We had previously reported a close association between pathological response and the maximum tumor standardized uptake value (SUVmax) measured by $^{18}$F-fluorodeoxyglucose positron emission tomography prior to chemotherapy in estrogen receptor (ER)-positive breast cancer. We hypothesized that glucose hypermetabolism by luminal B tumors may result in chemotherapy responsiveness. Using a single-gene expression assay, TargetPrint® (Agendia) and a 70-gene expression classifier, MammaPrint® (Agendia), we divided 20 patients with ER-positive primary breast cancer into luminal A and luminal B subtypes and compared the tumor SUVmax value between the two groups. A significantly higher SUVmax was measured for luminal B tumors ($n=10$; mean± SD, $7.6±5.6$) than for luminal A tumors ($n=10$; mean± SD, $2.6±1.2$; $p=0.01$). Glucose hypermetabolism could help predict intrinsic subtyping and chemotherapy responsiveness as a supplement to ER, progesterone receptor, HER2, and Ki-67 histochemical scores.

Key Words: Breast neoplasms, Estrogen receptor, Fluorodeoxyglucose positron emission tomography, Glucose metabolism

We hypothesized glucose hypermetabolism in luminal B tumors may result in chemotherapy responsiveness. Using a single-gene expression assay, TargetPrint® (Agendia, Amsterdam, The Netherlands) and a 70-gene expression classifier, MammaPrint® (Agendia) [2,3], we divided 20 patients with ER-positive primary breast cancer into luminal A and luminal B subtypes and compared the tumor SUVmax value between the two groups. The demographics of these groups are shown in Table 1.

A significantly higher SUVmax was measured for luminal B tumors ($n=10$; mean± SD, $7.6±5.6$) than for luminal A tumors ($n=10$; mean± SD, $2.6±1.2$; $p=0.01$) (Figure 1). At the threshold of 5.0, the sensitivity and specificity of FDG-PET to identify tumors of the luminal B subtype were 60% and 100%, respectively. The area under the curve (AUC) analysis showed that SUVmax was an acceptable discriminator (AUC = 0.878; 95% confidence interval [CI], 0.647-0.981) with results comparable with those of the Ki-67 labeling index (LI) (AUC, 0.878; 95% CI, 0.647-0.981), a proliferative marker used to discriminate luminal B tumors in clinical practice (Figure 2). When SUVmax and Ki-67 LI were combined, the diagnostic performance improved (AUC = 0.933; 95% CI, 0.72-0.997).

Jin et al. [4] reported that among 273 breast cancer patients who received neoadjuvant chemotherapy, higher baseline glucose metabolism was associated with a lower rate of pathological complete response (pCR) and a poorer overall survival. These findings suggest that glucose hypermetabolism may be a useful biomarker for identifying patients who are likely to respond to chemotherapy.
SUVmax of the tumor and ER negativity were independent indicators of pCR. Despite the low number of ER-positive breast cancer patients who achieved pCR in that study, higher SUVmax in pCR than in non-pCR was in agreement with the results of our study. The role of glucose metabolism in ER-positive breast cancer was examined by Osborne et al. [5] from the Memorial Sloan-Kettering Cancer Center, who identified 43.7% of FDG SUV-correlated genes as ER signal-related genes by cDNA microarray analysis.

The present study has some limitations: the sample size was too small, including patients with relatively small tumors, which may have been a confounding factor that affected the SUVmax. Standardization is required for the use of quantitative FDG-PET as an imaging biomarker.

Currently, FDG-PET scanning is used for noninvasive detection of metastasis. In combination with one-stop examination, which evaluates the clinical staging of primary breast cancer, FDG-PET may provide invaluable information on intrinsic subtyping and chemotherapy responsiveness in addition to that obtained from ER, progesterone receptor, HER2, and Ki-67 histochemical scores.

CONFLICT OF INTEREST

The authors declare that they have no competing interests.

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