Metformin decreases the risk of recurrence of colorectal cancer.

Tina Fransgaard, MD¹, Lau C. Thygesen, PhD², Ismail Gögenur, MD, DMS⁰¹

¹ Dept. of Surgery, Zealand University Hospital and University of Copenhagen
² National Institute of Public Health, University of Southern Denmark

Background
Emerging evidence suggests that metformin decreases the risk of developing colorectal cancer in patients with diabetes. Only few studies have examined the potential survival benefits after surgery for colorectal cancer (CRC). Especially, the association between metformin use and risk of recurrence has been scarcely examined.

Aim
To examine the association between metformin and the risk of CRC recurrence.

Methods
Patients undergoing surgery for CRC in the entire Danish population between the January 1, 2003 and December 31, 2012 were identified through the Danish Colorectal Group’s National Clinical Database. The Danish National Patient Register records all hospital contacts in Denmark and the use of antidiabetic drugs were identified through the Danish National Prescription Registry. The risk of recurrence was assessed by a previously validated method using data from the Danish National Pathology Registry. Cumulative drug exposures after surgery were treated as time-dependent covariates in a Cox regression model adjusted for important clinical risk factors.

Results
A total of 20,485 patients were included in the study, 2,425 were diagnosed with diabetes and 1,158 treated with metformin at the time of surgery.

The adjusted hazard ratio (HR) for the risk of recurrence was 0.74 (95% confidence interval, 0.70-0.78, p = <.0001) for the metformin treated group compared with the insulin treated group. Compared with non-diabetic patients, the adjusted HR for metformin users was 0.90 (95% confidence interval, 0.87-0.92, p <.0001).

<table>
<thead>
<tr>
<th>Risk of recurrence</th>
<th>HRadjusted*</th>
<th>95% CI</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Insulin</td>
<td>1</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Metformin</td>
<td>0.74</td>
<td>0.70-0.78</td>
<td>&lt;.0001</td>
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<tr>
<td>Other oral antidiabetics</td>
<td>0.98</td>
<td>0.92-1.05</td>
<td>0.58</td>
</tr>
</tbody>
</table>

*Adjusted for: age, sex, ASA score, BMI, blood transfusions, smoking, alcohol consumption elective or emergency surgery, type of cancer (colon or rectum), T-stage, lymph node status and diabetic complications

Conclusion
Metformin use decreases the risk of recurrence by 26 % in diabetic patients with colorectal cancer compared with insulin users. Compared with non-diabetic patients metformin use decrease the risk of recurrence by 10%.

Take home message
Metformin treatment decreases the risk of recurrence after surgery for colorectal cancer.