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RESEARCH LETTER

Coronary Artery Calcium on Noncontrast Thoracic Computerized Tomography Scans and All-Cause Mortality

Genetic Epidemiology of COPD (COPDGene) Study

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Although coronary artery calcium (CAC) has extensive validation for predicting clinical events, little is known about how CAC interacts and predicts mortality in patients with chronic obstructive pulmonary disease (COPD). We evaluated the contribution of CAC to all-cause mortality and assessed the association of CAC with mortality varied by sex, race/ethnicity, and COPD GOLD category (Global Initiative for Chronic Obstructive Lung Disease) using the COPDGene study (Genetic Epidemiology of COPD). Smoking is not only the leading cause of lung cancer and COPD, but also a major risk factor for heart disease and associated with significantly higher atherosclerosis burden.[1] Smokers are more likely to die of cardiovascular disease (CVD) than lung cancer, which accounted for only 24.1% of all deaths in the National Lung Screening Trial.[1] Ungated low-dose multidetector row computerized tomography (CT), which is generally used for the assessment of lung cancer and COPD, can evaluate CAC.[2] Assessment of CAC during chest CT represents an opportunity to simultaneously identify asymptomatic individuals at increased CVD risk.[3] Thus, we sought to evaluate the relationship between the presence and severity of CAC and the risk of all-cause mortality in smokers with and without COPD.

COPDGene is a large, observational cohort study, evaluating the development of COPD in persons with a >10 pack-year smoking history and scientific data available at www.copdgene.org.[3,4] Overall, 6842 participants had both CAC measured from noncontrast CT scans and follow-up for mortality (median, 81.3 months). COPD GOLD stage is based on forced expiratory volume (FEV_1). Cox proportional hazards regression was used to evaluate the independent effect of CAC on all-cause mortality adjusting for age, sex, race, diabetes mellitus, self-reported hypercholesterolemia and hypertension, body mass index, cigarette pack-years, smoking status, and COPD GOLD stage. The study was approved by an institutional review board, and subjects gave informed consent.

Over a median of 81.3 months of follow-up, 850 of 6842 (12.4%) participants died. Mortality in the CAC=0 group was 8.4%; in the 1 to 100 group, mortality was 9.3%; in the 101 to 400 group, mortality was 12.7%; and in the >400 group, mortality was 24.4% (P<0.0001, Figure 1). GOLD 0 (no obstruction) included 3039, GOLD 1 (FEV_1 ≥80%) included 552, GOLD 2 (FEV_1 50-79%) included 1288, GOLD 3 (FEV_1 30-49%) included 751, and GOLD 4 (FEV_1 <30%) included 388 participants.

The highest CAC category (>400) was associated with increased mortality adjusted for known risk factors (hazard ratio [HR], 1.68; 95% CI, 1.30–2.03; P<0.0001), in comparison with individuals with no CAC. There was a strong interaction with COPD GOLD stage and CAC, where worsening mortality was independently associated with CAC and overall COPD (GOLD stages 1–4) (HR, 2.73; 95% CI, 2.27–3.28; P<0.0001). HRs increased across stages of COPD GOLD (stage 1 HR=1.24; stage 2 HR=2.16; stage 3 HR=3.96; and stage 4 HR=11.17).

Key Words: calcium ■ cardiovascular disease ■ mortality ■ pulmonary disease, chronic obstructive ■ tomography, x-ray computed

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CORRESPONDENCE

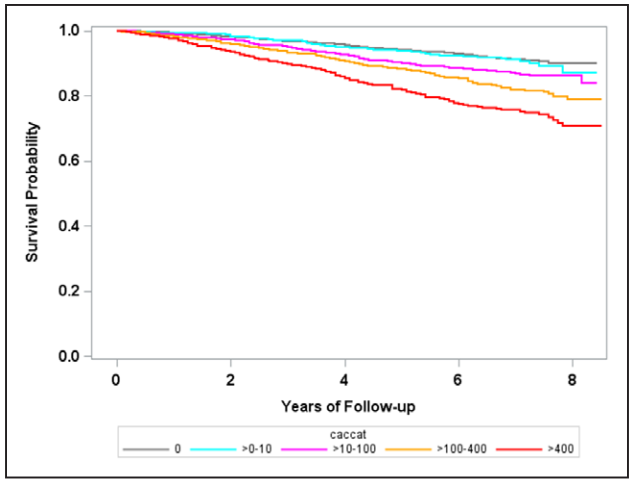

Figure. Kaplan-Meier survival curves.
All-cause mortality survival differed significantly by CAC severity (P<0.0001). Mortality in the CAC=0 group was 8.4%; in the 1 to 10 group, mortality was 9.3%; in the 11 to 100 group, mortality was 12.7%; in the 101 to 400 group, mortality was 17.3%; and in the >400 group, mortality was 24.4%. caccat indicates coronary artery calcium category.

Patients with high CAC burden and advanced COPD GOLD stage had ≈3-fold higher risk of all-cause mortality. In comparison with other cohorts without lung disease, the prediction of CAC on all-cause mortality is quite comparable,[5] suggesting no attenuation or competing risk from COPD. Considering that CVD is a more frequent cause of morbidity and mortality in this vulnerable population, there is a need to increase the awareness among persons with COPD that there is an underlying risk for clinical and subclinical CVD. Almost half of this cohort of smokers had no detectable CAC on ungated lung CT scans. The clinical importance of this study is the predictive power for mortality of CAC on routine CT scans, and the potential to screen for CVD among the 19 million ungated thoracic scans done annually in the United States, without additional radiation, cost, or participant burden.

ARTICLE INFORMATION

Data sharing: The data, analytic methods, and study materials will not be made available to other researchers for purposes of reproducing the results or replicating the procedure.

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Disclosures

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