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Cancer History Portends Worse Acute and Long-term Noncardiac (but Not Cardiac) Mortality After Primary Percutaneous Coronary Intervention for Acute ST-Segment Elevation Myocardial Infarction

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Abstract

Objective: To define the effect of a history of cancer on in-hospital and long-term mortality after primary percutaneous coronary intervention (PCI) for ST-segment elevation myocardial infarction (STEMI).

Patients and Methods: In this retrospective cohort study of 2346 patients with STEMI enrolled in the Mayo Clinic PCI registry from November 1, 2000, through October 31, 2010, we identified 261 patients (11.1%) with a history of cancer. The in-hospital and long-term outcomes (median follow-up, 6.2 years; interquartile range=4.3-8.5 years), including cardiac and noncardiac death and heart failure hospitalization, of these patients were compared with those of 1313 cancer-negative patients matched on age, sex, family history of coronary artery disease, and date of STEMI.

Results: Patients with cancer had higher in-hospital noncardiac (1.9% vs 0.4%; P=.03) but similar cardiac (5.8% vs 4.6%; P=.37) mortality as matched controls. The group at highest acute mortality risk were those diagnosed as having cancer within 6 months before STEMI (hazard ratio [HR]=7.0; 95% CI, 1.4-34.4; P=.02). At 5 years, patients with cancer had similar cardiac mortality (4.2% vs 5.8%; HR=1.27; 95% CI, 0.77-2.10; P=.35) despite more heart failure hospitalizations (15% vs 10%; HR=1.72; 95% CI, 1.18-2.50; P=.01) but faced higher noncardiac mortality (30.0% vs 11.0%; HR=3.01; 95% CI, 2.33-3.88; P<.001) than controls, attributable solely to cancer-related deaths.

Conclusion: One in 10 patients in this contemporary registry of patients undergoing primary PCI for STEMI has a history of cancer. These patients have more than a 3 times higher acute in-hospital and long-term noncardiac mortality risk but no increased acute or long-term cardiac mortality risk with guideline-recommended cardiac care.

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For editorial comment, see page 1675; for related articles, see pages 1693 and 1706

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Since the 1990s there has been a steady decline in cancer-related mortality.[1] As a consequence, the number of cancer survivors has been steadily rising to now nearly 15 million in the United States alone.[2] A third of the survivors are deemed to be at high lifetime risk for cardiotoxicity due to exposure to anthracyclines.[1] Although this cardiotoxicity can present within 1 year of therapy, it may become evident only several years after therapy.[3] Before the clinical presentation of cardiomyopathy, however, these patients may already have a reduced contractile reserve.[4,5]

Lasting cardiovascular effects of cancer therapy may also reduce the compensatory reserve to acute clinical events such as acute myocardial infarction (AMI). Indeed, experimental studies found that sorafenib markedly increases the mortality of acute coronary occlusive episodes.[6] Interestingly, this detrimental effect did not seem to be related to precipitation of more extensive infarctions but rather to inhibition of c-kit–mediated stem

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cell proliferation and repair. In distinction from anthracyclines, these effects of targeted cancer therapies are to abate over time.[1] Thus, there might be a time dimension to the risk of vulnerability of patients with cancer to cardiac injuries depending on the type of therapy and the proximity to an acute cardiac event.

A study from the National Heart, Lung, and Blood Institute Dynamic Registry identified a history of cancer as a significant independent predictor of 1-year death and AMI for patients with AMI.[7] Moreover, patients with AMI with a history of cancer were noted to have higher overall but not cardiac in-hospital mortality.[8] In the most comprehensive and specific analysis so far, patients with ST-segment elevation myocardial infarction (STEMI) with a cancer history were noted to have higher 1-year overall and cardiac mortality.[9] The increased risk of death was eminent during the acute hospitalization but not thereafter and was confined to patients diagnosed as having cancer in the 6 months before the acute event.

The present retrospective cohort study was performed to further define the acute and long-term outcome dynamics of patients with STEMI with a history of cancer compared with an age- and sex-matched group of control patients without cancer. In extension of the previous studies, the present study specifies in greater detail the type of chemotherapeutic subgroups for analysis and acute in-hospital and long-term outcomes.

METHODS

Patient Population

The centralized Mayo Clinic Catheterization Laboratory percutaneous coronary intervention (PCI) registry prospectively collects clinical information, angiographic and procedural characteristics, postprocedural cardiac events, and outcomes of all patients undergoing PCI at the Rochester campus of Mayo Clinic since 1979. For this analysis, all patients enrolled in the database from November 1, 2000 (start date for entry differentiation between STEMI and non-STEMI in the registry), through October 31, 2010 (end date to allow for 5-year follow-up data), were screened according to a predesigned search strategy (cross-referencing with the Mayo Clinic cancer database and clinical data repository search software using *International Classification of Diseases, Ninth Revision* coding) to identify those with a cancer history. All patients with cancer were included in this study except those with nonmelanoma skin tumors given their borderline malignant nature and difficulty of group allocation.[9] The medical records of patients with cancer were reviewed for details of their cancer history and cancer therapy. Chemotherapeutic agents were defined as cardiotoxic if a decrease in cardiac function or heart failure was listed as one of their well-described adverse effects. They were considered vasotoxic if they had been associated with symptomatic coronary, carotid, or peripheral arterial disease. Radiation therapies were further divided into chest and nonchest based on the radiation field. A cohort of patients with STEMI with no history of cancer was matched to these patients with cancer, as further detailed later herein. Acute cardiovascular events were adjudicated as outlined elsewhere.[10] After PCI, each patient was surveyed for major adverse cardiovascular events by telephone using a standardized questionnaire at 6 months, 1 year, and then annually after the procedure by trained data technicians. All long-term follow-up events were confirmed and adjudicated by review of medical records, as detailed elsewhere.[11] Patients lost to follow-up were treated as censored on the last day of contact.

Classification of Cause of Death

As previously outlined elsewhere,[11] deaths were primarily ascertained via scheduled surveillance telephone contact. The Mayo Clinic registration office, which serves as a central repository of all patient death notifications, provided an additional source. Once confirmed, details of a death were obtained through telephone contact with family and external providers and through review of local and external medical records. Death certificates were requested for all patients. Experienced data technicians recorded the details of each death and performed the initial classification. When cause of death could not initially be obtained (10% of total deaths), information was requested from the National Death Index. Two physicians reviewed each death, rescreened medical records where appropriate, and resolved disparity by consensus. Final classification (subclassification) was performed into