vrieling et al., 2012, Kwan et al., 2013)	0.94 (0.88 1.01)	10%	(Saxe et al., 1999, Kwan et al., 2010, Kwan et al., 2013)	0.98 (0.88 1.11)	0%
>10g/d	(Ewertz et al., 1991, Rohan et al., 1993, Fuchs et al., 1995, Thun et al., 1997, Holmes et al., 1999, Jain et al., 2000, Reding et al., 2008, Franceschi et al., 2009, Flatt et al., 2010, Hellmann et al., 2010, Allemani et al., 2011, Breslow et al., 2011, Harris et al., 2012, Vrieling et al., 2012, Kwan et al., 2013, Newcomb et al., 2013)	1.03 (0.97 1.10)	51%	(Kwan et al., 2013)	1.09 (0.94 1.26)	
<15g/d	(Ewertz et al., 1991, Rohan et al., 1993, Fuchs et al., 1995, Zhang et al., 1995, Thun et al., 1997, Holmes et al., 1999, Saxe et al., 1999, Jain et al., 2000, Reding et al., 2008, Franceschi et al., 2009, Flatt et al., 2010, Hellmann et al., 2010, Kwan et al., 2010, Allemani et al., 2011, Breslow et al., 2011, Harris et al., 2012, Vrieling et al., 2012, Kwan et al., 2013, Newcomb et al., 2013)	0.95 (0.90 1.01)	9%	(Saxe et al., 1999, Kwan et al., 2010, Kwan et al., 2013)	1.00 (0.91 1.10)	0%
>15g/d	(Ewertz et al., 1991, Fuchs et al., 1995, Thun et al., 1997, Holmes et al., 1999, Jain et al., 2000, Franceschi et al., 2009, Hellmann et al., 2010, Kwan et al., 2010, Kwan et al., 2013, Newcomb et al., 2013)	1.08 (0.98 1.18)	36%	(Kwan et al., 2013)	1.04 (0.83 1.30)	
<20g/d	(Ewertz et al., 1991, Rohan et al., 1993, Fuchs et al., 1995, Zhang et al., 1995, Thun et al., 1997, Holmes et al., 1999, Saxe et al., 1999, Jain et al., 2000, Reding et al., 2008, Franceschi et al., 2009, Flatt et al., 2010, Hellmann et al., 2010, Kwan et al., 2010, Allemani et al., 2011, Breslow et al., 2011, Harris et al., 2012, Vrieling et al., 2012, Kwan et al., 2013, Newcomb et al., 2013)	0.96 (0.92 1.01)	14%	(Saxe et al., 1999, Kwan et al., 2010, Kwan et al., 2013)	1.00 (0.91 1.10)	0%
>20g/d	(Fuchs et al., 1995, Thun et al., 1997, Jain et al., 2000, Franceschi et al., 2009, Hellmann et al., 2010, Kwan et al., 2013)	1.14 (1.02 1.27)	49%	(Kwan et al., 2013)	1.04 (0.83 1.30)	

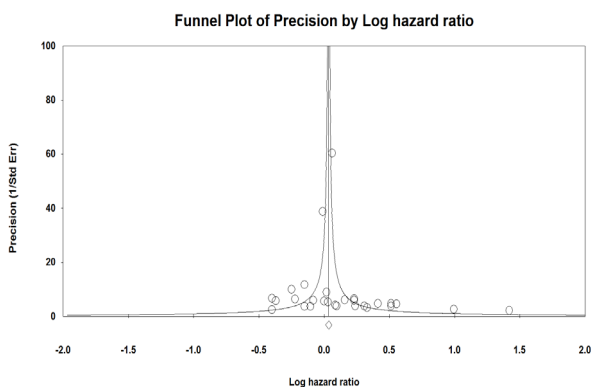


Figure 4. publication Bias Analysis Based Funnel Plot

Subgroup analysis of different alcohol consumption

Although the relationships of different alcohol consumption (<10 g/d, >10 g/d, <15 g/d, >15 g/d, and <20 g/d) with breast cancer mortality and recurrence were not significant, there seemed to be a dose-response relationship of alcohol consumption with breast cancer mortality and recurrence. Only one dose of alcohol consumption (>20 g/d) was associated with increased breast cancer mortality, but not with increased breast cancer recurrence (Table 3).

Publication bias

There was no significant publication bias based on funnel plot (Figure 4). Egger’s test indicated that there was not a possibility of publication bias for the relationship of alcohol drinking with breast cancer mortality (intercept 0.26, 95%CI -0.54 1.07 p=0.26).

Discussion

Summary of finding: We included 25 cohort studies. The meta-analysis results showed that alcohol consumption was not associated with increased breast cancer mortality and recurrence after pooling all data from highest versus lowest comparisons. Subgroup analyses showed that pre-diagnostic or post-diagnostic, and ER

negative or ER positive did not affect the relationship of alcohol consumption with breast cancer mortality and recurrence. Subgroup analysis of menopausal statuses showed that menopausal statuses did not affect the relationship of alcohol consumption with breast cancer mortality. But menopausal statuses might affect the relationship of alcohol consumption with breast cancer recurrence. Although the relationships of different alcohol consumption (<10 g/d, >10 g/d, <15 g/d, >15g/d, and <20 g/d) with breast cancer mortality and recurrence were not significant, there seemed to be a dose-response relationship of alcohol consumption with breast cancer mortality and recurrence. Only alcohol consumption of >20 g/d was associated with increased breast cancer mortality, but not with increased breast cancer recurrence.

The association between alcohol consumption and an increased risk of breast cancer has been established (Longnecker 1994; Suzuki et al., 2008). Studies have shown that mechanisms underlying the association of alcohol intake and breast cancer risk included increased estrogen and androgen levels, enhanced mammary gland susceptibility to carcinogenesis, increased mammary carcinogen DNA damage, and greater metastatic potential of breast cancer cells (Singletary et al., 2001; Reding et al., 2008). That is why reductions in alcohol intake were expected to improve breast cancer survival through similar mechanisms (Newcomb et al., 2013). However, our meta-analysis showed alcohol consumption was not associated with increased breast cancer mortality and recurrence. This is consistent with the result from a recent systematic review (Hauner et al., 2011). So based on available evidence, alcohol consumption did not affect breast cancer survival.

Cancer survivors face significant morbidity and mortality associated with their disease and treatment regimens, some of which can be improved through modifying behavioral and psychosocial risk factors (Carmack et al., 2011). However, a recent study showed that women with breast cancer did not modify their alcohol use compared with cancer-free women (Bidstrup et al.,

2013). Even so, based on the results of our meta-analysis, pre-diagnostic and post-diagnostic alcohol consumption were not associated with increased breast cancer mortality and recurrence. This is to say, both pre-diagnostic and post-diagnostic alcohol consumption did not affect breast cancer survival.

It is reported that the magnitude of damage by alcohol intake likely depends on the amount of alcohol consumed (Stroup et al., 2000; Bagnardi et al., 2013). A meta-analysis (Longnecker 1994) showed there was a modest dose-response relationship between alcohol drinking and breast cancer. Our meta-analysis showed that the relationships of different alcohol consumption (<10 g/d, >10 g/d, <15 g/d, >15g/d, and <20 g/d) with breast cancer mortality and recurrence were not significant, but there seemed to be a dose-response relationship of alcohol consumption with breast cancer mortality and recurrence. And alcohol consumption of >20g/d was associated with increased breast cancer mortality, but not with increased breast cancer recurrence. Combining with the results of the associations of pre-diagnostic and post-diagnostic alcohol consumption with breast cancer mortality and recurrence, we could suggest that too much alcohol intake (>20 g/d) should be avoided.

It is said ER statuses could affect the relationship of alcohol consumption with breast cancer risk (Suzuki et al., 2008), as increased estrogen and androgen levels in women consuming alcohol appear to be important mechanisms underlying the association (Breslow et al., 2011). But based on the results of our meta-analysis, ER statuses did not affect the relationship of alcohol consumption with breast cancer mortality and recurrence. This might be due to few studies that stratified ER statuses when they evaluated the relationship of alcohol consumption with breast cancer mortality and recurrence. Available evidence showed that menopausal statuses could not affect the relationship of alcohol intake with breast cancer mortality, but might affect the relationship of alcohol intake with breast cancer recurrence. But there were also few studies that evaluated the relationship of alcohol intake with breast cancer mortality and recurrence by stratifying the menopausal statuses.

Strength and limitation: Our meta-analysis is the first meta-analysis that evaluated the relationship of alcohol intake with breast cancer mortality and recurrence. Our meta-analysis also conducted subgroup analyses of different ER statuses, menopausal statuses and different doses. Even though, our meta-analysis has its own limitations: first: few studies evaluated the relationship of alcohol intake with breast cancer mortality and recurrence by stratifying the menopausal and ER statuses. And few studies evaluated the relationship of alcohol intake with breast cancer recurrence. Second, as we did not find a suitable criterion to evaluate quality of these included studies, we skipped this part. It could make our analysis not as powerful as we expected.

Implications to research and practice: Based on our meta-analysis, alcohol drinking was not associated with increased breast cancer mortality and recurrence. Menopausal and ER statuses did not affect the relationship of alcohol drinking with breast cancer mortality,

but whether menopausal and ER statuses affect the relationship of alcohol drinking with breast cancer recurrence deserves further researches. And as few studies evaluated the relationship of alcohol intake with breast cancer recurrence and evaluated the relationship of alcohol intake with breast cancer mortality by stratifying the menopausal and ER statuses, so these kinds of studies should be conducted.

And our meta-analysis also showed that the relationships of different alcohol consumption (<10 g/d, >10 g/d, <15 g/d, >15 g/d, and <20 g/d) with breast cancer mortality and recurrence were not significant, there seemed to be a dose-response relationship of alcohol consumption with breast cancer mortality and recurrence. And alcohol consumption of >20 g/d was associated with increased breast cancer mortality, but not with increased breast cancer recurrence. So in clinical practice, breast cancer patients should avoid too much alcohol drinking, such as alcohol consumption of >20 g/d.

Conclusion: Although our meta-analysis showed alcohol drinking was not associated with increased breast cancer mortality and recurrence, there seemed to be a dose-response relationship of alcohol consumption with breast cancer mortality and recurrence and alcohol consumption of >20 g/d was associated with increased breast cancer mortality. So in clinical practice, breast cancer patients should avoid too much alcohol drinking, such as alcohol consumption of >20 g/d. And studies that evaluated the relationship of alcohol intake with breast cancer recurrence and the relationship of alcohol intake with breast cancer mortality by stratifying the menopausal and ER statuses should be conducted.

Acknowledgements

The author(s) declare that they have no competing interests.

References

- Allemani C, Berrino F, Krogh V, et al (2011). Do pre-diagnostic drinking habits influence breast cancer survival? *Tumori*, **97**, 142-8.
- Bagnardi V, Rota M, Botteri E, et al (2013). Light alcohol drinking and cancer: a meta-analysis. *Ann Oncol*, **24**, 301-8.
- Barnett GC, Shah M, Redman K, et al (2008). Risk factors for the incidence of breast cancer: do they affect survival from the disease? *J Clin Oncol*, **26**, 3310-6.
- Beasley JM, Newcomb PA, Trentham-Dietz A, et al (2011). Post-diagnosis dietary factors and survival after invasive breast cancer. *Breast Cancer Res Treat*, **128**, 229-36.
- Bidstrup PE, Dalton SO, Christensen J, et al (2013). Changes in body mass index and alcohol and tobacco consumption among breast cancer survivors and cancer-free women: A prospective study in the Danish Diet, Cancer and Health Cohort. *Acta Oncologica*, **52**, 327-35.
- Borugian MJ, Sheps SB, Kim-Sing C, et al (2004). Insulin, macronutrient intake, and physical activity: are potential indicators of insulin resistance associated with mortality from breast cancer? *Cancer Epidemiol Biomarkers Prev*, **13**, 1163-72.
- Breslow RA, Chen CM, Graubard BI, Mukamal KJ (2011). Prospective study of alcohol consumption quantity and

- frequency and cancer-specific mortality in the us population. *Am J Epidemiol*, **174**, 1044-53.
- Carmack CL, Basen-Engquist K, Gritz ER (2011). Survivors at higher risk for adverse late outcomes due to psychosocial and behavioral risk factors. *Cancer Epidemiol Biomarkers Prev*, **20**, 2068-77.
- Dal Maso L, Zucchetto A, Talamini R, et al (2008). Effect of obesity and other lifestyle factors on mortality in women with breast cancer. *Int J Cancer*, **123**, 2188-94.
- Ewertz M, Gillanders S, Meyer L, Zedeler K (1991). Survival of breast cancer patients in relation to factors which affect the risk of developing breast cancer. *Int J Cancer*, **49**, 526-30.
- Flatt SW, Thomson CA, Gold EB, et al (2010). Low to moderate alcohol intake is not associated with increased mortality after breast cancer. *Cancer Epidemiol Biomarkers Prev*, **19**, 681-8.
- Franceschi S, Dal Maso L, Zucchetto A, et al (2009). Alcohol consumption and survival after breast cancer. *Cancer Epidemiol Biomarkers Prev*, **18**, 1011-2.
- Fuchs CS, Stampfer MJ, Colditz GA, et al (1995). Alcohol consumption and mortality among women. *N Engl J Med*, **332**, 1245-50.
- Harris HR, Bergkvist L, Wolk A (2012). Alcohol intake and mortality among women with invasive breast cancer. *Br J Cancer*, **106**, 592-5.
- Hauner D, Janni W, Rack B, Hauner H (2011). The effect of overweight and nutrition on prognosis in breast cancer. *Deutsches Arzteblatt*, **108**, 795-801.
- Hebert JR, Toporoff E (1989). Dietary exposures and other factors of possible prognostic significance in relation to tumour size and nodal involvement in early-stage breast cancer. *Int J Epidemiol*, **18**, 518-26.
- Hellmann SS, Thygesen LC, Tolstrup JS, Gronbaek M (2010). Modifiable risk factors and survival in women diagnosed with primary breast cancer: Results from a prospective cohort study. *Eur J Cancer Prev*, **19**, 366-73.
- Holm M, Olsen A, Christensen J, et al (2013). Pre-diagnostic alcohol consumption and breast cancer recurrence and mortality: Results from a prospective cohort with a wide range of variation in alcohol intake. *Int J Cancer*, **132**, 686-94.
- Holmes MD, Stampfer MJ, Colditz GA, et al (1999). Dietary factors and the survival of women with breast carcinoma. *Cancer*, **86**, 826-35.
- Jain MG, Ferrence RG, Rehm JT, et al (2000). Alcohol and breast cancer mortality in a cohort study. *Breast Cancer Res Treat*, **64**, 201-9.
- Kwan ML, Chen WY, Flatt SW, et al (2013). Postdiagnosis alcohol consumption and breast cancer prognosis in the after breast cancer pooling project. *Cancer Epidemiol Biomarkers Prev*, **22**, 32-41.
- Kwan ML, Kushi LH, Weltzien E, et al (2010). Alcohol consumption and breast cancer recurrence and survival among women with early-stage breast cancer: The life after cancer epidemiology study. *J Clin Oncol*, **28**, 4410-6.
- Longnecker MP (1994). Alcoholic beverage consumption in relation to risk of breast cancer: meta-analysis and review. *Cancer Causes Control*, **5**, 73-82.
- McDonald PA, Williams R, Dawkins F, Adams-Campbell LL (2002). Breast cancer survival in African American women: is alcohol consumption a prognostic indicator? *Cancer Causes Control*, **13**, 543-9.
- Newcomb PA, Kampman E, Trentham-Dietz A, et al (2013). Alcohol Consumption Before and After Breast Cancer Diagnosis: Associations With Survival From Breast Cancer, Cardiovascular Disease, and Other Causes. *J Clin Oncol*, **31**, 1939-46.
- Poli A, Marangoni F, Visioli F (2012). Alcohol consumption and breast cancer risk. *JAMA*, **307**, 666.
- Reding KW, Daling JR, Doody DR, et al (2008). Effect of prediagnostic alcohol consumption on survival after breast cancer in young women. *Cancer Epidemiol Biomarkers Prev*, **17**, 1988-96.
- Rohan TE, Hiller JE, McMichael AJ (1993). Dietary factors and survival from breast cancer. *Nutr Cancer*, **20**, 167-77.
- Saxe GA, Rock CL, Wicha MS, Schottenfeld D (1999). Diet and risk for breast cancer recurrence and survival. *Breast Cancer Res Treat*, **53**, 241-53.
- Singletary KW, Gapstur SM (2001). Alcohol and breast cancer: review of epidemiologic and experimental evidence and potential mechanisms. *JAMA*, **286**, 2143-51.
- Stroup DF, Berlin JA, Morton SC, et al (2000). Meta-analysis of observational studies in epidemiology: a proposal for reporting. Meta-analysis of Observational Studies in Epidemiology (MOOSE) group. *JAMA*, **283**, 2008-12.
- Suzuki R, Orsini N, Mignone L, et al (2008). Alcohol intake and risk of breast cancer defined by estrogen and progesterone receptor status--a meta-analysis of epidemiological studies. *Int J Cancer*, **122**, 1832-41.
- Thun MJ, Peto R, Lopez AD, et al (1997). Alcohol consumption and mortality among middle-aged and elderly U.S. adults. *N Engl J Med*, **337**, 1705-14.
- Vrieling A, Buck K, Heinz J, et al (2012). Pre-diagnostic alcohol consumption and postmenopausal breast cancer survival: A prospective patient cohort study. *Breast Cancer Res Treat*, **136**, 195-207.
- Zhang S, Folsom AR, Sellers TA, et al (1995). Better breast cancer survival for postmenopausal women who are less overweight and eat less fat. The Iowa Women's Health Study. *Cancer*, **76**, 275-83.