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Light Alcohol Intake Increases Risk for Breast Cancer CME

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Clinical Context

Since the early 1980s, an association has been shown between alcohol consumption and risk for breast cancer in case-control studies. The risk from light alcohol consumption is not well known.

This is an epidemiological review of other studies to examine the association between breast cancer risk and light and heavy alcohol consumption, and the mechanisms that may underlie the association.

Study Synopsis and Perspective

Women should not exceed 1 drink of alcohol a day, concludes a new meta-analysis of 113 studies of light drinking and breast cancer. However, even such light drinking is a little risky, say the authors.

"A significant increase of the order of 4% in the risk of breast cancer is already present at intakes of up to one alcoholic drink/day," write the authors, led by Helmut K. Seitz, PhD, from the Centre of Alcohol Research at the University of Heidelberg in Germany.

This comment refers to the finding that the relative risk (RR) for breast cancer in light drinkers versus nondrinkers in the 113 studies was 1.04 (95% confidence interval [CI], 1.02 - 1.07). This is a "modest but significant association between light drinking and breast cancer," the authors write in their paper, published online March 28 in *Alcohol and Alcoholism*.

In other words, drink at your own risk, they suggest.

The definition of light drinking in the new analysis was no more than 12.5 g of ethanol per day or 1 drink per day or less.

For women at elevated risk for breast cancer, the authors are clearer and more authoritative in their advice: Such women "should avoid alcohol or consume alcohol occasionally only."

Overall, up to 1% to 2% of breast cancers in Europe and North America are "attributable to light drinking alone," the authors estimate.

Just exactly how alcohol increases breast cancer risk is not certain, said an expert not associated with the study.

"The new article focuses on the effects of light drinking and shows that even light drinking can increase breast cancer risk," Béatrice Lauby-Secretan, PhD, from the IARC in Lyon, France, told Medscape Medical News via email.

But she continued: "The mechanisms involved are not clearly established and can be diverse."

"Synergistic effects with other carcinogenic agents must be evaluated" because alcohol drinking — even light drinking — "can be very prevalent in certain populations and countries," added Dr. Lauby-Secretan, who was the lead author of a review on alcohol and general cancer risk published in 2009.

The conclusion of the new meta-analysis echoes the conclusion of an original study published in 2011.

"I tell my patients to limit consumption to a few drinks per week or less, which is what I also practice," lead of author of that study, Wendy Y. Chen, MD, MPH, told Medscape Medical News at the time. "It is important to remember that we were looking at cumulative average alcohol intake over a long period of time," she said about the 28-year study period.

In Dr. Chen and colleagues' study, which used data from the large Nurses' Health Study, the regular consumption of a light amount of alcohol — 3 to 6 glasses of wine per week — over a long period of time increased a woman's risk for invasive breast cancer by a small but statistically significant amount (*JAMA*. 2011;306:1884-1890).

What the Meta-Analysis Looked at

The authors of the new meta-analysis say it is not known whether any amount of alcohol intake is safe. "It is still unclear whether there is any threshold in intake below which no effect of alcohol on breast cancer is evident," they write.

The authors found 113 papers reporting breast cancer risk estimates for light drinkers.

The analysis included 44,552 breast cancer cases in the reference category of nondrinkers and 77,539 cases in the light drinkers' category. Case-control was the most common study design (64% of studies); 90% of the included studies were from North America or Europe.

About one third of the studies (36%) were adjusted for the main breast cancer risk factors (age, family history, parity, menopausal status, oral contraceptive/hormonal replacement therapy use).

Of note, the results did not "appreciably change" from those of the overall analysis when only estimates adjusted for the main risk factors were considered (pooled RR, 1.03 [95% CI, 1.00 - 1.07]).

The authors also did an epidemiologic review — but not a meta-analysis — of studies that included heavy alcohol consumption.

Heavy alcohol consumption, defined as 3 or more drinks per day, is associated with a 40% to 50% increased relative risk compared with not drinking at all, they report. "This translates into up to 5% of breast cancers attributable to alcohol in northern Europe and North America for a total of approximately 50,000 alcohol-attributable cases of breast cancer worldwide," they write.

The new paper also commented on biological mechanisms that may be at work in this relationship. They cite the often-mentioned findings that alcohol increases estrogen levels, and estrogens may exert a carcinogenic effect on breast tissue.

Other potential mechanisms may include the effects of acetaldehyde, oxidative stress, epigenetic changes, and "decreased retinoic acid concentrations associated with an altered cell cycle," they suggest.

The analysis was funded by the Italian Association for Cancer Research (AIRC), the Dietmar Hopp Foundation, and the Manfred Lautenschläger Foundation, Heidelberg, Germany. The authors have disclosed no relevant financial relationships.

Alcohol Alcoholism. Published online March 29, 2012. Abstract

Study Highlights

A literature search was conducted in MEDLINE, ISI Web of Science, and EMBASE on epidemiological studies performed before November 2011.

Included were case-control or cohort studies with reports that included odds ratios, hazard ratios, or RRs.

A pooled RR was constructed for light drinkers vs nondrinkers, using a random effects model.

Heterogeneity among studies was assessed.

113 papers were included, with 44,552 cases of nondrinkers and 77,539 cases of light drinkers.

The most common study design was case-control (64%).

51% of studies were from North America, 38% from Europe, 6% from Asia, and 10% from other regions.

There was substantial heterogeneity among the studies.

The summary RR for light drinkers vs nondrinkers was 1.04, and this remained after adjustment for other risk factors.

In the available studies that examined heavy drinking, defined as 3 or more drinks daily for women, an increased risk for breast cancer was seen.

In 1 collaborative reanalysis, the RRs were 1.32 for alcohol consumption of 35 to 44 g/day and 1.46 for consumption of more than 44 g daily compared with nondrinkers.

The results from this and other reviews suggest a consistent increase of 40% to 50% in risk for breast cancer with heavy drinking in women.

The RR for breast cancer increased by 7.1% for each additional 10 g/day of alcohol intake.

In 1 report, the RR was 1.5 at consumption of 40 g/day and increased further for higher levels of intake.

In another study, the increase in risk for each additional 10 g/day varied from 10% to 13%.

1 study showed a linear association between dose of alcohol and breast cancer risk.

Some studies examined the association between drinking and estrogen receptor (ER) and progesterone receptor (PR) status of the breast cancer.

Studies indicated that alcohol consumption increased the risk for all ER+ cancers by 27%, with a 14% risk for all ER- breast cancers for the highest vs lowest level of alcohol drinking.

Based on 15 studies, the RR was 1.22 for ER+/PR+ cancers, 1.28 for ER+/PR- cancers, 1.31 for ER-/PR+ cancers, and 1.10 for ER-/PR- cancers.

Later studies supported a stronger relationship between heavy drinking and ER+/PR+ cancers.

Because alcohol ingestion increases estrogen levels and a carcinogenic effect has been reported for estrogen on breast tissue, estrogen is 1 of the potential mediators of breast cancer risk.

Acetaldehyde, a toxic metabolite of alcohol, and oxidative stress are also cited as potential mechanisms of carcinogenesis.

The authors conclude that alcohol consumption is causally related to risk for breast cancer, with a stronger association for ER+ cancers.

A small increased risk of 4% is present, even for intake of 1 drink a day, and heavy consumption of 3 or more drinks a day increases risk by 40% to 50%.

There is thus no safe threshold for alcohol and breast cancer risk.

The authors estimate that 5% of breast cancers in Europe and North America could be attributed to alcohol intake (for a total of 50,000 attributable cases). That percentage is 10% in Italy and France, where drinking rates are higher.

Up to 1% to 2% of cases in North America are attributed to drinking alone.

The authors advise that healthy women should not exceed 1 drink of alcohol a day, whereas women with breast cancer risk factors should avoid alcohol or consume it only occasionally.

Clinical Implications

In women, light alcohol consumption of 1 drink a day is associated with a 4% increased risk for breast cancer.

In women, heavy alcohol consumption is associated with a 40% to 50% increased risk in breast cancer, with higher risk for ER+ cancers.

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