Risk of myocardial infarction following capecitabine treatment in patients with gastrointestinal cancer - a nationwide registry-based study


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Background: Myocardial infarction is a cardiac adverse event associated with fluoropyrimidines such as 5-fluorouracil and its orally available prodrug capecitabine. There are limited data on the incidence, risk, and prognosis of capecitabine associated myocardial infarction.

Purpose: The aim of this study was to examine the risk of myocardial infarction in patients with gastrointestinal (GI) cancer treated with capecitabine compared with age- and sex-matched population control subjects without cancer (1:2 ratio).

Methods: Patients with GI cancer treated with capecitabine between 2004-2016 were identified within the Danish National Patient Registry. Those with a history of ischemic heart disease were excluded. Absolute and relative risks of myocardial infarction at 6 months and 1 year were derived from multivariable Cox regression with average treatment effect modeling. Estimates were standardized to the distributions of age, sex, selected comorbidities, and pharmacotherapies of all included subjects.

Results: A total of 71,460 patients were included in the final analysis of whom 23,820 had GI cancer treated with capecitabine, and 47,640 were population control subjects without cancer. Differences in the prevalences of selected comorbid conditions, including diabetes, hypertension, and other risk factors for coronary artery disease and antianginal medications were not significant (P > 0.05 for all). The 6-month absolute risk (AR) of myocardial infarction was significantly higher for capecitabine-treated patients at 0.6% [95% confidence interval (CI): 0.5%-0.7%] versus 0.3% [95% CI: 0.2%-0.3%] in population control subjects, corresponding to a relative risk (RR) of 2.00 [95% CI 1.53-2.48; P < 0.001]. The corresponding 1-year ARs were 0.7% [95% CI: 0.6%-0.9%] versus 0.6% [95% CI: 0.5%-0.6%]; RR 1.28 [95% CI 1.03-1.52; P = 0.03]. Six-month and one-year all-cause mortality ARs for patients treated with capecitabine versus controls were 15.2% vs. 0.7% and 29.7% vs. 1.6% respectively.

Conclusions: The risk of myocardial infarction of capecitabine-treated patients both 6- and 12-month risks were significantly higher compared with population controls. Despite the absolute risk were low, the clinical significance of the differences appears limited in the context of the significant competing risk of death in this population.
Mortality

![Graph showing mortality over follow-up time in months. The graph compares capcitabine-treated patients to age- and sex-matched controls.](image-url)