Response to Meurs, Menke-Pluijmers, Seisling, and Westenend

Shi-Yi Wang, MD, PhD1,2 Peiyin Hung, PhD,3 Brigid K. Killelea, MD,2,4 Sarah S. Mougalian, MD,2,5 Suzanne B. Evans, MD,2,6 Cary P. Gross, MD2,7

1 Department of Chronic Disease Epidemiology, Yale School of Public Health, New Haven, Connecticut
2 Cancer Outcomes, Public Policy, and Effectiveness Research (COPPER) Center, Yale Cancer Center, New Haven, Connecticut
3 Department of Health Services Policy and Management, Arnold School of Public Health, University of South Carolina, Columbia, South Carolina
4 Department of Surgery, Yale School of Medicine, New Haven, Connecticut
5 Section of Medical Oncology, Department of Internal Medicine, Yale School of Medicine, New Haven, Connecticut
6 Department of Therapeutic Radiology, Yale School of Medicine, New Haven, Connecticut
7 Section of General Internal Medicine, Department of Internal Medicine, Yale School of Medicine, New Haven, Connecticut

Corresponding author: Shi-Yi Wang, MD, PhD,
Department of Chronic Disease Epidemiology
Yale School of Public Health
60 College Street, P.O. Box 208034
New Haven, CT 06520
Phone number: 203-737-8096
Fax number: 203-785-6980
Email: shiyi.wang@yale.edu

© The Author(s) 2020. Published by Oxford University Press.
This is an Open Access article distributed under the terms of the Creative Commons Attribution Non-Commercial License (http://creativecommons.org/licenses/by-nc/4.0/), which permits non-commercial re-use, distribution, and reproduction in any medium, provided the original work is properly cited. For commercial re-use, please contact journals.permissions@oup.com
We appreciate the correspondence from Meurs et al. about our study and value their interest in expanding the discussion of sentinel lymph node biopsy (SLNB) for older women with ductal carcinoma in situ (DCIS). They raised several interesting questions about the study design and interpretation of our findings.

First, Meurs and colleagues appeared to over-interpret our conclusions. We disagree with their assertion that SLNB is a staging for DCIS. SLNB is a staging procedure for invasive cancer. Furthermore, acknowledging that SLNB can be considered for patients who undergo mastectomy, we conclude that our findings do not support the routine performance of SLNB for older patients with DCIS amenable to breast conservation.1 The clinical guidelines from NCCN and ASCO are not vague,2, 3 and our conclusions are indeed aligned with them. Our findings that SLNB leads to side effects but does not improve outcomes are particularly important1, 4 given the increasing trend of SLNB among patients with DCIS who underwent breast conserving surgery (BCS).5 For example, the percentage of the older patients with DCIS receiving BCS who underwent SLNB in the United States increased from 7.2% in 1998 to 39.4% in 2011,5 which is concerning.

Second, we concur that our cohort was limited to patients who had a final diagnosis of DCIS. Patients who were initially diagnosed with DCIS but were later upstaged to invasive cancer were not included in our sample. Thus, it is important to delineate how this study design may have impacted the results: The group that did not undergo SLNB in our study might consist of a larger number of patients who harbor unidentified positive nodes, compared to the SLNB group. In other words, the SLNB group excluded women with node positive disease detected on SLNB, while the non-SLNB group included these patients (because they did not have the SLNB that might have detected the positive nodes). If we found statistically significantly worse
outcomes (recurrence and breast cancer mortality) among the group of patients who did not undergo SLNB, we would have concluded that SLNB should not be omitted for this patient population. On the other hand, and in fact, we found no difference in outcomes between older patients with DCIS undergoing BCS who did and did not undergo SLNB; our findings therefore support that the SLNB procedure is unnecessary for this group.

Finally, while patients with biopsy-proven DCIS may actually have invasive cancer, little is known about the risk of underestimation among older patients who are amenable to BCS. We agree that research identifying patients with a biopsy diagnosis of DCIS who harbor invasive breast cancer is needed. However, older patients with biopsy-proven DCIS have a low risk of being upstaged to invasive breast cancer, as well as a low likelihood of benefiting from SLNB. The authors argued that finding a lymph node that contains cancer (and thus treating invasive cancer rather than DCIS) affects the ultimate outcome in our target population, yet our data suggests similar outcomes without SLNB. Furthermore, SLNB use was associated with higher risks of complications, including lymphedema, pain, and infection. At this point, given the lack of evidence that routine SLNB use improves clinical outcomes in older patients who undergo BCS, clinician investigators should derive and validate evidence to support this procedure or move away from its routine use.

References:

1. Hung P, Wang SY, Killelea BK, Evans SB, Mougalian SK, Sedghi T, Gross CP. Long term outcomes of sentinel lymph node biopsy for ductal carcinoma in situ. JNCI Cancer Spectrum 2019 Aug 7;3(4):pkz052. doi: 10.1093/jncics/pkz052. eCollection 2019 Dec.
2. NCCN Clinical Practice Guidelines in Oncology. Breast Cancer. Version 5. Available at www.nccn.org/patients. Assessed on July 31, 2020.

3. Lyman GH, Temin S, Edge SB, et al. Sentinel lymph node biopsy for patients with early-stage breast cancer: american society of clinical oncology clinical practice guideline update. J Clin Oncol. 2014;32(13):1365-1383. doi:10.1200/JCO.2013.54.1177.

4. Killelea BK, Long JB, Dang W, Mougalian S, Evans SB, Gross CP, Wang SY. Associations between sentinel lymph node biopsy and complications for patients with ductal carcinoma in situ. Ann Surg Oncol 2018; 25(6):1521-1529.

5. Mitchell KB, Lin H, Shen Y, et al. DCIS and axillary nodal evaluation: compliance with national guidelines. BMC Surg. 2017;17(1):12. doi:10.1186/s12893-017-0210-5.

6. Meurs CJC, van Rosmalen J, Menke-Pluijmers MBE, et al. A prediction model for underestimation of invasive breast cancer after a biopsy diagnosis of ductal carcinoma in situ: based on 2892 biopsies and 589 invasive cancers. Br J Cancer. 2018;119(9):1155-1162. doi:10.1038/s41416-018-0276-6.