JNCI Cancer Spectrum (2017) 1(1): pkx005

doi: 10.1093/jncics/pkx005
First published online September 21, 2017
Editorial

EDITORIAL

Survival Benefits of Smoking Cessation After Breast Cancer Diagnosis

Michael N. Passarelli, Polly A. Newcomb

Affiliations of authors: Department of Epidemiology, Geisel School of Medicine, Dartmouth College, Hanover, NH (MNP); Cancer Prevention Program, Fred Hutchinson Cancer Research Center, Seattle, WA (PAN); Department of Epidemiology, School of Public Health, University of Washington, Seattle, WA (PAN).

Correspondence to: Michael N. Passarelli, PhD, Department of Epidemiology, Geisel School of Medicine at Dartmouth, Dartmouth-Hitchcock Medical Center, One Medical Center Dr, HB 7927, Lebanon, NH 03756 (e-mail: michael.n.passarelli@dartmouth.edu).

We now recognize that cigarette smokers have about a 10% increased risk of developing breast cancer over never smokers, albeit far from the 600% to 800%, or more, increased risk for cancers of organs in direct contact with carcinogens in smoke such as lung, head and neck, bladder, and others (1). For established smoking-related malignancies, continued smoking after diagnosis is associated with increased risk of disease progression and death (2), but much less is known about postdiagnosis smoking and outcomes for cancers, such as breast, for which smoking is not a particularly strong risk factor. Postdiagnosis assessments of smoking habits are frequently missed, both in the clinic (3) and as part of follow-up in longitudinal research studies (4), making it a challenge to estimate any association with change in smoking behavior.

Many breast cancer patients who smoke at the time of their diagnosis deny that the habit was a cause of their own cancer, but about 60% of these women acknowledge that smoking may be a cause of breast cancer for some women (5). Regardless of their beliefs on the causes of their own malignancy, it is unclear whether a similar proportion would deny that continuing to smoke is a cause of complications and earlier death from metastatic breast cancer, given that nearly all oncology care providers agree that smoking impacts outcomes (3). About one-third of women with breast cancer who smoke successfully quit within two years following diagnosis (6). This exceeds the proportion of cancer-free women who quit during the same period (6), but still falls short of quit rates reported for patients with lung and head and neck cancers (7).

The accompanying article by Parada et al. (8) describes an analysis from the Long Island Breast Cancer Study Project (LIBCSP), which followed 1508 women with breast cancer recruited from Nassau and Suffolk counties in New York between 1996 and 1997, and measured smoking at diagnosis and again an average of 5.5 years after diagnosis. Consistent with age-standardized smoking prevalence estimates for American women at the time (9), the overall prevalence of current smoking at diagnosis in LIBSCP was about 19%, with about half of those at-diagnosis smokers reporting they had quit after diagnosis (8% of the total were still smoking at the follow-up assessment).

The study found that continuing to smoke after breast cancer results in poorer overall survival relative to women who quit upon receiving their diagnosis. The increased risk of death from any cause for continued smokers should not come as a surprise given the litany of recognized adverse outcomes of smoking, including increased risk of wound infections from mastectomy and breast conserving surgery (10), respiratory and cardiovascular comorbidities (11), second primary malignancies (12), and poorer overall quality of life (13). A disease-specific association, on the other hand, may be indicative of more direct effects on tumor burden, including potentially poorer response to endocrine therapy (14) or subsequent contralateral breast cancer (15).

Parada et al. estimated an adjusted hazard ratio (HR) for breast cancer–specific survival comparing women who continued to smoke after diagnosis with never smokers of 1.60 (95% confidence interval [CI] = 0.79 to 3.23). Although imprecise because only 125 of 426 (29%) total deaths were from breast cancer, the magnitude of this association is very similar to that previously reported by the Collaborative Women's Longevity Study (CWLS) (16). A fixed-effect meta-analysis of LIBCSP and CWLS would put this HR estimate at 1.69 (95% CI = 1.18 to 2.41), without exclusion of women with in situ carcinoma from LIBCSP. Also consistent between the two studies is the association for breast cancer–specific survival comparing women who quit at the time of diagnosis with never smokers, similarly combined as 1.10 (95% CI = 0.73 to 1.64). Dividing these estimates suggests approximately one-third lower risk of death from breast cancer for women who quit upon receiving news of their

Received: July 13, 2017; **Accepted:** July 19, 2017

diagnosis compared with those who continued to smoke (HR = 0.65, 95% CI = 0.38 to 1.11). A disease-specific survival improvement of this magnitude, albeit not statistically significant here, should be considered encouraging news for women contemplating the value of cessation after learning of their diagnosis.

Extending results from CWLS, the LIBCSP cohort also included 235 (16%) women diagnosed with in situ carcinoma at study enrollment, a group for which it is expected that less than 5% will develop fatal breast cancer (17). Exclusion of these women did not alter the primary study conclusions. Whether smoking cessation at the time of diagnosis of preinvasive disease could prevent subsequent fatal breast cancer should be confirmed in future studies. Such studies would need to be very large, but may be feasible as smoking quit rates following a diagnosis of in situ lesions appear to mirror those following a diagnosis of invasive breast cancer (18).

Unfortunately, cessation support for breast cancer survivors who are unwilling or unable to stop smoking has proved challenging. A clinical trial of physician-based smoking cessation guidelines, which included some women with advanced-stage breast cancer, did not result in a statistically significant change in quit rates six or 12 months postintervention (19). Specific to breast cancer, a clinical trial in Denmark of a one-time personalized cessation support and nicotine replacement therapy within a week prior to breast cancer surgery did not reduce postoperative complications relative to standard care (20). These studies reinforce the notion that new behavioral or pharmacological approaches to smoking cessation will require intense, long-term, continual patient support.

Prospective survival cohorts such as LIBSCP help quantify the mortality burden faced by active smokers with malignancies not traditionally thought to be smoking related. Evidence that smoking cessation benefits even those who quit soon after diagnosis should serve as continued motivation for breast cancer survivors to pursue positive health behavior changes.

References

1. US Department of Health and Human Services. *The Health Consequences of Smoking—50 Years of Progress: A Report of the Surgeon General*. Atlanta, GA: US Department of Health and Human Services, Centers for Disease Control and Prevention, National Center for Chronic Disease Prevention and Health Promotion, Office on Smoking and Health; 2014.
2. Parsons A, Daley A, Begh R, Aveyard P. Influence of smoking cessation after diagnosis of early stage lung cancer on prognosis: Systematic review of observational studies with meta-analysis. *BMJ*. 2010;340:b5569.
3. Warren GW, Marshall JR, Cummings KM, et al. Addressing tobacco use in patients with cancer: A survey of American Society of Clinical Oncology members. *J Oncol Pract*. 2013;9(5):258–262.
4. Land SR. Methodologic barriers to addressing critical questions about tobacco and cancer prognosis. *J Clin Oncol*. 2012;30(17):2030–2032.
5. Wold KS, Byers T, Crane LA, Ahnen D. What do cancer survivors believe causes cancer? (United States). *Cancer Causes Control*. 2005;16(2):115–123.
6. Westmaas JL, Newton CC, Stevens VL, Flanders WD, Gapstur SM, Jacobs EJ. Does a recent cancer diagnosis predict smoking cessation? An analysis from a large prospective US cohort. *J Clin Oncol*. 2015;33(15):1647–1652.
7. Gritz ER, Fingeret MC, Vidrine DJ, Lazev AB, Mehta NV, Reece GP. Successes and failures of the teachable moment: Smoking cessation in cancer patients. *Cancer*. 2006;106(1):17–27.
8. Parada H, Bradshaw PT, Steck SE, et al. Postdiagnosis changes in cigarette smoking and survival following breast cancer. *JNCI Cancer Spectrum*. 2017;1(1): 10.1093/jncics/pkx001.
9. Ng M, Freeman MK, Fleming TD, et al. Smoking prevalence and cigarette consumption in 187 countries, 1980-2012. *JAMA*. 2014;311(2):183–192.
10. Sorensen LT, Horby J, Friis E, Pilsgaard B, Jorgensen T. Smoking as a risk factor for wound healing and infection in breast cancer surgery. *Eur J Surg Oncol*. 2002;28(8):815–820.
11. Hooning MJ, Botma A, Aleman BM, et al. Long-term risk of cardiovascular disease in 10-year survivors of breast cancer. *J Natl Cancer Inst*. 2007;99(5): 365–375.
12. Trentham-Dietz A, Newcomb PA, Nichols HB, Hampton JM. Breast cancer risk factors and second primary malignancies among women with breast cancer. *Breast Cancer Res Treat*. 2007;105(2):195–207.
13. Jang S, Prizment A, Haddad T, Robien K, Lazovich D. Smoking and quality of life among female survivors of breast, colorectal and endometrial cancers in a prospective cohort study. *J Cancer Surviv*. 2011;5(2):115–122.
14. Persson M, Simonsson M, Markkula A, Rose C, Ingvar C, Jernstrom H. Impacts of smoking on endocrine treatment response in a prospective breast cancer cohort. *Br J Cancer*. 2016;115(3):382–390.
15. Li CI, Daling JR, Porter PL, Tang MT, Malone KE. Relationship between potentially modifiable lifestyle factors and risk of second primary contralateral breast cancer among women diagnosed with estrogen receptor-positive invasive breast cancer. *J Clin Oncol*. 2009;27(32):5312–5318.
16. Passarelli MN, Newcomb PA, Hampton JM, et al. Cigarette smoking before and after breast cancer diagnosis: Mortality from breast cancer and smoking-related diseases. *J Clin Oncol*. 2016;34(12):1315–1322.
17. Schairer C, Mink PJ, Carroll L, Devesa SS. Probabilities of death from breast cancer and other causes among female breast cancer patients. *J Natl Cancer Inst*. 2004;96(17):1311–1321.
18. Sprague BL, Trentham-Dietz A, Nichols HB, Hampton JM, Newcomb PA. Change in lifestyle behaviors and medication use after a diagnosis of ductal carcinoma in situ. *Breast Cancer Res Treat*. 2010;124(2):487–495.
19. Schnoll RA, Zhang B, Rue M, et al. Brief physician-initiated quit-smoking strategies for clinical oncology settings: A trial coordinated by the Eastern Cooperative Oncology Group. *J Clin Oncol*. 2003;21(2):355–365.
20. Thomsen T, Tonnesen H, Okholm M, et al. Brief smoking cessation intervention in relation to breast cancer surgery: A randomized controlled trial. *Nicotine Tob Res*. 2010;12(11):1118–1124.