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Use of Positron Emission Tomography Imaging: Another Nonbiological Source of Racial Disparities in US Cancer Care

Aaron P. Mitchell, MD, MPH, Peter B. Bach, MD, MAPP

Department of Epidemiology and Biostatistics, Memorial Sloan Kettering Cancer Center, New York, NY, USA

Correspondence to: Peter B. Bach, MD, MAPP, Department of Epidemiology and Biostatistics, Center for Health Policy and Outcomes, 485 Lexington Ave, 2nd Floor, New York, NY 10017, USA (e-mail: bachp@mskcc.org).

Racial disparities in cancer treatment and outcomes in the United States are well documented. A substantial body of work has identified worse outcomes for non-white cancer patients compared with their white counterparts. Proposed explanations for this disparity include two broad categories of mechanisms: biological factors (differences in cancer biology resulting in intrinsically more aggressive and faster growing cancers among non-white patients) and social factors (differences in the care received in cancer screening and/or treatment).

In this issue of the Journal, Morgan et al. report on racial disparities in the utilization of positron emission tomography (PET) in the initial staging of non-small cell lung cancer (NSCLC) (1). In their analysis of the Surveillance, Epidemiology, and End Results-Medicare database, they find that patients with black or Hispanic race or ethnicity who are newly diagnosed with NSCLC are less likely to receive PET imaging during staging compared with white patients despite guideline recommendations that PET should be a standard component of staging (2). In unadjusted analysis, the receipt of PET imaging was 63% among non-Hispanic black patients, 70% among Hispanic patients, and 78% among non-Hispanic white patients. After adjustment for other demographic and socioeconomic characteristics, the likelihood of PET remained lower for non-Hispanic black patients (odds ratio = 0.57, 95% confidence interval [CI] = 0.51 to 0.64) and Hispanic patients (odds ratio = 0.76, 95% CI = 0.67 to 0.88) compared with white patients. After further adjustment for imaging modality and treatment received, the authors found improved survival at 1 year among non-Hispanic black and Hispanic patients compared with white patients. Receipt of PET imaging during staging was noted to be statistically significantly associated with reduced likelihood of cancer-specific mortality at 1 year among both squamous (hazard ratio [HR] = 0.61, 95% CI = 0.57 to 0.65) and nonsquamous (HR = 0.62, 95% CI = 0.60 to 0.65) histology.

These findings are consistent with the existing literature on racial disparities in treatment of NSCLC. Non-white patients appear less likely to receive many components of lung cancer care. In particular, eligible non-white patients are less likely to receive potentially curative surgery for early-stage disease (3–5). Additionally, those non-white patients who do receive surgery or other treatment modalities such as chemotherapy and radiation are more likely to experience delays in treatment initiation (6). The current study suggests that appropriate staging imaging is another source of racial differences in lung cancer care delivery, with the potential to harm long-term outcomes. A prior study of PET utilization for NSCLC staging, done within the Veterans Affairs health-care system from 2003 to 2005, found the absolute, unadjusted utilization of PET to be approximately 7% greater in white than non-white patients (7). The current findings suggest that the disparity may have grown since 2003– 2005 or may be greater outside the VA system.

This report comes in the context of a growing literature supporting the hypothesis that racial differences in cancer outcomes are due to social, rather than biological, factors. One recent study reported that nearly one-half of the racial disparity in presentation with locally advanced (stage III) breast cancer (vs stage I–II) was mediated by a single social factor: insurance status (8). Similarly, adjustment for social factors has been found to erase the racial disparity in survival among patients with resectable pancreatic cancer (9,10). Even prostate cancer for which outcome disparities between black and white men have long been attributed to biology—has been found to have similar outcomes in treatment settings where black and white patients receive similar care (11). The work by Morgan et al. further suggests that inequality is a story of "socioeconomics, not biology" (12).

Although receipt of appropriate staging imaging likely improves patient outcomes, the magnitude of this effect is likely to be overstated in the current study. The authors find a large, favorable association between PET and 1-year cancer-specific death (HR = 0.62, 95% CI = 0.60 to 0.65) for nonsquamous NSCLC and a similar reduction for squamous NSCLC. In absolute terms, this observed effect corresponded to a 20% improvement in 1-year survival. But studies that have examined the incremental improvement in staging achieved through PET rather than CT have found that only 20% of patients' staging changes (13). In other words, the absolute percent change in survival essentially equals the absolute change in restaging, a finding that

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could be mathematically correct only if mis-staging were associated with 100% mortality and correct staging 100% survival. This is not plausible.

This is why we believe that the observed association between PET and survival is more likely to be a reflection of confounding factors. First, restaging resulting from PET would be expected to cause a "Will Rogers Effect," in which apparent stage-specific survival improves for all stages of disease without any actual improvement for any individual patient. This can occur because the fraction of patients at a given stage who will be up-staged on PET were the "most advanced" of those at that stage and after restaging will then be the "least advanced" of all patients in their new stage group. Hence, average survival within each stage will increase even though survival across stages does not. Additionally, there is a high likelihood of "confounding by indication," in which patients with unmeasured clinical factors indicating a better prognosis were more likely to receive PET. Residual confounding by unmeasured socioeconomic factors is also likely. It should be noted that in the same multivariate model, MRI brain was found to be associated with increased likelihood of death (HR = 1.19, 95% CI = 1.14 to 1.24 for nonsquamous NSCLC). If we follow the authors' interpretation of their findings, this means that MRI scans must be accelerating death, which runs counter to everything we know about the clinical care of patients with lung cancer.

In summary, Morgan et al. highlight a persistent disparity in guideline-concordant cancer staging. These findings contribute to an understanding of US racial health-care disparities resulting from social, rather than biological, processes. Additional research is needed to better understand the contribution of staging with PET imaging to patient survival in NSCLC, although that impact is almost certainly overstated in their study.

Notes

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References

- Morgan R, Karam SD, Bradley CJ. Ethnic disparities in PET/CT utilization at diagnosis of non-small cell lung cancer. J Natl Cancer Inst. 2020;112(12):djaa034.
- National Comprehensive Cancer Network. NCCN guidelines: non small cell lung cancer. 2020. https://www.nccn.org/professionals/physician_gls/pdf/ nscl.pdf. Accessed February 14, 2020.
- Check DK, Albers KB, Uppal KM, et al. Examining the role of access to care: racial/ethnic differences in receipt of resection for early-stage non-small cell lung cancer among integrated system members and non-members. Lung Cancer. 2018;125:51–56.
- Farjah F, Wood DE, Yanez ND, et al. Racial disparities among patients with lung cancer who were recommended operative therapy. Arch Surg. 2009; 144(1):14–18.
- Sineshaw HM, Wu X-C, Flanders WD, Osarogiagbon RU, Jemal A. Variations in receipt of curative-intent surgery for early-stage non-small cell lung cancer (NSCLC) by state. J Thorac Oncol. 2016;11(6):880–889.
- Shugarman LR, Mack K, Sorbero MES, et al. Race and sex differences in the receipt of timely and appropriate lung cancer treatment. *Med Care*. 2009;47(7): 774–781.
- Gould MK, Schultz EM, Wagner TH, et al. Disparities in lung cancer staging with positron emission tomography in the Cancer Care Outcomes Research and Surveillance (CanCORS) study. J Thorac Oncol. 2011;6(5):875–883.
- Ko NY, Hong S, Winn RA, Calip GS. Association of insurance status and racial disparities with the detection of early-stage breast cancer. JAMA Oncol. 2020; doi: 10.1001/jamaoncol.2019.5672 [Epub ahead of print]
- Heller DR, Nicolson NG, Ahuja N, Khan S, Kunstman JW. Association of treatment inequity and ancestry with pancreatic ductal adenocarcinoma survival. JAMA Surg. 2020;155(2):e195047. doi:10.1001/jamasurg.2019.5047.
- Moaven O, Richman JS, Reddy S, Wang T, Heslin MJ, Contreras CM. Healthcare disparities in outcomes of patients with resectable pancreatic cancer. Am J Surg. 2019;217(4):725–731.
- Dess RT, Hartman HE, Mahal BA, et al. Association of Black Race with prostate cancer-specific and other-cause mortality. JAMA Oncol. 2019;5(7): 975–983.
- 12. Paller CJ, Wang L, Brawley OW. Racial inequality in prostate cancer outcomes—socioeconomics, not biology. JAMA Oncol. 2019;5(7):983.
- Maziak DE, Darling GE, Inculet RI, et al. Positron emission tomography in staging early lung cancer: a randomized trial. Ann Intern Med. 2009;151(4): 221–228, W-48.