

Are BMI and Negative Hormone Receptors Prognostic Factors in HER2⁺ Early-stage Breast Cancer?

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To The Editor:

We read the recently reported article by Cantini et al.¹ They had retrospectively analyzed the role of the body mass index (BMI) and hormone receptor (HR) status in 238 patients with human epidermal growth factor receptor 2-positive (HER2⁺) early-stage breast cancer (BC).¹ The patients had received chemotherapy and trastuzumab (Herceptin) for 1 year.¹ The authors reported a higher risk of relapse for patients with HR⁻ status and BMI of ≥ 25 kg/m². Although these results were very interesting, we would like to underline some points.

At present, the duration of adjuvant treatment with trastuzumab for patients with HER2⁺ BC is still very much open to debate. Conte et al.² recently reported a phase III randomized trial comparing 9 weeks and 12 months of adjuvant trastuzumab combined with chemotherapy in this setting. However, the results failed to show the noninferiority of a shorter trastuzumab administration.² Although other studies have also been conducted on this topic,^{3,4} 1-year trastuzumab has remained the standard adjuvant treatment of HER2⁺ BC. Furthermore, 2 large meta-analyses of 43 and 82 international studies showed poorer outcomes for obese patients with BC compared with nonobese patients, independently of menopausal and HR status.^{5,6}

We agree with Cantini et al.¹ that their retrospective study, albeit of a small case series, has produced provocative and hypothesis-generating findings. It prompted us to evaluate the BMI in 53

patients with HER2⁺ early-stage BC who had received adjuvant chemotherapy and trastuzumab therapy (excluding patients who had received neoadjuvant treatment). These 53 patients were enrolled from 2007 to 2015 at Istituto Scientifico Romagnolo per lo Studio e la Cura dei Tumori, IRCCS (Meldola, Italy), in a study reviewed and approved by the local ethics committee (C.E.ROM. approval no. 2157). The median patient age was 55 years (range, 32-77 years). All the patients were followed up for ≥ 5 years after the diagnosis. The patients with and without relapse were matched by age at the start of adjuvant treatment and estrogen receptor (ER) status.

Of the 53 included patients, 23 had experienced relapse, defined as the presence of local recurrence or distant metastasis. Also, 30 of the 53 patients (56.6%) had had a high BMI (≥ 25 kg/m²). Our data differ from those reported by Cantini et al.,¹ who reported a greater proportion of patients with relapse and a BMI of ≥ 25 kg/m² and HR⁻ status. Of the 6 patients with ER⁻ BC and a high BMI in our series, 3 (50%) had developed a relapse. In contrast, in the 7 patients with ER⁻ status and a low BMI, 3 (34.7%) had developed a relapse ($P = .764$; Table 1). Our analysis revealed that the BMIs were similar in patients with and without relapse ($P = \text{NS}$; Table 2). Thus, in our case series, BMI and ER⁻ status did not appear to influence the risk of recurrence in this setting.

Further research is warranted to understand the real impact of BMI on patients with BC in the adjuvant setting and to establish

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Table 1 BMI Stratified by ER⁻ Status

| BMI, kg/m ² | ER ⁻ Breast Cancer, n | | | P Value ^a |
|------------------------|----------------------------------|-----------------|--------------------|----------------------|
| | All Patients (n = 13) | Relapse (n = 6) | No Relapse (n = 7) | |
| <25 | 7 | 3 | 4 | .764 |
| ≥ 25 | 6 | 3 | 3 | |

Abbreviations: BMI = body mass index; ER = estrogen receptor.
^a χ^2 test with Yates correction.

Table 2 Mean and Median BMI for Overall Case Series

| BMI | Overall Case Series (n = 53) | No Relapse (n = 30) | Relapse (n = 23) | P Value |
|---------------------------|------------------------------|---------------------|------------------|-------------------|
| Mean, kg/m ² | 25.1 | 24.7 | 25.7 | .365 ^a |
| Median, kg/m ² | 25.1 | 25.0 | 26.0 | .342 ^b |

Abbreviation: BMI = body mass index.

^aStudent's *t* test.

^bMann-Whitney *U* median test.

whether the BMI is an independent prognostic factor or correlates with other known prognostic parameters such as ER⁻ status, proliferative index, or HER2 status.

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