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INSULIN RESISTANCE (IR) AND PROGNOSIS OF METASTATIC BREAST CANCER (MBC) PATIENTS

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Background: Higher insulin levels have been associated with a worse prognosis in early BC patients. The effect of higher insulin levels on MBC prognosis has not been explored so far. The aim of this study was to evaluate the influence of IR on the prognosis of HER2 negative, non-diabetic, MBC patients receiving first line CT.
Methods: The relationship between IR, identified by HOMA index >2.5 (fasting glucose [mmol/L] × insulin [mU/L]/22.5), and progression free (PFS) or overall survival (OS) was assessed in 125 MBC patients enrolled in a clinical trial of first line CT with non-pegylated liposomal doxorubicin 60 mg/sqm plus cyclophosphamide 600 mg/sqm Q21 days. PFS and OS were calculated by Kaplan-Meier estimation; multivariate. Cox analysis was performed adjusting for age, PS, endocrine status, metastatic site and BMI.
Results: Information on patient's IR status at baseline was available on 116 women. Median follow up was 17.9 months (IQR 1–49). Overall, 46.95% patients were classified as insulin resistant (HOMA >2.5), 40.51% were overweight (BMI 25–30) and 16.37% were obese (BMI >30). Median age was 60 years (range 36–86); PS was 0 in 74.13% of the patients. Endocrine status was positive in 75.08% and visceral disease was present in 65.79%. Overall, median PFS was 10 months (IQR 8.5–12.8): Median PFS was 11.5 months (IQR 9.6–14.6) in patients with HOMA index ≤2.5 and 8.5 months (IQR 5.7–12.4), in patients with HOMA index >2.5; HR = 1.332 (95% CI: 1.01–3.18, p = 0.04). By multivariate analysis, after adjustment for age, PS, endocrine status, visceral disease and BMI, a statistically significant higher risk of disease progression was detected in patients with HOMA Index >2.5 (HR = 2.28; 95%CI: 1.06–4.89, p = 0.035).
Conclusions: In this study IR, indicated by an HOMA Index >2.5, was associated with a significantly worse prognosis; after adjusting for other acknowledged prognostic factors, the IR status together with the ER status, were the only two to maintain their adverse prognostic effect. These data suggest that host metabolic status might influence the prognosis of MBC treated with CT and therefore additional alternative strategies, targeting host metabolism, should be considered in this unfavorable subset of patients.