Citrus Fruit Consumption May Be Associated With Increased Melanoma Risk

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ASCO Perspective
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“This study adds to the growing discussion around food and cancer risk. While the findings are intriguing, it’s far too soon to recommend any broad changes to grapefruit or orange consumption. Until conclusive data are available, we should continue to be cautious about protecting our skin from sun exposure.”

A new analysis of dietary patterns among more than 100,000 Americans suggests that frequent consumption of citrus — namely whole grapefruit and orange juice — may be associated with an increased risk of melanoma. Melanoma risk was 36% higher in people who consumed citrus fruit or juice at least 1.6 times daily compared to those who consumed them less than twice per week.

Consumption of grapefruit and oranges was not associated with an increased risk for any other non-skin cancers. This analysis, along with an accompanying editorial, “Dietary Advice for Melanoma: Not Ready for Prime Time,” was published online today in the *Journal of Clinical Oncology*.

The study researchers argue that the apparent link between melanoma and citrus fruit consumption may be due to high levels of substances called furocoumarins found in citrus fruits. Prior research showed that furocoumarins make the skin more sensitive to sunlight, including to melanoma-causing ultraviolet (UV) rays.

“While our findings suggest that people who consume large amounts of whole grapefruit or orange
juice may be at increased risk for melanoma, we need much more research before any concrete recommendations can be made,” said lead study author Shaowei Wu, PhD, a postdoctoral research fellow at the Department of Dermatology, the Warren Alpert Medical School of Brown University in Providence, Rhode Island. “At this time, we don’t advise that people cut back on citrus but those who consume a lot of grapefruit and/or orange juice should be particularly careful to avoid prolonged sun exposure.”

The analysis included data on 63,810 women in the Nurses’ Health Study (1984 - 2010) and 41,622 men in the Health Professionals Follow-Up Study (1986 – 2010). Questionnaires were mailed at various intervals to assess dietary intake (at least every four years) and collect information on medical history and lifestyle factors (every two years). For the purposes of the survey, a serving of citrus fruit was defined as the equivalent of half of a grapefruit, one orange, or a small (6 oz) glass of grapefruit or orange juice. People with a history of cancer were excluded from the analysis.

Over a follow-up period of up to 26 years, 1,840 (1.7%) study participants were diagnosed with melanoma. Higher overall citrus fruit consumption (the total number of servings of whole grapefruit, whole oranges, and juices from those fruits) was associated with increased risk of malignant melanoma in both men and women. The association was strongest for grapefruit, followed by orange juice. Conversely, and interestingly, consuming either grapefruit juice or whole oranges was not associated with melanoma risk.

Furthermore, the association between eating whole grapefruit and melanoma was independent of age and lifestyle factors, such as physical activity, cigarette smoking, alcohol and coffee intake, and use of vitamin C supplements. However, the association was more apparent among those who were more susceptible to sunburn as a child or adolescent and those who spent more time in direct sunlight.

The authors speculate that the levels of furocoumarins may be higher in whole fruit than in processed juices. They suspect that the significant effect of orange juice on melanoma risk can be explained by its consumption level, which was several times higher than any other citrus product. There was no significant association between other furocoumarin-rich foods, such as carrots and celery, and melanoma risk. “People often cook these vegetables, and heat treatment reduces the amount of furocoumarins in food,” said Dr. Wu. Further research into furocoumarin levels in citrus fruit and juice and participants’ blood samples is planned to confirm these hypotheses.

According to the authors, this is the first large study to investigate the link between dietary furocoumarin and melanoma risk. Prior research has shown that tanning lotions containing psoralens (a group of naturally occurring furocoumarins) increase the risk for melanoma. Long-
term use of oral psoralen as part of therapy for severe psoriasis can also increase risk of melanoma.

In an accompanying editorial, Marianne Berwick, PhD, MPH, professor of the Department of Internal Medicine and Dermatology at the University of New Mexico, acknowledges that this study was quite large and data were collected prospectively. However, she identified several important limitations of the study worth noting. This includes a study population of health professionals, which is not representative of the general population.

According to Dr. Berwick, this is a potentially important study because citrus consumption is widely promoted as an important part of the diet. Citrus has demonstrated benefit for coronary heart disease, cancer prevention, and overall health effects. “At this point in time, a public overreaction leading to avoidance of citrus products is to be avoided,” said Dr. Berwick. “For people who would be considered at high risk, the best course might be to advise individuals to use multiple sources of fruit and juice in the diet and to use sun protection, particularly if one is sun sensitive. There is clearly a need for replication of the study findings in a different population prior to modifying current dietary advice to the public.”

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Helpful Links from Cancer.Net, ASCO’s cancer information website:

- Guide to Melanoma
- Understanding Cancer Risk

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