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Impact of diabetes on outcome and toxicity of neoadjuvant (chemo)radiation for rectal cancer

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Purpose

For patients with locally advanced rectal cancer, the German S3- guideline recommends neoadjuvant chemoradiation (nCRT) or short-course neoadjuvant radiotherapy (nRT) before surgery to improve local control rates. While complete pathologic responses and a lower rate of progression after neoadjuvant treatment are more commonly seen in patients without diabetes, there are conflicting results regarding the impact of diabetes mellitus type 2 (DMT2) on survival. Diabetic patients had a significantly lower 5-year survival rate and overall survival (OS). Other authors found no difference in OS, disease-free survival (DFS) and progression-free survival (PFS).

Aim of this study was to compare oncologic outcome and toxicity between diabetic and non-diabetic patients undergoing neoadjuvant chemoradiation or short-course neoadjuvant radiotherapy before surgery.

Patients and Methods

In total, 73 patients with locally advanced rectal cancer who underwent surgery after neoadjuvant chemoradiation or neoadjuvant short-course radiotherapy, were included in this analysis. Median age was 63 years (Range: 43-85 years). 63.0% were male and 37.0% female. 90.2% had a regional disease (UICC Stage II and III) and 9.7% had an advanced rectal cancer (UICC Stage IV). Within this cohort, we identified 20 patients with diabetes mellitus type 2 with a median haemoglobin A1c (HbA1c) of 6.2%. Baseline and tumor characteristics, oncologic outcome and toxicity of these patients were compared to 53 patients without diabetes.

For statistical analysis IBM SPSS Statistics (Version 25.0) was used. OS and PFS were calculated with Kaplan-Meier curves, followed by uni- and multivariable Cox regression models. Pathologic complete response and toxicity were compared using Fisher's exact test.

Results

Patients with DMT2 were significantly older than patients without diabetes (median age 68 vs. 60 years; p=0.006). In addition we observed higher body mass index (BMI) for patients with DMT2 (median BMI 26.8 vs. 24.6 kg/m², p=0.09). After nCRT, pathologic complete response was seen in 10.0% of patients with DTM2 and in 7.1% of patients without DTM2, (p=0.944). After a median follow-up of 49.7 months, there were no significant differences regarding PFS between both groups. In contrast, OS times were significantly shorter in diabetic patients compared to patients without DMT2 (patients with DMT2 had a median OS of 45.2 months, median OS for patients without DMT2 was not reached, p=0.006) (Figure 1). In a multivariable Cox regression model including DMT2, age, sex and UICC stages, DMT2 still independently affected OS (p=0.029).

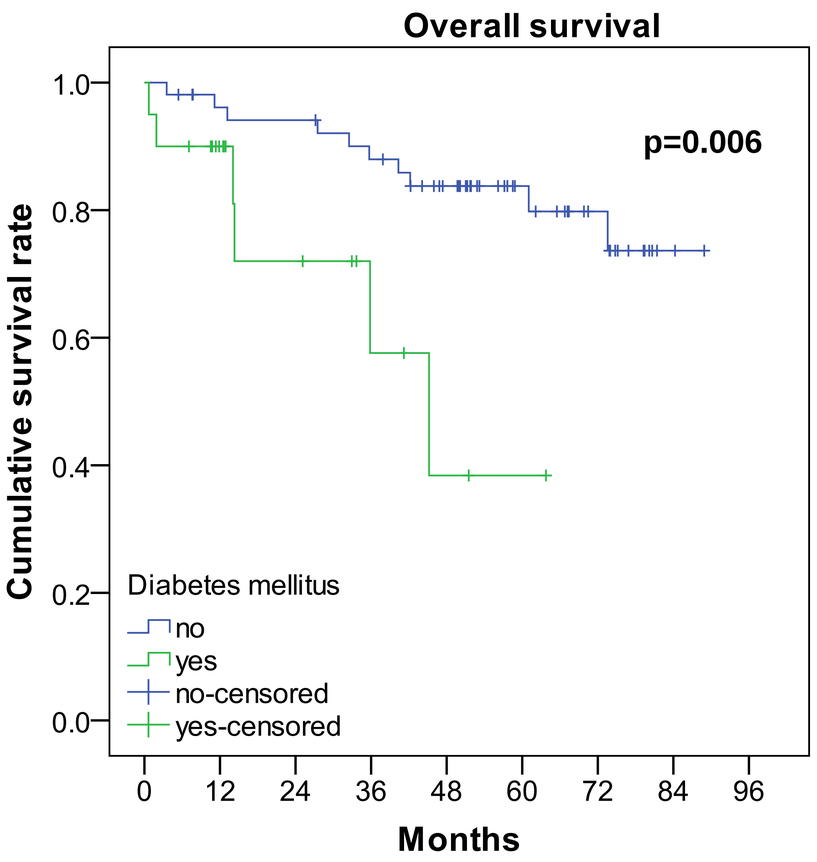

Figure 1: Overall Survival for diabetic and non-diabetic patients with rectal cancer

Regarding toxicity, diabetic patients had a higher rate of anemia than patients without diabetes (≥II° 42.9% vs. 9.5%, p=0.004) (Figure 2). However, no significant differences were seen for the rates of leukopenia (≥II° 21.4% (DTM2) vs. 14.3% (no DMT2), p=0.377) (Figure 3) and thrombocytopenia (≥II° 0.0% (DTM2) vs. 0.0% (no DMT2)).

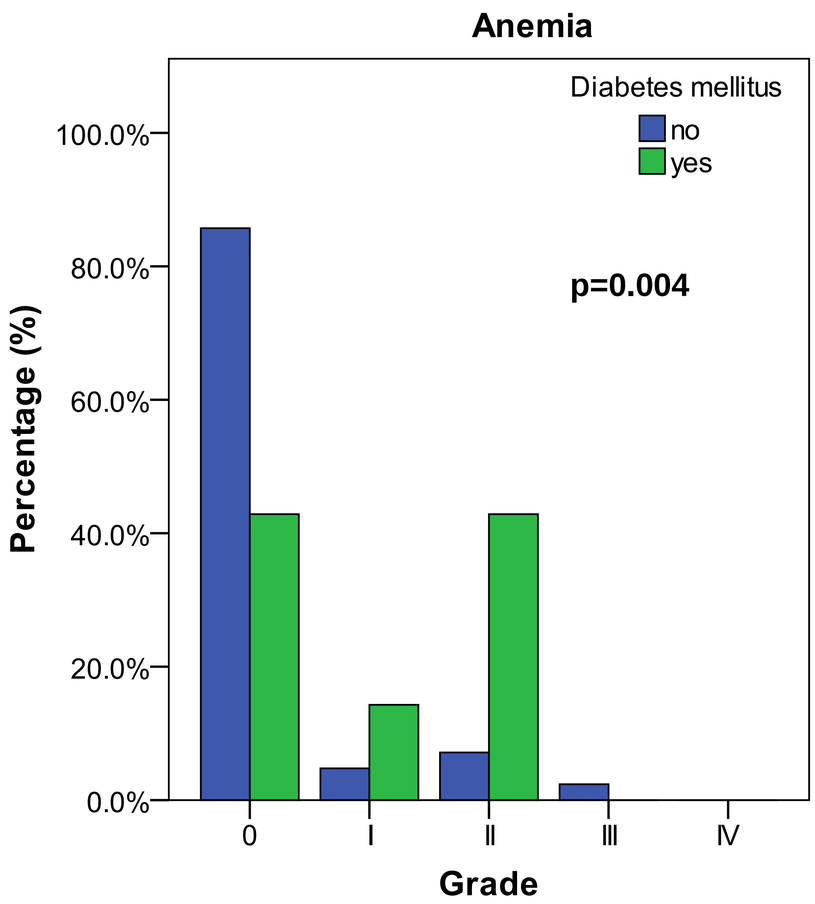

Figure 2: Rates of anemia for diabetic and non-diabetic patients with rectal cancer

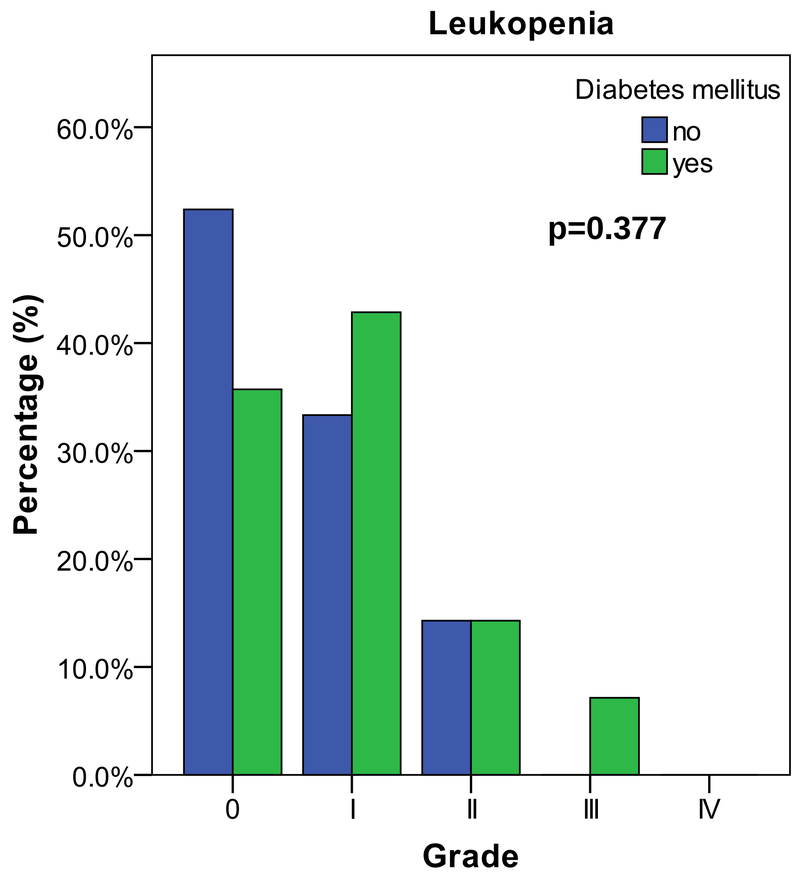

Figure 3: Rates of leukopenia for diabetic and non-diabetic patients with rectal cancer

Conclusion

While there were no significant differences for PFS or the rate of complete pathologic response after nCRT, median OS was significantly higher in patients without DMT2 than in diabetic patients. A significant difference was also seen for the rate of anemia after nCRT, but not for leukopenia or thrombocytopenia.

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