Cardiovascular diseases mortality following cancer during childhood: long term risk, role of chemotherapy and of radiation dose to heart and brain

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Abstract

Background: A multi-centric French-UK cohort study was performed to evaluate the role of treatment in the long-term overall and cause-specific mortality among childhood cancer survivors.

Methods: This study cohort included 4,120 patients treated for a solid tumours before the age of 17 between 1942-1986, in 8 centres in France and UK and who survived at least 5 years from diagnosis. Detailed clinical and therapeutic data were extracted for each patients from medical records. For 2868 of the 2868 patients who received radiotherapy, radiation doses were estimated using DOS_EG software at 188 anatomical sites, including heart (7 sites) and lungs (10 sites). We obtained the death causes of 95% of dead patients. Overall and cause-specific mortality standardized ratios (SMR), absolute excess risk (AER) of death were studied using Poisson regression.

Results: 603 patients died during the follow-up, i.e. 8.5-fold (95%CI: 7.7-9.1) more than that expected in the general population. A total of 32 patients died of cardiovascular diseases, i.e. 4.8-fold (95%CI, 3.3 to 6.7) more than expected, 21 of which were cardiac diseases, i.e. 6.0-fold more (95%CI, 3.8 to 9.0). Overall, patients who had received radiotherapy had a 5.4-fold (95%CI, 1.5 to 32.1) higher risk of mortality due to cardiovascular disease than those who had not. Mortality due to cardiac disease was related to the administration of alkylating agents and / or vinca alkaloids, and to that of anthracyclines. Each additional 100 mg of anthracyclines per m² of body surface area increased the mortality rate due to heart diseases by 92% (95%CI, 16% to 318%). Patients who had received between 5 to 14.9 Gy to the heart during radiotherapy had a 14.5-fold (95%CI, 2.0 to 291) higher risk of mortality from cardiac diseases than patients who had not received radiotherapy, this ratio being 32.6 (95% CI, 5.6 to 622) in those who had received more than 15 Gy.

Conclusion: Childhood cancer survivors are at high long-term risk of mortality from cardiovascular pathologies when treated with radiotherapy if the average radiation dose to the heart or to the brain is higher than 5 Gy, or when treated with anthracyclines, alkylating agents and / or vinca alkaloids.

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