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The Effect of the Lifestyle, Exercise, and Nutrition (LEAN) Study on Alcohol Consumption
Among Breast Cancer Survivors

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ABSTRACT

Background Alcohol use is an established risk factor for the development of breast cancer. Additionally, there is evidence that consuming alcohol increases the risk of breast cancer recurrence among survivors. A randomized controlled weight loss intervention called the Lifestyle, Exercise, and Nutrition (LEAN) Study resulted in clinically meaningful weight loss and improvements in aspects of diet among a population of breast cancer survivors. Since the LEAN intervention included some content related to alcohol consumption, we hypothesized that the LEAN intervention would result in a reduction in alcohol consumption at 6 months.

Methods A total of 151 overweight and obese breast cancer survivors, who had been diagnosed with Stage 0 to III breast cancer in the last 5 years, had completed chemotherapy and/or radiation, and had a BMI greater than 25, were randomized in the 6-month LEAN study to either the weight loss intervention or usual care. Alcohol consumption was assessed for the analytic sample size of 123 women via a dietary questionnaire at baseline and 6-months. t-tests were used to determine change in g/day of alcohol by group and McNemar's test was used to determine change in the proportion of non-drinkers and drinkers. All statistical analyses were conducted in SAS Version 9.4.

Results Of the 123 women in the analytic sample size, the intervention group (n=73) had a mean age of 59.0 ± 7.0 years, and a mean BMI of 32.3 ± 6.1 kg/m^2, while the control group (n=50) had a mean age of 56.9 ± 7.8 years, and a mean BMI of 34.3 ± 6.8 kg/m^2. The population was mostly white and highly educated. At baseline, the mean grams of alcohol consumed per day were 8.1 ± 14.4 g/day among the intervention group, and 7.7 ± 12.2 g/day among the control group. The mean change in the grams of alcohol consumed per day was -0.5 ± 8.5 g/day among the intervention group, and $+0.2 \pm 13.2$ g/day among the control group, but this difference was

not statistically significant (p-value=0.72). The intervention group did have an increase in the proportion of non-drinkers from baseline to 6 months, but the change over time between groups of drinking category was not statistically significant.

Conclusions The LEAN intervention did not result in a significant reduction in consumption of alcohol. This may have been due to the LEAN intervention targeting dietary changes, and not focusing on alcohol. In addition, the low-drinking level in this population of breast cancer survivors at baseline may have made it difficult for the population to further reduce consumption. Given the data on alcohol and breast cancer risk and recurrence, an intervention like LEAN or one with an additional component targeting alcohol would be an important study to evaluate in a breast cancer survivor population with a higher drinking level at baseline.

TABLE OF CONTENTS

LIST OF TABLES

LIST OF FIGURES

BACKGROUND

In 2019, breast cancer was estimated to be the second leading cause of cancer-related deaths among women in the US.[1] Obesity at the time of breast cancer diagnosis is associated with an increased risk of recurrence and mortality.[2] The prevalence of obesity, defined as an individual having a body mass index (BMI) greater than or equal to 30, has reached a prevalence of 42.4% among adults in the US based on 2017-2018 National Health and Nutrition Examination Survey data.[3]

The relationship between obesity and breast-cancer associated mortality served as the rationale for the initial Lifestyle, Exercise, and Nutrition (LEAN1) study, which enrolled 100 overweight and obese breast-cancer survivors and randomly assigned them to either in-person counseling, telephone counseling, or usual care[4]. The counseling focused on how to reduce caloric intake and eat healthily, while increasing physical activity[4]. Women assigned to the LEAN intervention had significantly greater weight loss than those assigned to the usual care group, with weight loss of 6.4%, 5.4%, and 2% for the in-person intervention, telephone intervention, and the usual care group, respectively[4]. A subsequent iteration of the LEAN study (LEAN2) was conducted for which the primary endpoint was change in breast tissue biomarkers.[5] LEAN2 enrolled an additional 51 overweight and obese breast-cancer survivors that were randomly assigned to the 6-month LEAN weight loss intervention (delivered either in-person, via telephone, or a combination based on participant preference) or usual care.[5]

A dietary analysis of women enrolled in LEAN1 looked at changes in diet quality between the intervention and usual care groups over 6 months using the Healthy Eating Index-2010 (HEI-2010)[6]. There was no statistically significant difference in the average HEI score between the intervention group and the usual care group at 6 months, but women in the

intervention group reported statistically significant increases in their fruit and fiber intake compared to the usual care group.[7] There was also a statistically significant decrease in the percent of their total energy coming from total fat and saturated fat.[7]

The American Institute for Cancer Research (AICR) has put out a recommendation regarding alcohol consumption and cancer prevention. The AICR recommends against drinking any alcohol for cancer prevention due to the evidence that alcohol increases the risk of developing a number of different cancers, including breast cancer.[8] There is strong evidence that consuming even small amounts of alcohol increases the risk of developing both premenopausal and postmenopausal breast cancer,[9] and alcohol is a known carcinogen for many other cancer types.[8]

In terms of the relationship between alcohol consumption and breast cancer risk, specifically, a seminal meta-analysis found that alcohol intakes of up to one alcoholic drink a day increases breast cancer risk by 4%.[10] Researchers found that heavy alcohol consumption (three or more drinks per day) increases breast cancer risk by 40-50%.[10] In terms of mortality, another study found that 56% to 66% of alcohol-attributed cancer deaths among women were from breast cancer.[11] There is a strong relationship between alcohol consumption and developing breast cancer, but questions still remain about the risk of recurrence and mortality associated with alcohol consumption in a population of breast cancer survivors.

At present, the recommendation for all cancer survivors from the AICR is to not consume alcohol, but the data supporting the recommendation for survivors are more limited and the guidance for breast cancer survivors is largely based on the etiologic data described above. Some evidence suggests that alcohol consumption before or after diagnosis is not associated with increased mortality from breast cancer or all-cause mortality.[12] However, another study found

that regular consumption of alcohol (greater than 6 grams per day) resulted in an increased risk of breast cancer recurrence and death due to breast cancer.[13] There is also evidence that risk of recurrence associated with alcohol intake is higher in postmenopausal women and in overweight and obese women.[13] Given these studies and several others, a seminal systematic review concluded that there is evidence that consumption of alcohol results in a modest, but significant, increased risk of breast cancer recurrence.[14]

It is unclear if breast cancer survivors learn about and follow the AICR alcohol recommendation, but given the potential relationship with recurrence, and the known relationship for alcohol and breast cancer risk, it is important to see if a weight loss intervention that includes diet counseling is also effective in reducing alcohol consumption among breast cancer survivors. Therefore, we investigated changes in alcohol consumption among overweight and obese breast cancer survivors enrolled in a lifestyle intervention.

METHODS

Study Population

We evaluated change in consumption of alcohol between the intervention and control groups over the course of a 6-month lifestyle intervention utilizing data from both LEAN1 and LEAN2.[4,5] The LEAN studies were randomized controlled 6-month weight loss trials. The LEAN1 study enrolled 100 breast cancer survivors who had been diagnosed with Stage 0 to III breast cancer in the last 5 years, had completed chemotherapy and/or radiation, and had a BMI greater than 25.[4] They were randomly assigned to in-person counseling (n=33), telephone counseling (n=34), or usual care (n=33).[4] The LEAN2 study[5] enrolled 51 more breast cancer survivors meeting the same inclusion criteria, and they were randomly assigned either the weight

loss intervention group (n=26) or to the usual care group (n=25). BMI, diet, physical activity, and blood markers were measured at baseline and at 6 months for both LEAN1 and LEAN2.

Assessment of Lifestyle, Medical, and Dietary Characteristics

At baseline all women completed questionnaires related to medical history and demographics. Dietary information was collected via the Fred Hutchinson Cancer Research Center food frequency questionnaire (FFQ)[15] at both baseline and 6 months. In terms of alcohol, the FFQ queried how often individuals drank beer (all types), red wine, white or rosé wine, and liquor and mixed drinks over the last month. Both the frequency of consumption, and the portion size of each beverage consumed were recorded. To calculate the total grams of alcohol per day, the portion size was multiplied by the frequency and by the alcohol content. The value for each alcoholic beverage was divided by 365, and then summed to get total alcohol in grams per day. Additionally, for some individuals, there were small amounts of sugar alcohol derived from foods that were added to the total grams per day calculated.

Figure 1: Sample Alcohol FFQ Question[15]

BEVERAGES and ALCOHOL													
	HOW OFTEN DID YOU DRINK THESE BEVERAGES? →									AMOUNT?			
	NEVER or less than once per month	1-3 per month	1 per week	2-4 per week	5-6 per week	1 per day	2-3 per day	4-5 per day	6+ per day	Medium serving size	S	M	L
	Note that the frequency headings are different.												
Liquor and mixed drinks	○	○	○	○	○	○	○	○	○	1 shot (1½oz) or 1 mixed drink	○	○	○

Intervention Group Counseling

The LEAN intervention consisted of 11 counselling sessions with a registered dietitian. The intervention focused on reduced caloric intake and improving diet quality, increasing physical activity, and behavioral therapy techniques to promote these behavior changes.[4] The participants in the intervention group also received non-judgmental and compassionate counseling in regards to their alcohol intake and reducing their alcohol consumption. Those who did not drink were urged not to start, and those who did drink were counseled that it should be in moderation (i.e. <1 drink/day). If patterns of alcohol misuse were seen among individuals, they were referred to a website specifically geared toward helping those with alcohol abuse. The approach also included broaching the subject of alcohol from a caloric standpoint in order to reduce stigma. Additionally, individuals were given strategies to curb their alcohol consumption, such as having a non-alcoholic drink after each alcoholic drink.

Usual Care

The participants in the usual care group received brochures from the AICR on nutrition and physical activity, and a referral to the Yale Cancer Center Survivorship Clinic.[4] At the conclusion of the study, participants in the usual care group were offered a counseling session with the study dietitian, and the same educational materials as the intervention group.[4]

Statistical Analysis

Our current analytic population consisted of the breast cancer survivors enrolled in the two LEAN studies described above where alcohol data was available at both baseline and 6 months. There were 21 women who did not complete the 6 month visit, and 7 women where complete alcohol data were not available, resulting in a total sample size of 123 breast cancer survivors for our analysis. Our sample included 73 individuals in the intervention group and 50

individuals in the usual care group. No significant weight loss difference was shown for those

who received telephone versus in-person counseling,[4] so the intervention groups were combined

for analysis.

Baseline characteristics were assessed and compared between the intervention and

control groups using the χ^2 test for categorical variables and t-tests for continuous variables.

Descriptive analyses were also conducted to evaluate the type of alcohol (g/day) (i.e. beer, red

wine, white/rose wine, liquor) consumed at both baseline and 6 months.

We used t-tests to compare change in total alcohol consumption (g/day) between the

intervention and control group as well as between those who had greater than the median weight

loss, and those who had less than the median weight loss within only the intervention group.

We also conducted an additional analysis in which we classified women as non-drinkers

and drinkers. Some alcohol in the FFQ was derived from other sources, such as foods with sugar

alcohols, like vanilla extract. Therefore, a non-drinker was defined as an individual who had a

baseline alcohol consumption that was less than the maximum alcohol consumption for

individuals who had an alcohol frequency of 0 for each alcohol type – which equated to an

individual only having alcohol from food sources. The cutoff for being defined as a non-drinker

was having an alcohol consumption ≤ 0.102 g/day, which is much lower than a standard

medium drink (14g of alcohol). Otherwise, individuals were defined as drinkers. Differences

between the intervention and usual care groups in the change in drinking category (drinker; non-

drinker) between baseline and 6-months was assessed via the McNemar's Test. Differences

between the intervention and usual care groups using another drinking cut-point (<1 drink/day;

>1 drink/day) between baseline and 6-months was also assessed via the McNemar's Test.

Additionally, generalized estimating equation (GEE) models were used to compare these

changes in drinking categories by group over time. All analyses were conducted using SAS

Version 9.4 and findings with a p-value less than 0.05 were considered statistically significant.

RESULTS

Among these 123 breast cancer survivors, the mean age was 59.0 ± 7.0 (SD) years for the

intervention group (n=73) and 56.9 ± 7.8 years for the control group (n=50) (Table 1). At

baseline, the intervention group had a mean BMI of 32.3 ± 6.1 kg/m^2 and the control group had a

mean BMI of 34.3 ± 6.8 kg/m^2. The population was mostly white and highly educated. There

were no statistically significant differences in baseline characteristics between the intervention

and control groups.

For individuals in the intervention group, the majority of alcohol at baseline came from

red wine (38.8%) and white/rose wine (38.8%). This was also the case for individuals in the

control group, who got 51.9% of their alcohol from red wine and 29.8% of their alcohol from

white/rose wine at baseline. At 6 months, these proportions remained relatively similar with the

majority of individuals in both the intervention and control groups deriving most of their alcohol

from red wine and white/rose wine.

At baseline, the mean grams of alcohol consumed per day were 8.1 ± 14.4 g/day among

the intervention group, and 7.7 ± 12.2 g/day among the control group. The mean change in the

grams of alcohol consumed per day was -0.5 ± 8.5 g/day among the intervention group, and +0.2

± 13.2 g/day among the control group, but this difference was not statistically significant (p-

value=0.72) (Table 2). At baseline, the intervention group consisted of 16.4% non-drinkers and

83.6% drinkers, and the control group consisted of 26% non-drinkers and 74% drinkers (Table

3). Within the intervention group, there were a greater proportion of drinkers who moved to the

non-drinker category between baseline and 6 months, than there was among the control group. In the intervention group, the proportion of non-drinkers increased by 8.2%, which approached statistical significance (p=0.06). In the control group, the proportion of non-drinkers increased by 4%, and was not significant (p=0.57). However, the comparison of these changes over time by group revealed no statistically significant differences (p=0.45). Additionally, there was not a statistically significant change in the proportion of individuals in the <1 drink/day and the >1 drink/day categories from baseline to 6 months by group (Table 4).

Within the intervention group, those who had a greater-than-median weight loss (>4.6kg) had a reduction in alcohol consumption of -1.0 ± 3.7 grams/day, while those with less-than-median weight loss (<4.6kg) had no change in alcohol consumption (0.0 ± 11.3 grams/day) (Table 5). The between group difference in change in alcohol at 6 months was not statistically significant (p=0.60).

DISCUSSION

We did not find a statistically significant difference in change in alcohol consumption from baseline to 6 months between the intervention and control groups. Nor was there a difference by intervention group in the proportion of women who changed drinking status over the course of the study. Thus our results did not indicate that the LEAN intervention resulted in a significant reduction of alcohol consumption.

The overall low alcohol consumption in our population is an important consideration when interpreting our findings. A study with a similar population of breast cancer patients, but a much larger sample size (n=9,329), had a total alcohol consumption of 5.79 ± 11.15 g/day[16]. This is a similar range to the alcohol consumption of all of the LEAN participants (intervention and

control groups), who had a total alcohol consumption of 7.96 ± 13.5 g/day. However, these averages are much lower than the 14 g/day of alcohol that constitutes 1 drink. The LEAN intervention language regarding alcohol counseled individuals who did not consume alcohol to not begin, and counseled those who did consume alcohol to limit their consumption to <1 drinks/day. However, as 79.4% of individuals in the intervention group already had an alcohol level that was <1 drink/day at baseline, the guidance regarding alcohol may not have had a large impact in the LEAN study population. Also, the LEAN intervention targeted overall dietary changes and was not solely focused on women reducing alcohol intake.

Strengths of this analysis were the randomized longitudinal nature of the data, and the LEAN study's high proportion of overweight/obese and postmenopausal individuals, who have a higher alcohol-attributed risk of breast cancer recurrence.[13] The findings are generalizable to a population of non-Hispanic, white breast cancer survivors with similar alcohol intake, but due to the specific characteristics of this population, they are not generalizable to populations not meeting these criteria. As mentioned earlier, our study population had low levels of alcohol consumption, so it is possible the LEAN intervention would be more effective in a population of breast cancer survivors that had a higher drinking level to begin with. We also had a limited sample size. The small sample size combined with the low level of alcohol consumption greatly limited the alcohol categorizations we could use in our analysis.

Larger studies are needed to establish an effective intervention that curbs alcohol consumption among breast cancer survivors. There is an established need for these types of interventions because of the evidence for increased risk of breast cancer recurrence due to alcohol consumption.[13] An effective evidence-based alcohol intervention for breast cancer survivors is urgently needed to help mitigate risk of recurrence due to alcohol.

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Table 1: Baseline Characteristics of Participants in the LEAN Study (N=123)

Characteristic	Intervention N=73 N (%)[a] Or Mean ± SD	Control N=50 N (%)[a] Or Mean ± SD	p-value[b]
Age (y)	59.0 ± 7.0	56.9 ±7.8	0.12
BMI (kg/m^2)	32.3 ± 6.1	34.3 ± 6.8	0.09
% Obese	37 (50.6)	34 (68.0)	0.06
Race/Ethnicity			0.29
Black/African American	4 (5.5)	3 (6.0)	
White	68 (93.2)	44 (88.0)	
Other	0 (0)	2 (4.0)	
Refused to Answer	1 (1.4)	0 (0)	
Education			0.43
High school/GED/Vocational	8 (11.0)	8 (16)	
Bachelor/Associate Degree	39 (53.4)	21 (42.0)	
Graduate Degree	26 (35.6)	21 (42.0)	
Marital status			0.33
Not Married	23 (31.5)	20 (40.0)	
Married/Living as Married	50 (68.5)	30 (60.0)	
Received Chemotherapy	39 (53.4)	24 (0.48)	0.55
Current Smoker	1 (1.4)	0 (0)	0.41
Stage of Cancer at Diagnosis			0.94
0-I	48 (65.8)	33 (66.0)	
II-III	24 (32.9)	16 (32.0)	

[a]May not sum to total due to missing values
[b]χ^2 test

Table 2: Change in Total Alcohol (grams/day) Consumption in Intervention and Control From Baseline to 6 Months

Alcohol Mean ± SD (g/day)	LEAN Intervention N=73			Control N=50		
	Baseline	6 Months	Change in Alcohol	Baseline	6 Months	Change in Alcohol
Total Alcohol	8.1 ± 14.4	7.6 ± 17.2	-0.5 ±8.5	7.7 ± 12.2	7.9 ± 19.1	0.2 ± 13.2
P-value[*]			0.72			

*t-test comparing change in alcohol

Table 3: Changes in Drinking Status From Baseline to 6 Months

Alcohol Level	LEAN Intervention N=73			Control N=50		
	Baseline	6 Months	Change in %	Baseline	6 Months	Change in %
Non-Drinker	12 (16.4)	18 (24.6)	+8.2%	13 (26.0)	15 (30.0)	+4%
Drinker	61 (83.6)	55 (75.3)	-8.2%	37 (74.0)	35 (70.0)	-4%
p-value Within Groups[a]		p=0.06			p=0.57	
p-value By Group Over Time[b]			p=0.45			

[a]McNemar's Test
[b]GEE Model, Interaction

Table 4: Changes in Alcohol Level From Baseline to 6 Months

Alcohol Level	LEAN Intervention N=73			Control N=50		
	Baseline	6 Months	Change in %	Baseline	6 Months	Change in %
<1 Drink/Day	58 (79.4)	61 (83.6)	+4.2%	40 (80.0)	43 (86.0)	+6%
>1 Drink/Day	15 (20.6)	12 (16.4)	-4.2%	10 (20.0)	7 (14.0)	-6%
p-value Within Groups[a]		p=0.18			p=0.08	
p-value By Group Over Time[b]			p=0.62			

[a]McNemar's Test
[b]GEE Model, Interaction

Table 5: Change in Total Alcohol From Baseline to 6 Months By Weight Loss in the Intervention Group (N=73)

	Weight Loss > Median (4.60kg) N=36 Mean ± SD (g/day)	Weight Loss < Median (4.60kg) N=37 Mean ± SD (g/day)	P-value*
Change in Total Alcohol	-1.0 ± 3.7	0.0 ± 11.3	0.60

*t-test