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Congenital heart disease and cancer

Cancer risk, risk factors and outcomes after cancer diagnosis

Akademisk avhandling

som för avläggande av medicine doktorsexamen vid Sahlgrenska akademin, Göteborgs universitet kommer att offentligen försvaras i konferensrum Europa på Wallenberg konferenscentrum, Medicinaregatan 20, Göteborg
torsdagen den 23 maj 2024, klockan 09:00

av Christina Karazisi, leg läkare

Fakultetsopponent:
Professor Michael A. Gatzoulis
National Heart & Lung Institute, Imperial College, London, Storbritannien

Avhandlingen baseras på följande delarbeten

I. Mandalenakis Z, Karazisi C, Skoglund K, Rosengren A, Lappas G, Eriksson P, Dellborg M. Risk of Cancer Among Children and Young Adults With Congenital Heart Disease Compared With Healthy Controls.
JAMA Netw Open. 2019 Jul 3;2(7):e196762.

II. Karazisi C, Dellborg M, Mellgren K, Giang KW, Skoglund K, Eriksson P, Mandalenakis Z. Risk of cancer in young and older patients with congenital heart disease and the excess risk of cancer by syndromes, organ transplantation and cardiac surgery: Swedish health registry study (1930-2017).
Lancet Reg Health Eur. 2022 May 29;18:100407

III. Karazisi C, Dellborg M, Mellgren K, Giang KW, Skoglund K, Eriksson P, Mandalenakis Z. Outcomes after cancer diagnosis in children and adult patients with congenital heart disease in Sweden – a registry-based cohort study.
Accepted for publication in BMJ Open

IV. Karazisi C, Dellborg M, Mellgren K, Giang KW, Skoglund K, Eriksson P, Mandalenakis Z. Heart failure in patients with congenital heart disease after cancer diagnosis.
Submitted

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Cancer risk, risk factors and outcomes after cancer diagnosis

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Abstract
Background: Congenital heart disease (CHD) is the most common congenital defect. The aim of this thesis was to study whether there is a higher cancer risk in CHD patients than in the general population (papers I and II), to explore possible risk factors for cancer development such as syndromes, organ transplantation and cardiac surgery (paper II) and study outcomes after cancer diagnosis: mortality (paper III) and heart failure (HF) (paper IV).

Methods: In paper I, 21 982 CHD patients born 1970–1993 were identified through the Swedish National Patient Register and matched by birth year, sex and county with 219 816 non-CHD controls from the Total Population Register. In paper II, 89 542 CHD patients born 1930–2017 were matched by sex and birth year with 890 472 controls. In paper III, CHD patients born 1970–2017 were matched by birth year and sex with 10 non-CHD controls. Included in the study were those with a cancer diagnosis born in Sweden: 758 CHD patients and 3670 non-CHD controls. The Cause of Death Register was used to identify causes of death. In paper IV, CHD patients with cancer born 1952–2017 were matched by propensity score with non-CHD controls with cancer and, in a separate analysis, with CHD patients without cancer. Individuals with HF prior to cancer diagnosis were excluded. Incidence rates for cancer, mortality and HF were calculated as total events divided by the cumulative follow-up time for the study population. Hazard ratios (HR) for cancer, mortality and HF risk were derived using Cox hazard regression models.

Results: The cancer risk among CHD patients was more than double that of controls (HR 2.24; 95% CI 2.01–2.48) (paper I). The elevated risk was confirmed in paper II, with children having the highest relative risk (HR 3.21; 95% CI 2.90–3.56). After excluding patients with syndromes and transplant recipients the risk remained. Children who underwent cardiac surgery had a higher cancer risk (paper II). Across all CHD patients, cancer accounted for less than 2% of deaths. The mortality risk was about 1.5 times higher in cancer patients with CHD than in non-CHD controls; however, the difference was no longer statistically significant after adjustments and exclusion of patients with syndromes and transplant recipients (paper III). The HF risk after cancer diagnosis was more than four times higher in CHD patients than in non-CHD controls and about 1.5 times higher than in CHD patients without cancer (paper IV).

Conclusion: We found an elevated cancer risk in CHD patients. The risk remained after excluding patients with syndromes and transplant recipients. Cardiac surgery during childhood appears to be a risk factor for cancer development. Mortality risk did not differ between cancer patients with or without CHD after adjustments and exclusion of patients with syndromes and transplant recipients. The excess HF risk for CHD patients with cancer compared to CHD patients without cancer is on a similar level to that previously reported in general for cancer survivors. Thus, the higher HF risk relative to non-CHD cancer patients may be more attributable to CHD itself rather than to cancer treatment related side effects.

Keywords: congenital heart disease; cancer; cancer risk; risk factors; outcome

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