

Impact of diabetes and metformin use on recurrence and outcome in early colon cancer (CC) patients – a pooled analysis of 3 adjuvant trials

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Background

Obesity and diabetes mellitus type 2 are associated with an increased risk of colorectal cancer. Recent studies have suggested beneficial effects of metformin in patients with cancer and diabetes. We sought to investigate the impact of metformin on recurrence and survival in a large, pooled analysis of non-metastatic colon cancer (CC) patients.

Methods

A patient-level meta-analysis from three randomized adjuvant trials was performed. All patients had resection with curative intent of a stage II or III CC and were treated with standard adjuvant fluoropyrimidine and oxaliplatin (+/- cetuximab). We investigated the impact of metformin on time to recurrence (TTR) and overall survival (OS). Multivariable analyses were adjusted for age, ECOG, T-stage, N-stage, grade, and primary tumor location.

Results

5922 patients were available for this analysis with a median follow-up of 6.8 years. 621 of 5922 patients (10.5%) had diabetes at the time of their diagnosis of CC. Of those with diabetes, 327 (52.7%) were defined as metformin-users and 294 patients (47.3%) as non-metformin-users. As expected, baseline characteristics associated with diabetes differed between non-diabetic, metformin-diabetic and non-metformin-diabetic CC patients whereas tumor-related characteristics were shown to be well balanced. CC patients with diabetes had a significantly shorter median TTR (adjHR: 1.21; 95% CI, 1.03 to 1.42; $p=0.027$) and median OS (adjHR: 1.29; 95% CI, 1.09 to 1.52; $p=0.002$) compared to non-diabetic CC patients. Diabetic CC patients not receiving metformin had a significantly worse OS (adjHR: 1.41; 95% CI, 1.13 to 1.77; $p=0.017$); however, use of metformin appeared to attenuate this effect on OS (adjHR: 1.18; 95% CI, 0.95 to 1.48; $p=0.017$).

Conclusions

CC patients with diabetes type 2 had a significantly worse survival as well as shorter TTR. Furthermore, our data suggest that metformin may attenuate the detrimental effect of diabetes on CC patient outcomes.