

COMMENTARY

The Influence of Aspirin Intake on Survival after Primary Resection of Pancreatic Ductal Adenocarcinoma

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DESCRIPTION

Pancreatic cancer is the third leading cause of cancer-related deaths worldwide. Even when diagnosed in localized and thus potentially resectable stages, the 5-year relative survival rate remains limited. This is primarily attributed to the aggressive nature of pancreatic carcinoma, which frequently leads to rapid recurrence, particularly in the form of metastasis, even among patients who have undergone resection of the pancreatic tumor.

Metastasis formation is a complex process involving numerous factors, with platelets is suggested to play a significant role in this context. Thrombocytosis has frequently been associated with poorer survival in cancer patients. As a platelet inhibitor, aspirin is attributed various anti-carcinogenic effects, including a reduction in metastasis formation. Although the precise pathogenesis of these effects remains unclear, several potential pathways are proposed: Some regard aspirin as a chemopreventive agent and a suppressor of bioactivities of cancer cells. Others speculate that its effects are related to the inhibition of COX-2, cancer-related inflammatory reactions, prostaglandins, and the NF- κ B signaling pathway. Additionally, there is discussion about the impact of aspirin on circulating tumor cells. In this context, it is hypothesized that activated platelets may surround circulating tumor cells, providing protection against immune cells and killer cells, thereby preventing effective immune-mediated degradation. Patients who have undergone surgical resection are particularly susceptible to metastasis formation due to the release of a higher number of circulating tumor cells

into the bloodstream through tumor manipulation during surgery. Furthermore, postoperative immunosuppression weakens cell-mediated immunity.

While the effects of aspirin have been extensively studied for other cancer types, such as colorectal carcinoma, data on its effects in patients with pancreatic carcinoma are scarce, particularly in those who have undergone primary resection. Therefore, we conducted a retrospective single-center analysis of 213 patients who underwent primary resection of Pancreatic Ductal Adenocarcinoma (PDAC) from January 2000 to December 2018 at the University Hospital of Erlangen. Patients were stratified according the aspirin intake in three groups: Continuous aspirin intake (cASS), perioperatively Interrupted Aspirin Intake (iASS) and no Aspirin Intake (no ASS) at the timepoint of surgery [1].

Our results showed that postoperative morbidity (iASS:54% vs. cASS: 53% vs. no ASS:64%, $p=0.448$) and in-hospital mortality (iASS:4% vs. cASS:10% vs. no ASS: 3%, $p=0.198$) did not differ in the ASS-intake groups. Similarly, there were no differences in Overall Survival (OS) and Disease-Free Survival (DFS) between the groups comparing the ASS-intake status (OS: iASS 17.8 months vs. cASS 19.6 months vs. no ASS 21.6 months, $p=0.489$; DFS: iASS 14.0 months vs. cASS 18.3 months vs. no ASS 14.7 months, $p=0.957$). In multivariate analysis, age (Hazard Ratio (HR) 2.2, $p<0.001$), lymph node positive (HR 2.0, $p<0.001$), R-status 1 or 2 (HR 2.8, $p<0.001$) and differentiation with a grading of 3 (HR 1.7, $p=0.005$) could be identified as independent prognostic factors regarding the OS. Moreover, multivariate analysis revealed age (HR 1.5, $p = 0.040$), lymph node positive (HR 1.8, $p=0.002$) and high grade (G3) carcinomas (HR 1.5, $p=0.037$) as independent prognostic parameters for DFS [1].

In the existing literature, two other studies have explored the impact of aspirin intake on survival in comparable patient cohorts with pancreatic cancer. In contrast to our findings, both of these studies reported a favorable prognostic effect of aspirin intake on postoperative survival [2, 3]. However, all three studies, including our own, are retrospective in nature and conducted with a limited number of patients, which

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could potentially introduce bias. Therefore, high-quality randomized controlled trials are essential to elucidate the influence of aspirin on long-term survival in patients with pancreatic carcinoma.

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