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### **Breast**

# Identification of Risk of Cardiovascular Disease by Automatic Quantification of Coronary Artery Calcifications on Radiotherapy Planning CT Scans in Patients With Breast Cancer.

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#### **IMPORTANCE**

Cardiovascular disease (CVD) is common in patients treated for breast cancer, especially in patients treated with systemic treatment and radiotherapy and in those with preexisting CVD risk factors. Coronary artery calcium (CAC), a strong independent CVD risk factor, can be automatically quantified on radiotherapy planning computed tomography (CT) scans and may help identify patients at increased CVD risk.

#### **OBJECTIVE**

To evaluate the association of CAC with CVD and coronary artery disease (CAD) in patients with breast cancer.

#### DESIGN, SETTING, AND PARTICIPANTS

In this multicenter cohort study of 15,915 patients with breast cancer receiving radiotherapy between 2005 and 2016 who were followed until 31 December 2018, age, calendar year, and treatment-adjusted Cox proportional hazard models were used to evaluate the association of CAC with CVD and CAD.

#### **EXPOSURES**

Overall CAC scores were automatically extracted from planning CT scans using a deep learning algorithm. Patients were classified into Agatston risk categories (0, 1-10, 11-100, 101-399, >400 units).

#### MAIN OUTCOMES AND MEASURES

Occurrence of fatal and nonfatal CVD and CAD were obtained from national registries.

#### **RESULTS**

Of the 15,915 participants included in this study, the mean (SD) age at CT scan was 59.0 (11.2; range, 22-95) years, and 15,879 (99.8%) were women. Seventy percent (n = 11,179) had no CAC. Coronary artery calcium scores of 1 to 10, 11 to 100, 101 to 400, and greater than 400 were present in 10.0% (n = 1584), 11.5% (n = 1825), 5.2% (n = 830), and 3.1% (n = 497) respectively. After a median follow-up of 51.2 months, CVD risks increased from 5.2% in patients with no CAC to 28.2% in patients with CAC scores

higher than 400. After adjustment, CVD risk increased with higher CAC score (hazard ratio [HR]CAC = 1-10 = 1.1; 95% CI, 0.9-1.4; HRCAC = 11-100 = 1.8; 95% CI, 1.5-2.1; HRCAC = 101-400 = 2.1; 95% CI, 1.7-2.6; and HRCAC>400 = 3.4; 95% CI, 2.8-4.2). Coronary artery calcium was particularly strongly associated with CAD (HRCAC>400 = 7.8; 95% CI, 3.0-11.2). The association between CAC and CVD was strongest in patients treated with anthracyclines (HRCAC>400 = 5.8; 95% CI, 3.0-11.4) and patients who received a radiation boost (HRCAC>400 = 6.1; 95% CI, 3.8-9.7).

#### **CONCLUSIONS AND RELEVANCE**

This cohort study found that coronary artery calcium on breast cancer radiotherapy planning CT scan results was associated with CVD, especially CAD. Automated CAC scoring on radiotherapy planning CT scans may be used as a fast and low-cost tool to identify patients with breast cancer at increased risk of CVD, allowing implementing CVD risk-mitigating strategies with the aim to reduce the risk of CVD burden after breast cancer.