Cancer therapeutics-related heart failure from a cohort study using big data of electronic health record in Japan.

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Background: The prognosis of cancer patients has been improved partly because of the progress in cancer therapy, which increases the cancer survivors in the society. It may raise a concern regarding the development of heart failure (HF), because the anticancer agents have some serious side effects on cardiovascular system, especially in the aging society including Japan. However, the epidemiological data for the risk of HF in the cancer survivors is limited due to the lack of comprehensive dataset in the aging society. In this regard, the electronic health record (EHR), a big data, from the National Health Insurance in Japan provides a unique opportunity to obtain the suitable dataset.

Purpose: The purpose of this study was to clarify the prevalence and the risk factors of HF in cancer survivors, focusing on the impact of their age, using EHR in Japan.

Methods: We examined the EHR of 17.8 million patients, covering 14% of the total Japanese population. The EHR includes the diagnoses as coded with International Classification of Diseases, 10th revision (ICD-10), and the information for therapeutics. We extracted 159,380 patients who received anticancer agents between April 2008 to January 2017. HF patients were identified according to ICD-10 codes and the record for the use of therapeutic drugs for HF at least once after the HF diagnosis following the treatment with anticancer agents. We excluded the patients if they had other conditions indistinguishable from HF or if they had past history of HF before receiving anticancer agents.

Results: The mean follow-up period was 1.75 years and mean age (standard deviation) was 68.9 (11.6) years. The population over 75 years old were 37%, while males were 59.5%. There were prostate cancer (28.1%), lung cancer (13.4%), and colon cancer (12.6%) in males, and breast cancer (42.8%), colon cancer (11.5%), and lung cancer (8.6%) in females. Among them, 5,529 patients were diagnosed with HF, corresponding to the prevalence of 3.8%. The mean time form the initiation of chemotherapy to the HF onset was 1.03 year. In the Cox’s proportional hazard model after the adjustments for comorbidity, HF was more prevalent in males with hazard ratio (HR) 1.07 and 95% C.I. 1.01-1.13 (p<0.05) and in those with obesity (HR 1.18, 95% C.I. 1.09-1.26, p<0.01). We divided the subjects into three age groups (younger; <65 years, intermediate; 65-74 years, older; ≥75 years). HF was more prevalent in older group than younger group (HR 1.72, 95% C.I. 1.60-1.85, p<0.01). Among the anticancer agents, doxorubicin showed HR 2.09 (95% C.I. 1.89-2.3, p<0.01), and trastuzumab showed HR 1.47 (95% C.I 1.25-1.73, p<0.01).

Conclusion: We showed that the average prevalence of HF after anticancer agent was 3.8%. The independent risk factors for HF were older age, male, obesity, and the use of doxorubicin or trastuzumab. This study also demonstrated the usefulness of EHR in Japan, to investigate the cardiovascular risk associated with the anticancer agents.