



Smoking and Melanoma Outcomes—Another Reason to Quit

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Do you need another reason to encourage your patients to stop smoking? Smoking increases the risk of a myriad of diseases and is associated with cancer incidence and mortality. Smoking increases the risk of dying of cancer of the lung, oropharynx, pancreas, bladder, and cervix, to name just a few.¹ Jackson and colleagues² found that a substantial proportion of patients (1077 of 6279 patients [17.2%]) who presented with clinically localized melanoma were current smokers. Perhaps this is an ideal moment to recommend against smoking because the diagnosis of melanoma, in my experience, has often been a teachable moment. Many patients dramatically alter their sun exposure habits, returning for follow-up visits without a trace of sunburn or tan (even in the summer months), despite a lack of evidence that modification of this behavior is associated with long-term outcomes for melanoma. While it is certainly not as addictive as nicotine, UV exposure shares features of addiction as well.³ Jackson and colleagues² use the data from 2 large, well-conducted clinical trials in patients with clinically localized melanoma to determine the association of smoking with melanoma-specific survival (MSS) and melanoma-associated death (MAD). The Multicenter Selective Lymphadenectomy Trials (MSLT-I and MSLT-II) provided the data and were conducted to determine whether sentinel lymph node (SLN) biopsy was associated with improved MSS compared with wide excision and observation (MSLT-I)⁴ and whether completion node dissection in patients with SLN-positive melanoma was associated with MSS advantage compared with nodal basin observation (MSLT-II).⁵ These 2 trials were practice-changing (neither study found an association) and provided the foundation for the current treatment of patients with clinically localized melanoma or microscopic regional nodal disease.

Although cigarette smoking has been associated with a lower incidence of melanoma, the association of smoking with melanoma survival has not been determined.⁶ The Jackson et al study² provides a perfect opportunity to ask this question with a large prospectively collected database of patients. Indeed, over 6000 patients comprised the study group and the median (IQR) follow-up was 78.4 (30.5-119.6) months.

The investigators found that current smokers had an increased risk of MAD compared with former or nonsmokers (hazard ratio [HR], 1.48; 95% CI, 1.26-1.75; $P < .001$).² The analysis controlled for cofounders such as age, Breslow thickness, ulceration, primary site, and SLN status. The negative association of smoking with MSS was greatest for patients with SLN-negative melanoma (HR, 1.85; 95% CI, 1.35-2.52).²

Further supporting the association of smoking with MAD was that the amount of smoking reported was associated with increased MAD risk, with an HR of 1.63 (95% CI, 1.33-2.01) for heavy smokers and 1.48 (95% CI, 1.13-1.93) for moderate smokers.² This study confirms a report by Mattila and colleagues,⁷ who identified an increased risk of melanoma death in 1359 patients treated between 2005 and 2019 in southern Finland. In this population-based study,⁷ current smokers had an increased risk of melanoma death (HR, 1.81; 95% CI, 1.27-2.58) when compared with nonsmokers.

The reason for the association of smoking with increased risk of MAD is unclear. It is well known that smoking diminishes cutaneous blood flow, potentially leading to promotion of tumor growth due to hypoxia, as the investigators point out.² Smoking has additional negative outcomes on tumor containment and immunity, and further studies are needed to elucidate the specific factors that contribute to poor outcomes.

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We did not really need another reason to recommend against smoking, but here we have it. Congratulations to the investigators² for providing an answer to the commonly asked query, "Is there anything I can do to decrease my risk of melanoma recurrence?"

ARTICLE INFORMATION

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REFERENCES

1. Gandini S, Botteri E, Iodice S, et al. Tobacco smoking and cancer: a meta-analysis. *Int J Cancer*. 2008;122(1):155-164. doi:[10.1002/ijc.23033](https://doi.org/10.1002/ijc.23033)
2. Jackson KM, Jones PC, Fluke LM, et al. Smoking status and survival in patients with early-stage primary cutaneous melanoma. *JAMA Netw Open*. 2024;7(2):e2354751. doi:[10.1001/jamanetworkopen.2023.54751](https://doi.org/10.1001/jamanetworkopen.2023.54751)
3. Nguyen NT, Fisher DE. MITF and UV responses in skin: from pigmentation to addiction. *Pigment Cell Melanoma Res*. 2019;32(2):224-236. doi:[10.1111/pcmr.12726](https://doi.org/10.1111/pcmr.12726)
4. Faries MB, Thompson JF, Cochran AJ, et al. Completion dissection or observation for sentinel-node metastasis in melanoma. *N Engl J Med*. 2017;376(23):2211-2222. doi:[10.1056/NEJMoa1613210](https://doi.org/10.1056/NEJMoa1613210)
5. Morton DL, Thompson JF, Cochran AJ, et al; MSLT Group. Final trial report of sentinel-node biopsy versus nodal observation in melanoma. *N Engl J Med*. 2014;370(7):599-609. doi:[10.1056/NEJMoa1310460](https://doi.org/10.1056/NEJMoa1310460)
6. DeLancey JO, Hannan LM, Gapstur SM, Thun MJ. Cigarette smoking and the risk of incident and fatal melanoma in a large prospective cohort study. *Cancer Causes Control*. 2011;22(6):937-942. doi:[10.1007/s10552-011-9766-z](https://doi.org/10.1007/s10552-011-9766-z)
7. Mattila K, Vihinen H, Karlsson A, Minn H, Vihinen P, Heervä E. Smoking is an independent marker of poor prognosis in cutaneous melanoma. *Acta Derm Venereol*. 2023;103:adv00860. doi:[10.2340/actadv.103.3209](https://doi.org/10.2340/actadv.103.3209)