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Are cancer patients at increased risk of diabetes?

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Diabetes mellitus (DM) is an established risk factor for cancer (1-2). To this day, however, there are only limited data on the risk of cancer patients developing diabetes.

This risk was recently investigated in South Korea in a large retrospective observational study (4) based on data from NHIS-NSC (*) covering the period from January 2003 to December 2013. None of the participants had any history of cancer or diabetes. About 500 000 subjects, age range 20-70 years (mean 41.8 ± 12.5), 50% women, were enrolled.

During the period of observation, 15139 participants (3%) developed a cancer, and 26510 (5.3%) DM. In 834/26610 diabetics (3.1%), the diagnosis of DM followed that of cancer (incidence 17.4/1000/year). In the remaining 25776 cases (96.9%), the diagnosis of DM preceded that of cancer, or was made in patients who did not develop a tumor (incidence 7.5/1000/year).

After adjusting for age, sex, pre-existing risk factors, metabolic factors and comorbidity, the hazard ratio (HR) for the development of DM following the diagnosis of neoplasia was 1.35 (95% CI 1.26-1.45, p <0.001). The HR was significant in 9 kinds of cancers: pancreas (HR 5.15), kidney (HR 2.06), liver (HR 1.95), gallbladder (HR 1.79), lung (HR 1.74), blood (HR 1.61), breast (HR 1.60), stomach (HR 1.35), and thyroid (HR 1.33). It is noteworthy that the increased risk of DM did not manifest in all obesity-related tumors, as shown by the absence of increased risk of DM in patients with cancer of the endometrium and colorectal cancer.

The excess risk was prominent in the two years preceding the diagnosis of cancer. After adjusting for all the risk factors, the risk of developing diabetes after the diagnosis of cancer was:

- first 2 years: HR 1.47 (95% CI 1.35-1.60);
- between third and fifth year: HR 1.14 (95% CI 0.97-1.33);
- between sixth and tenth year: HR 1.19 (95% CI 1.00-1.43).

Comments and Conclusions

The study shows a significant increase in the risk of DM in the 10 years following the diagnosis of neoplasia, particularly in the first two years.

Among the limits of the study:

- Absence of data on the stage of the cancer at diagnosis;
- Study limited to Korean population, hence difficulty in extrapolating its results to populations with different genetic backgrounds. Interestingly, in a USA study the risk of breast cancer was significantly increased in women with prediabetes (OR 1.16) (5), supporting a possible oncogenic role for the hyperinsulinism that precedes the diagnosis of DM (6).

In the current Korean study, the presence of cancer was associated to higher risk of DM in patients who survived the tumor. This may suggest that cancer patients are at higher risk of DM than non-cancer patients, and should therefore be evaluated for DM.

The study also suggests that the evolution and the response to therapy of DM could be related to the type of cancer and its treatment. The cancer treatment itself (chemo-therapy, steroids) may promote the development of DM (as suggested by the higher increase in risk of DM in the two years after the diagnosis of cancer). In conclusion, these data generate hypotheses, which, if confirmed by further research, should lead to an adequate metabolic follow-up in patients with cancer.

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(*) Since 1963, the republic of South Korea provides health coverage (*National Medical Insurance Act*), which in 1989 has been extended to the totality of the resident population. Since 2000, a single insurance system (derived from the integration of over 366 insurance companies) (*National Health Insurance Service, NHIS)* provides further preventive, diagnostic and therapeutic services, including screening. Data from participants are recorded in a national register and fed into a database (*National Health Information Database, NHID*). This database, however, is complex to use, due to its size and the difficulty to verify individual patient data. This prompted the South Korean government to establish a new database (*National Health Insurance Service – National Sample Cohort*) finalized to research purposes and covering only a representative sample of 2.2% of the population (7).

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