Heart failure (HF) and cancer are two major public health challenges worldwide. The ageing demographics, along with increasing prevalence of antecedents e.g. hypertension, diabetes, coronary artery disease, obesity and atrial fibrillation are driving the epidemic of HF globally. The improvement of HF management has further extended the longevity and increased the clinical relevance of non-cardiac morbidity and mortality in patients with HF. Recent epidemiologic studies have demonstrated that cancer is the leading cause of non-cardiac death in patients with HF. Besides shared risk factors, such as diabetes mellitus, smoking, dyslipidemia, it has been hypothesized that HF is an oncogenic condition, possibly related to links between neurohormonal activation to tumorigenesis, systemic pathological processes such as inflammation and oxidative stress, common genetic predisposition and clonal hematopoiesis of cancer and HF. Preventive strategies to reduce the burden of cancer in HF patients is hence urgently needed.

Methodology

Propensity score (PS) approach was used to address biases in the allocation of treatment. Covariates that were considered prognostically significant as well as those influenced treatment selection were logistically regressed to the probability of receiving treatment. An inverse propensity of treatment weighting (IPTW) was used, allowing a pseudo-population to be created through assigning individuals with weights that corresponded to the inverse of their probability of receiving treatment given observed covariates.

The differences in the prevalence of covariates between statin users and nonusers were considered insignificant if the standardized mean difference (SMD) was ≤0.10. Cox proportional-hazards modelling was used, and statin exposure was further entered as a time-dependent variable to determine the effect of statin use, including covariates used in calculating the propensity score in “doubly robust estimation”. A Fine and Gray model was used to adjust for competing risks, with the competing events being all-cause mortality and non-cancer-related death. Associations were considered significant if the p-value was below 0.05.

Results

Of all eligible subjects, the mean age was 76.5±12.8 years, 47.8% was male. Over a median follow-up of 4.1 years (interquartile range [IQR]: 1.6 to 6.8), 11,052 (12.7%) were diagnosed with cancer. Figure 1 Statin use (vs. none) was associated with a 16% lower risk of cancer incidence (multivariable adjusted subdistribution hazard ratio [SHR]=0.84; 95% Confidence Interval [CI], 0.80 to 0.89). (Table 1, Figure 2) This inverse association with risk of cancer was duration-dependent, as compared with short-term statin use (3 months to <2 years), the adjusted SHR were 0.99 (95% CI, 0.87 to 1.13) for 2 to < 4 years of use, 0.82 (95% CI, 0.70 to 0.97) for 4 to < 6 years of use, and 0.78 (95% CI, 0.65 to 0.93) for ≥ 6 years of use. (Table 2) Ten-year cancer-related mortality was 3.8% among statin users and 5.2% among nonusers (absolute risk difference, −1.4% percentage points [95% CI, −1.6% to −1.2%]; adjusted SHR=0.74; 95% CI, 0.67 to 0.81). Statin use (vs. none) was associated with a 26% lower risk of cancer incidence (SHR =0.74; 95%CI, 0.67 to 0.81). (Table 1, Figure 3)