The Breast xxx (2017) 1–2

Contents lists available at ScienceDirect

The Breast

journal homepage: www.elsevier.com/brst

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Do cut-off values of lymph node ratio and presence of perineural invasion affect survival in breast cancer patients with pathologic N3a lymph node stage? Reply to Kadri Altundag

Lymph node ratio (LNR) is an emerging prognostic factor in different types of cancer [1–4] and has been proposed for a revision of breast cancer staging [5]. Despite several studies have been published on this issue, a definitive cut-off value useful for predicting long-term outcome in patients affected by breast cancer has not been established yet.

In our study we included LNR among the variables to be evaluated as prognostic factor in a cohort of patients with pN3 breast cancer [6]. Using 0.6 as cut-off, we found that LNR did not influence prognosis.

Kadri Altundag, who personally thank for his comment, has emphasized the importance to set a cut-off for LNR at least at 0.65 in order to appreciate a difference in overall survival (OS), as suggested by Schiffman et al. [7], a value higher than that used in our study. Actually, in Schiffman's study a LNR more than 0.65 was predictive of poor prognosis. However, it is important to note that this result was referred to the outcome of the whole population included in the study, i.e. patients affected by breast cancer at different lymph node stage: 309 (21.5%) pN1, 138 (9.6%) pN2, and 109 (7.6%) pN3, while our study was carried out exclusively in a pN3 population. In a subgroup analysis, the differences in OS resulted statistically significant only for patients at pN1 or pN2 stage, not pN3, consistent with our result.

A subsequent study by Zhu et al., specifically focused on patients at stage III, reported that 0.6 was the most sensitive LNR cut-off to apply in this subset of patients to observe the greatest difference in OS [8]. Based on this finding, we adopted the cut-off value of 0.6. We did not find any statistically significant difference in outcome not only using 0.6, as reported in the published study, but also at higher cut-off values, 0.7, 0.8, or 0.9 (data not shown). Our study, with the limits of a retrospective study with small sample size, seems to indicate that once more than 10 lymph nodes are involved, LNR fails to maintain a predictive prognostic value.

Regarding perineural invasion, we did not include this factor in the statistical analysis since it was not available in our institution database. Perineural invasion is not routinely performed by our pathologists. Kadri Altundag comment gave us the interesting suggestion to perform ad hoc analysis to evaluate the prognostic relevance of this parameter in our cohort.

Conflicts of interest

The authors have no conflicts of interest.

http://dx.doi.org/10.1016/j.breast.2017.05.006
0960-9776/

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Please cite this article in press as: Grassadonia A, et al.Do cut-off values of lymph node ratio and presence of perineural invasion affect survival in breast cancer patients with pathologic N3a lymph node stage? Reply to Kadri Altundag, The Breast (2017), http://dx.doi.org/10.1016/j.breast.2017.05.006

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6 May 2017
Available online xxx