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RESEARCH LETTERS

Incidental Coronary Artery Calcification in Cancer Imaging

Cardiovascular (CV) disease is a leading cause of death among 15 million cancer survivors in the United States today (1). Mitigating CV risk in this population should be a priority for both oncologists and cardiologists. Most patients with cancer undergo nongated chest computed tomography (NGCCT) imaging for diagnosis, staging, and/or surveillance. Incidental detection of coronary artery calcification (CAC) on NGCCT in oncology patients may present an opportunity to detect and modify CV risk through lifestyle interventions, or pharmacological therapy as appropriate (e.g., use of statin and/or aspirin), especially for those without known atherosclerotic CV disease (ASCVD). We hypothesize that knowledge of CAC rarely influences preventive practices in the cancer population in clinical practice, and it may constitute a missed opportunity for reducing CV risk.

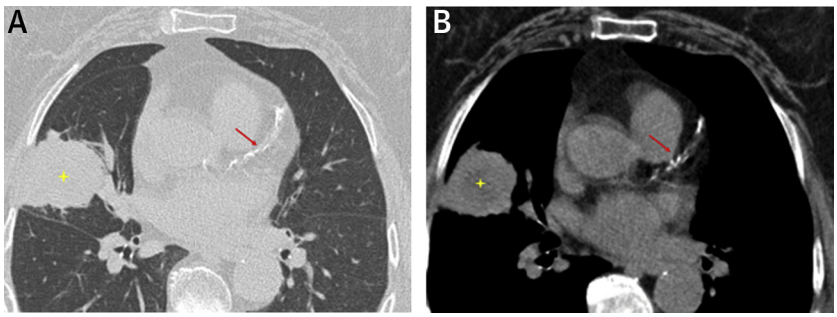
Five-year survival rates for non-small cell lung cancer (NSCLC) now reach 70% to 90% for small, localized tumors (2,3). Because of shared risk factors, adverse CV events are frequently observed among NSCLC survivors (4). In this retrospective study, we sought to assess the prevalence of CAC on NGCCT performed at diagnosis of early-stage NSCLC, and to determine whether the incidental finding of CAC influenced subsequent prescription of statin and/or aspirin.

Noncontrast NGCCT scans performed across 25 hospitals in 164 patients at diagnosis of early-stage NSCLC were assessed for CAC (**Figure 1**). The mean age was 68 ± 10 years, 64 (39.0%) were men, and 132 (80.5%) had stage 1 disease. A radiologist and a cardiologist with advanced training in CV imaging independently and blindly reviewed CT images. The readers provided a simple, overall visual assessment of none, mild, moderate, or severe CAC for the entire coronary arterial circulation. A third reader provided consensus in cases of disagreement. CAC was classified as mild if there were only isolated flecks of calcification; severe if there was continuous CAC within one or more coronary artery; and moderate if there was more than mild calcification but less than the description of severe calcification. This overall visual assessment approach to CAC quantification on NGCCT scans was validated by the National Lung Screening Trial investigators who reported good agreement with Agatston scoring, good inter-reader agreement among different radiologists, and that this approach was sufficient for CV risk classification (5).

CAC was present in 50 (98.0%) of 51 patients with known ASCVD and in 78 (69.0%) of 113 patients without pre-existing ASCVD. Of these 78 patients with CAC and no known ASCVD, CAC was graded as mild in 40 (51.3%), moderate in 24 (30.8%), and severe in 14 (17.9%); 51 (65.4%) were not on aspirin, 48 (61.5%) were not on statin therapy, and 36 (46.2%) were not on either therapy. Medication usage was reviewed again at a median of 198 (172 to 237) days after this index scan. Over this intervening period, among patients with CAC and no known ASCVD, aspirin was initiated in only 4 of 51 (7.8%) aspirin-naive patients and statin therapy was initiated in only 1 of 48 (2.1%) statin-naïve patients. Allergy or intolerance to either therapy was recorded for 3 patients. Aspirin was declined by 1 patient, and concurrent anticoagulation or gastrointestinal bleeding may have precluded aspirin prescription in 3 additional patients. No patients had abnormal liver function tests to deter statin therapy or severe thrombocytopenia to deter aspirin usage.

We demonstrate that CAC is prevalent (69%) among patients with early-stage NSCLC and no known ASCVD at time of cancer diagnosis, and that the incidental finding of CAC on NGCCT rarely results in prescription of either aspirin or statin therapy despite lack of contraindications to either therapy. This represents a missed opportunity to modify CV risk for a cohort of patients predisposed to adverse CV events. Similarly, existing data suggest underutilization of guideline-directed medical therapies including aspirin and statin therapy for secondary prevention in patients with cancer following acute myocardial infarction (AMI) (6,7). We recognize that safety concerns related to a higher prevalence of significant thrombocytopenia or hepatic dysfunction among patients with cancer compared with non-oncology cohorts may negatively influence prescription of aspirin and statin therapies, respectively. In a

FIGURE 1 Incidental Coronary Artery Calcification on Chest CT Performed in a Patient With Non-Small Cell Lung Cancer



(A) Lung window from a nongated, noncontrast chest computed tomography scan demonstrates a large mass in the right middle lobe **(yellow star)**, subsequently proven to be non-small cell lung carcinoma. **(B)** Corresponding mediastinal window demonstrates severe atherosclerotic calcification affecting the left anterior descending artery **(red arrow)**.

multivariable analysis of 456 patients with cancer and a discharge diagnosis of AMI, however, aspirin use was associated with a 23% decreased risk of death (7). Aspirin conferred a survival benefit in a small study of 70 patients with cancer with and without thrombocytopenia following an acute coronary syndrome (8). In another study of 118 patients with hematologic malignancies diagnosed with AMI, aspirin was associated with improved survival without increase in major bleeding, even in patients with severe thrombocytopenia (6). These data inform a consensus statement from the Society for Cardiovascular Angiography and Interventions that advocates to continue aspirin in patients with cancer who have an indication for antiplatelet therapy and a platelet count above 10,000/ml (9). Larger prospective multicenter studies to clarify safety of aspirin and statin therapy in patients undergoing active cancer care, particularly in the setting of thrombocytopenia, are needed to challenge the apparent underutilization of these therapies for primary and secondary prevention of adverse CV events in this cohort.

We observed a key obstacle that may have hindered an appropriate clinical response, in that the presence of CAC was included in NGCCT reports for only 27 (34.6%) patients with CAC and no pre-existing ASCVD. Radiologists need to recognize the opportunity to highlight the presence of coronary atherosclerosis in scans performed for cancer-specific indications. Similar attention should be awarded to atherosclerosis identified in other arterial territories. In addition to specific commentary on the presence and location of atherosclerosis in imaging reports, radiologists could specify the need for clinical correlation for these findings. This might reduce the likelihood that atherosclerosis is overlooked by clinicians more focused on cancer care. Cardiologists can also take advantage of existing cancer imaging when reviewing oncology patients by routinely conducting their own review of images for the presence, location, and burden of atherosclerotic calcification. When interpreting the clinical relevance of CAC identified during cancer imaging, cardiologists may underestimate cancer survival, whereas oncologists may underestimate the risk of adverse CV outcomes during survivorship. Better communication between oncologists and cardiologists might help improve and further optimize clinical management of cancer patients and survivors. The findings of this study performed in patients with NSCLC may also apply to patients with other malignancies who have NGCCT performed as part of their cancer care.

In an era when improving CV outcomes for cancer survivors is an important public health goal, the incidental finding of CAC on cancer imaging warrants specific recognition by reporting radiologists and careful consideration by clinicians, who should weigh potential merits of preventative pharmacological therapy in mitigation of CV risk throughout the period of cancer therapy and eventual survivorship.

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Current Management of Symptomatic Pericardial Effusions in Cancer Patients

Neoplasia and hematologic malignant diseases are common causes of acute pericardial effusion. The presence of malignant pericardial effusion (MPE) is associated with poor prognosis in these patients, with a shortened survival median time. The best management for symptomatic MPE (surgical drainage vs. percutaneous pericardiocentesis [PCC]) is controversial and is based on local experience. PCC could represent a less invasive, equally efficient, valuable option, although the lack of standardization of procedures could remain a confounding factor (1,2). The aim of our work was to evaluate the features and clinical outcomes (survival, effusion recurrence) of patients with symptomatic MPE that was managed by either PCC or surgical drainage.

We prospectively included as MPE all patients referred to our institution, the Institut Mutualiste Montsouris in Paris, France, who had a first episode of pericardial effusion requiring PCC or surgical drainage in the context of an ongoing or previous recent (<1 year) solid tumor or blood disorder between January 1, 2014, and December 31, 2017. Patients were excluded if they had pericardial effusion related to cardiac surgery, interventional procedures, or inflammatory disease.

Pericardial effusion drainage was considered in case of clinical symptoms and/or clinical tamponade. The procedure was chosen on the basis of a heart team decision according to the echocardiographic data, anatomic considerations, and surgical risk evaluation.

PCC was performed in a cardiac catheterization laboratory using fluoroscopic and echocardiographic guidance from the infrasternal angle, and a catheter was then inserted within the pericardial. A sample of pericardial liquid was analyzed (chemistry, cytology including fluid preparation evaluation and cell block evaluation with immunohistochemistry, and bacterial testing). Patients were all monitored in an intensive care unit, with echocardiographic evaluation once a day, and the pericardial catheter was removed when fluid drainage was <20 ml/day, without residual pericardial effusion. No sclerosing agent was used during the procedure. Echocardiography was performed a week later in our center to assess the disappearance of the effusion.

Surgical drainage was mostly performed by subxiphoid pericardiostomy, with a Redon drain positioned along the diaphragmatic surface of the heart. A pericardial window was performed only in case of recurrent MPE. Pericardial biopsy was sent for pathology analysis.

Recurrent pericardial effusion was documented by echocardiography and was defined as reaccumulation of pericardial fluid within 3 months after surgical drainage or pericardiocentesis. Management included repeated PCC, surgical drainage, and eventually placement of a surgical pericardial window.