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CORRESPONDENCE

Reply to A.C. Voogd et al

We would like to thank Voogd et al[1] for their interest and comments on our article. They hypothesize that age-related variations in the use of axillary staging may have explained the increased risk of axillary lymph node involvement in older women with breast cancer, mainly in small tumors, as observed in our study.[2] This potential bias was already commented on in our discussion. However, it is certainly a valuable argument that should be looked at in more depth, and we agree that great care is warranted to exclude selection bias as much as possible in these kinds of observational studies.

The advantage of the Leuven database is that it contains data from one large center, where the same surgeons (M.R.C., P.N. and A.S.[2]) have been active for many years, including the study period of 2000-2005. The policy has consistently been to perform axillary surgery independent of age of breast cancer diagnosis. In a previously reported series from Voogd et al,[3] the risk of finding a positive lymph node in patients with a clinically negative axilla was 34% and therefore unreliable to replace surgical staging of the axilla. If a patient was suitable for general anesthesia in our institution, as a matter of principle, axillary surgery (axillary lymph node dissection or sentinel lymph node procedure) was performed. As mentioned in our discussion, an axillary dissection was not performed in 48 of 2,568 patients (1.9%), 26 of these being $\leq$ 70 years of age. Rarely, in case of small tumors and contraindication for general anesthesia, a tumorectomy without axillary surgery has been performed under local anesthesia. To have concrete numbers for this approach, we asked our medical registration department to provide the number of patients who received a tumorectomy for invasive breast cancer under local anesthesia during the study period. In total, 17 patients were found with a median age of 83 years (range, 68 to 95 years), that is, 0.76% of the total study group population. None of these patients were included in the current study population.

A confirmation of the fact that the approach in Leuven is always to perform some form of axillary surgery for invasive tumors, is that during the year 2008 (which contains double-checked data from all patients receiving operations in Leuven), 100% (426 of 426) of patients with the same inclusion criteria as the study (female patients diagnosed with invasive breast cancer; patients who had received primary surgery at the University Hospitals Leuven, thus excluding patients who had neoadjuvant systemic therapy and patients who never had therapy or surgery before for breast cancer; patients whose pathology was performed in the University Hospitals Leuven; and patients with no metastases at diagnosis) had some form of axillary surgery: 41% sentinel procedure only, 44% axillary surgery only, and 15% both. This included 59 patients age 70 to 79 years and 23 patients age 80 years and older. This clearly contrasts with the data provided by Voogd et al,[1] where 13% and more than 40% of these age classes, respectively, did not receive axillary surgery (although not the same inclusion criteria were used in these data).

It is not possible to provide exact data on the number of older patients with early breast cancer who did not receive any breast and axillary surgery at all in Leuven. This number will be small, however, for operable breast cancer in Leuven, because the same policy of equal surgery in younger and older patients has been used from 2000 until present. Moreover, it is unlikely that there will be major differences in small (< 2 cm) and larger tumors, given that the decision for no surgery is probably more related to patient-related factors than tumor-related factors, so it is unlikely that this would have influenced our observations.

For the Eindhoven Cancer Registry database in our publication, it is more difficult to provide such detailed data, given they were retrieved from 17 different local hospitals and more bias might have been present there. However, our findings were replicated on this database after multiple imputation of the missing values under the assumption of missing at random (MAR, ie, missingness depends on other information in the data set). In some patients, a missing value for lymph node involvement may indeed be partly caused by clinical node negativity. The missing values were imputed using variables that are related to the missingness (eg, age, size, histology, ER status), which increases the plausibility of MAR.[4] Moreover, if MAR would not be fully satisfied (ie, missingness is not entirely explained by information that is present in the data set), the use of a rich imputation model may introduce little or no bias.[3] Nevertheless, it would be interesting to validate our findings on other databases where the same strategy of axillary surgery in older versus younger patients is present as in Leuven.

In conclusion, given the small percentage of patients in Leuven who did not receive any axillary surgery, it is unlikely that variations in axillary surgery had major influence on our finding that the risk of lymph node involvement decreases with age up to 70 years, but increases after 70 years of age, mainly in smaller tumors.

Hans Wildiers, Ben Van Calster, Thijs Van Dorpe, Anne-Sophie Dieudonné, Ann Smeets, Marie-Rose Christiaens, and Patrick Neven

Multidisciplinary Breast Centre, University Hospitals Leuven, Belgium

AUTHORS' DISCLOSURES OF POTENTIAL CONFLICTS OF INTEREST

The author(s) indicated no potential conflicts of interest.

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