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Expression of HIF-1α and markers of angiogenesis and metabolic adaptation in molecular subtypes of breast cancer

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Abstract

Hypoxic zones exist in solid tumors, where oxygen levels are significantly lower than in normal tissues. Hypoxia makes chemo-radiation therapeutics less effective and renders the metastatic potential more favorable. Emerging research has found that the transcriptional expression of hypoxia-inducible factor-1alpha (HIF-1α) promotes the transcription of vascular endothelial growth factor A (VEGF-A) and Hexokinase-I (HK-I), which are associated to cellular growth, angiogenesis, and metastatic invasion in many malignancies. However, it is still unclear whether VEGFA and HK-I expression has any influence on survival based on the intrinsic subtypes of breast cancer. Their prognostic significance remains a debatable topic. In the present study, quantitative Real-time polymerase chain reaction (qRT-PCR) was employed to check the relative expression of HIF-1α, VEGF-A and HK-I. The hazard ratios (HR) of breast cancer-specific and overall mortality were calculated using Cox proportional hazards model, which were adjusted for demographic, clinicopathological, and associated molecular variables, as well as the diagnosis year. The relative mRNA expression levels of HIF-1α ($p = 0.0010$) and VEGFA ($p = 0.0119$) were significantly higher in tumor tissues. The expression of both HIF-1α ($p = 0.0111$) and VEGFA ($p = 0.0078$) was higher in the TNBC group of breast cancers, while HK-I ($p = 0.0106$) was higher in ER/PR-positive, HER2-negative group. HIF-1α and HK-I overexpression were associated with a higher likelihood of survival, while overexpression of VEGFA was associated with a low survival rate, although it was not statistically significant.

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