The Risk of Second Primary Colorectal Adenocarcinomas is not Increased among Patients with Gastroenteropancreatic Neuroendocrine Neoplasms – A Nationwide Population Based Study

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AIM
In a nationwide population based study, we investigated the risk of second primary colorectal adenocarcinomas (SPCA) in patients with gastroenteropancreatic neuroendocrine neoplasms (GEP-NENs).

BACKGROUND
SPCAs may occur with a higher frequency in GEP-NEN patients. SPCAs are divided into synchronous (appear within the first six months after a diagnosis of NEN) or metachronous cancers (appear more than six months after a diagnosis of NEN).

METHODS
Using the nationwide Danish registries, we identified 2,831 GEP-NEN patients (median age 63 years (IQR 50-73 years), 53 % women) diagnosed in 1995-2010. We used Cox regression to compare the incidence of SPCA in GEP-NEN patients relative to a gender- and aged-matched general population sample of 56,044 persons. We used the cumulative incidence function to compare the cumulative risk of colorectal adenocarcinoma, considering death without colorectal adenocarcinoma as a competing risk.

CONCLUSION
In this population based study, there was no increased risk of SPCA among GEP-NEN patients. The clinical work-up in newly diagnosed GEP-NEN patients likely explains the positive short-term association followed by a negative association.

RESULTS
We observed 20 SPCAs among the 2,831 GEP-NEN patients with a total time at risk of 14,003 years (incidence = 143 per 100,00 person-years) and 770 colorectal adenocarcinomas in the general population of 56,044 persons with a total time at risk of 466,801 years (incidence = 165 per 100,000 person-years. The hazard ratio (HR) of SPCA from GEP-NEN diagnosis to end of follow up was 1.22 (95% CI: 0.78-1.92) in GEP-NEN patients compared to the general population. This nonsignificant association was the result of a strong positive association in the first 6 month after diagnosis of GEP-NEN (HR = 9.43 (95% CI: 4.98-17.86)) followed by a negative association in the remainder of the follow up period (HR = 0.50 (95% CI: 0.20-1.21)). The 10-year cumulative risk of colorectal adenocarcinoma was 0.7 % (95% CI: 0.5-1.1) for GEP-NEN patients vs. 1.4 % (95% CI: 1.3-1.6) for controls (figure 1).

Figure 1: Cumulative risk of colorectal adenocarcinomas for GEP-NEN patients (red) and controls (green)