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Cardiac morbidity

Quantitative coronary angiography findings of patients who received previous breast radiotherapy

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ABSTRACT

Purpose: To compare the coronary angiographic findings between patients who had previous left sided versus right sided breast cancer radiotherapy (RT).
Materials and methods: Between 1995 and 2009, 12,696 patients who underwent curative RT for breast cancer at Princess Margaret Hospital were screened to assess if they had been investigated with a post-RT coronary angiogram. Two cardiologists, blinded to the laterality of radiation treatment, assessed all angiograms and measured the percentage of stenotic lesions, the mean diameters of each segment of the left anterior descending artery (LAD) and the right coronary artery (RCA) using quantitative coronary angiography (QCA).
Results: Ninety-one patients were included, 49 patients with left sided RT and 42 with right sided RT. The median time from RT to coronary angiogram was 4.2 years (range: 22 days–16.9 years). Seventeen patients (35%) in the left sided RT group and 17 (40%) in the right sided RT group needed coronary revascularization (percutaneous coronary intervention or by-pass surgery). The LAD territory was revascularized in 12 (24%) and 11 (26%) patients, respectively. The proportion of clinically significant stenoses, degree of stenoses and mean vessel diameter were not significantly different between the two groups. In 33 patients who had coronary angiograms >5 years after breast RT (17 left-sided and 16 right-sided), the only statistically significant finding was marginally narrower mid RCA segments among those who had right sided RT: 2.52 mm versus 2.92 mm ($P = 0.039$).
Conclusions: In our patients, left sided breast cancer RT did not increase the risk of coronary artery disease within the first few years, when compared to right sided RT. However, with the limitation of short duration between radiotherapy and coronary angiogram, late development of coronary artery stenoses 10–15 years after left sided RT could not be excluded.

Adjuvant radiotherapy for breast cancer has been shown to reduce the risk of loco-regional recurrence and improve overall survival [1]. However, previous studies have shown that breast radiotherapy is also associated with increased cardiac mortality and morbidity [2–10], especially from ischemic heart disease. Correa et al. [7] showed that patients treated with left sided radiation had an increased risk of late, radiation-associated coronary artery disease (CAD), compared to those treated with right sided radiation. In addition, the predominant vascular territory affected was the left anterior descending artery (LAD). In this study, we evaluated the coronary angiographic findings of patients who previously had radiotherapy to the breast or chest wall for the treatment of breast cancer, to determine whether CAD was over-represented in patients who previously had left sided irradiation compared to right sided irradiation. The hypothesis of the study is that, given that the mid and distal LAD artery frequently falls within the tangential radiation field for the treatment of left sided breast cancer [11], and the radiation dose received by mid to distal LAD far exceeds other coronary arteries [12–15], this can lead to a disproportionately high occurrence of CAD within these segments among patients who had left sided irradiation.

Materials and methods

Patient selection

University Health Network is a medical network comprising of three teaching hospitals affiliated with the Faculty of Medicine, University of Toronto: Princess Margaret Hospital, Toronto General Hospital and Toronto Western Hospital. Between 1995 and 2009, 12,696 patients in the Princess Margaret Hospital radiotherapy database underwent curative radiotherapy for breast cancer. Over the same period, there were 61,136 patients/episodes of interventional cardiac procedures within the hospitals of the UHN,

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according to the database held at the Department of Interventional Cardiology of the Toronto General Hospital. When the two databases were matched, 178 patients appeared on both databases. Patients were further screened to check if they had coronary artery angiography after their breast radiotherapy, and were included for assessment if their coronary angiograms were retrievable for evaluation. Seventy-three patients had coronary angiography prior to their radiotherapy and were, therefore, excluded. One hundred and five patients had coronary artery angiography after their breast cancer radiotherapy; the coronary angiograms were not retrievable for evaluation for 14 of them, leaving 91 patients for further evaluation.

Angiographic analysis

The retrieved coronary angiograms were evaluated by two cardiologists using quantitative coronary angiography (QCA). The cardiologists performing the QCA evaluations were blinded to the laterality of the patient's previous breast irradiation.

QCA has become the standard tool to assess angiographic outcome in coronary interventional studies; reference diameter (RD), minimal lumen diameter and lesion length can be measured, and other parameters like diameter stenosis can be derived [16]. With medical software aiding the digital image analyses, this methodology allows increased accuracy and reduced inter-observer and intra-observer variation. The degree of any stenotic lesion(s) and the mean diameters of each of the segments (proximal, mid and distal segments) of both LAD and right coronary artery (RCA) were assessed (Fig. 1). A clinically significant or severe coronary lesion was defined as the presence of a percentage of stenosis $\geqslant$ 50% and 70%, respectively.

Statistical analysis

Baseline patient characteristics including age, underlying cardiac risk factors and radiotherapy treatment details were retrieved from the medical records. For the comparison of these baseline characteristics between the two groups, i.e., those who had left sided irradiation and those who had right sided irradiation, we

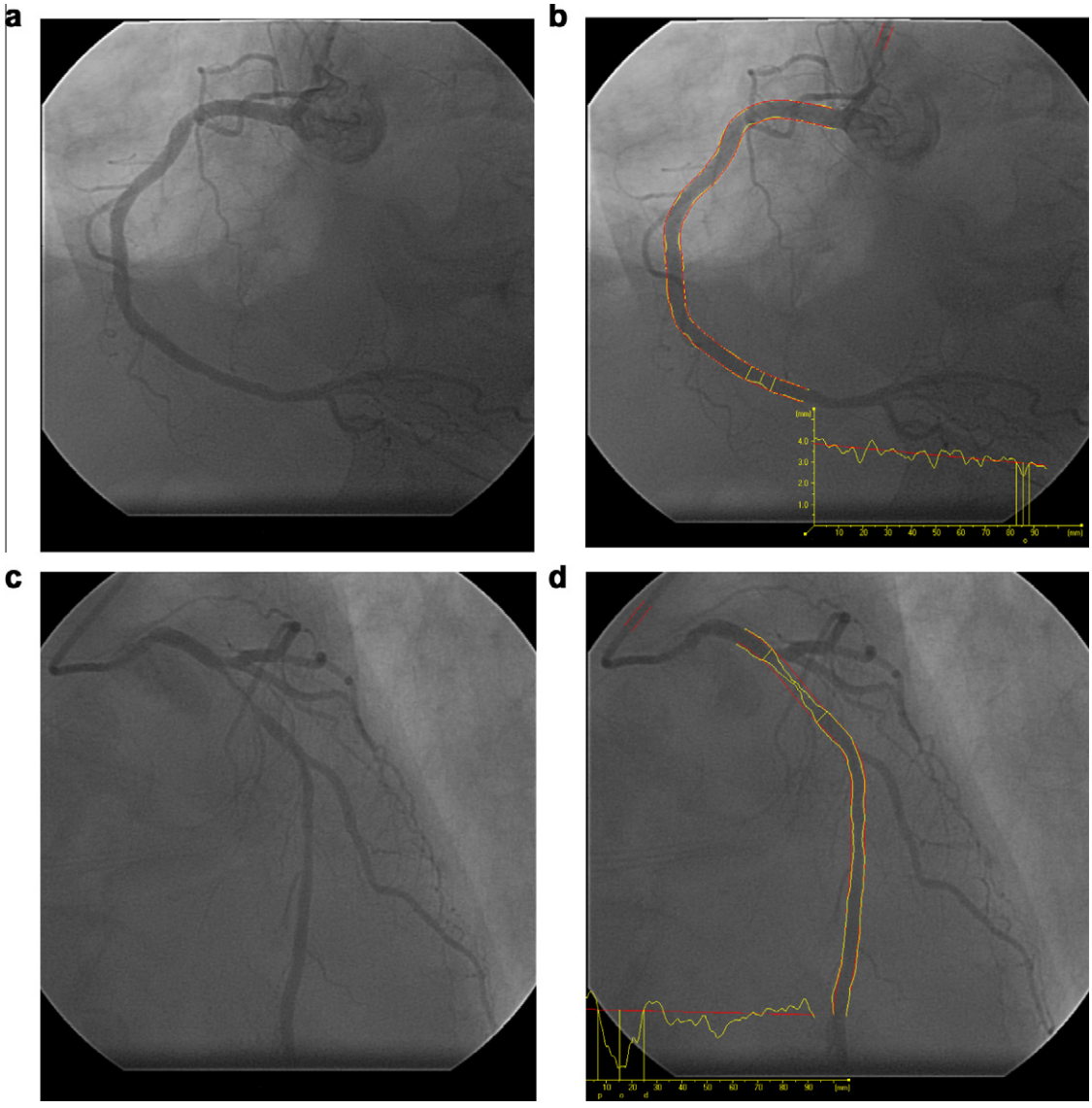

Fig. 1. (a) Digital angiogram of right coronary artery; (b) quantitative coronary angiography of right coronary artery; (c) digital angiogram of left anterior descending artery; (d) quantitative coronary angiography of left anterior descending artery. This patient has a 90% stenosis of the proximal LAD segment.