

## Correspondence

### Correlation does not always show a causal relationship

To the Editor

We have read the article by Homaei-Shandiz F et al.<sup>1</sup> It has already been shown that the tumors over-expressing the human epidermal growth factor receptor-2 (HER-2)/neu, have a higher metastatic tendency and a poor prognosis.<sup>2</sup> We would like to make a few comments about this article. The authors have reported that HER-2 positive breast tumors are possibly associated with higher frequency of nodal metastases; however, they could not find a significant association ( $p=0.538$ ). They reported that this is possibly due to the small sample size. We agree with this comment since there has been a large study showing this relationship.<sup>2,3</sup> Also, the authors have concluded that there is a relationship between tumor size and the HER-2 positive breast cancer. We do not agree with this conclusion: 1) the relationship that the authors mentioned did not reach a statistically significant value and the sample size was not sufficient to draw this conclusion; and 2) in recent published large studies, HER-2 and tumor size showed to be independent predictive factors for lymph node metastases.<sup>3</sup> We cannot concur with the result that the tumor fractions larger than 5 cm tended to have a higher probability and a greater tumor size. This is statistically a true result. However, we believe that the author's comment is wrong. Statistics can allow misleading interpretation of the data.

In this study, this is probably the case due to HER-2 positive tumors are more aggressive than the negative ones and the tumors are diagnosed at relatively higher stages. As the tumor size increases, the HER-2 positive tumors are diagnosed at later stages, we can find a positive correlation between

HER-2 positive tumors and the tumor size, however every correlation does not indicate causality.

*Hakan Buyukhatipoglu*  
Department of Internal Medicine  
Gaziantep University  
Gaziantep, Turkey

### Reply from the Author

I read the attached correspondence on our paper which was published last year in the Saudi Medical Journal. Although we found no statistical relationship between lymph node positive patient and human epidermal growth factor (HER-2)/neu, we agree with his comment that correlation does not always show a causal relationship, prospective studies with a large number of patients are necessary to determine the prognostic significant of HER-2/neu and tumor size. Especially, an amplification of HER-2/neu has been noted among in situ carcinoma as well and HER-2/neu over expression may identify in women with a small size tumor (>2 cm) and lymph node negative who are likely to experience early recurrences.

*Fatemeh Homaei-Shandiz*  
Department of Radiation Oncology  
Omid Hospital  
Mashhad, Iran

### References

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