

Influences of preoperative metformin on immunological factors in early breast cancer

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【Abstract】 【Purpose】 Metformin has been suggested to possibly reduce cancer risk. However, the mechanism underlying the positive effects of metformin on cancer treatment remains unclear. We conducted a prospective study to evaluate the effects of preoperative metformin in patients with early breast cancer.

【Method】 We evaluated the effects on immunological factors (TILs, CD4+, CD8+, PD-L1, IFN γ and IL-2) by comparing core needle biopsies (CNB) obtained before metformin treatment with surgical specimens. Seventeen patients were enrolled in this prospective study from January to December 2016. We also analyzed 59 patients undergoing surgery during the same period to reveal the correlation of immune factors between CNB and surgical specimen. **【Result】** There was a moderate correlation between CNB and surgical specimens on TILs and CD8+ lymphocyte. (TILs $R_s=0.63$, CD4+ $R_s=0.224$, CD8+ $R_s=0.42$) In the metformin group, TILs increases were confirmed in 5 (29%) patients, while a decrease was confirmed in 2 (12%). The expressions of CD4+ and CD8+ by TILs were increased in 41% and 18% of surgical specimens, respectively. However, TILs number ($p=0.0554$), CD4+ ($p=0.0613$) and CD8+ ($p=0.0646$) expressions did not significantly increase. Furthermore, IFN γ expression appeared to be increased in response to metformin ($p=0.08$). **【Conclusion】** Preoperative metformin tends to increase TILs, as well as the numbers of CD4 and CD8 positive lymphocytes, and IFN γ levels. Metformin might improve immune function and have a possibility of chemo-sensitivity and thereby increase the effectiveness of immunotherapy, based on the results of this preliminary study.