Available online at www.sciencedirect.com

ScienceDirect

journal homepage: www.JournalofCardiovascularCT.com

Original Research Article

Ascending and descending thoracic aorta calcification in type 2 diabetes mellitus

Timothy W. Churchill MD[a], *Suraj P. Rasania MD*[b], *Hashmi Rafeek MD*[c], *Claire K. Mulvey MD*[d], *Karen Terembula BS*[c], *Victor Ferrari MD*[c], *Saurabh Jha MD*[e], *Scott M. Lilly MD, PhD*[c], *Luis H. Eraso MD*[f], *Muredach P. Reilly MB, MSCE*[c], *Atif N. Qasim MD, MSCE*[g,*]

[a] *Department of Medicine, Brigham and Women's Hospital, Boston, MA, USA*
[b] *Department of Cardiovascular Medicine, Geisinger Medical Center, Danville, PA, USA*
[c] *Division of Cardiology, Hospital of the University of Pennsylvania, Philadelphia, PA, USA*
[d] *Division of Internal Medicine, University of California, San Francisco, San Francisco, CA, USA*
[e] *Department of Radiology, Hospital of the University of Pennsylvania, Philadelphia, PA, USA*
[f] *Jefferson Vascular Center, Thomas Jefferson University Hospital, Philadelphia, PA, USA*
[g] *Division of Cardiology, University of California, San Francisco, 505 Parnassus Avenue, San Francisco, CA 94143, USA*

ARTICLE INFO

Article history:
Received 30 January 2014
Received in revised form
24 February 2015
Accepted 18 April 2015
Available online 16 May 2015

Keywords:
Aorta
Arteriosclerosis
Calcium
Computed tomography
Diabetes mellitus type 2

ABSTRACT

Background: Calcification of the thoracic aorta is a risk factor for cardiovascular disease and peripheral arterial disease but has not been well studied in diabetics. In addition, many studies consider aortic calcium as a single anatomic entity, whereas calcification of the ascending and descending portions of the thoracic aorta may represent separate phenotypes. We sought to characterize the prevalence of ascending and descending aortic calcium among diabetics and to assess their associations with cardiovascular risk factors, coronary artery calcium, and peripheral arterial disease.

Methods: Within the Penn Diabetes Heart Study, a cross-sectional study of subjects with type 2 diabetes mellitus but without coronary or renal disease, we quantified Agatston scores of the ascending and descending thoracic aorta in 1739 subjects (63% male, 61% Caucasian). Multivariate logistic and Tobit regressions were used to assess associations with cardiovascular risk factors, coronary calcium, and peripheral arterial disease.

Results: Of all subjects, 54% had thoracic aortic calcium; of these, 37% had calcium solely in the ascending thoracic aorta and 20% solely in the descending thoracic aorta. In multivariate regression, age, Caucasian race, systolic blood pressure, low-density lipoprotein cholesterol, smoking, and diabetes duration were independently associated with calcium of both the ascending and descending thoracic aorta ($P < .001$ for all). Ascending and

Support: The Penn Diabetes Heart Study was supported by Clinical and Translational Science Award from the National Center for Research Resources (UL1RR024134) and a Diabetes and Endocrine Research Center award (P20-DK 019525), both from the National Institutes of Health to University of Pennsylvania.

Conflict of interest: Muredach P. Reilly receives research grants from GlaxoSmithKline and Merck Research Laboratories. All other authors have no industry relationships or conflicts of interest to disclose.

* Corresponding author.
E-mail address: aqasim@medicine.ucsf.edu (A.N. Qasim).

http://dx.doi.org/10.1016/j.jcct.2015.04.008

descending aortic calcium were each independently associated with coronary calcium in multivariate regression, but only calcification of the descending thoracic aortic was associated with low ankle-brachial index.

Conclusion: Ascending and descending thoracic aortic calcium have similar associations with traditional cardiovascular risk factors in diabetics and are independently associated with coronary artery calcium. Only calcium in the descending aorta is associated with peripheral arterial disease. Delineation of both phenotypes may provide information about the individualized vascular disease and risk profile of patients with type 2 diabetes mellitus.

1. Introduction

Cardiovascular disease is a major contributor to morbidity and mortality among those with type 2 diabetes mellitus (T2DM).[1] Individuals with T2DM are known to have increased arterial calcification across multiple vascular beds, including the coronary arteries, the great vessels, and peripheral arteries,[2–4] but the mechanisms underlying this process are incompletely understood. Thoracic aortic calcification is a common finding on cardiac and chest CTs among those with diabetes. Although coronary artery calcium is predictive of cardiovascular events in diabetics,[5] it is not clear whether aortic calcification is also associated with increased cardiovascular risk in this population.

In nondiabetic cohorts, data for thoracic aortic calcium as an independent risk factor for cardiovascular disease are mixed. Within a population of >5000 individuals in the Framingham Study, the presence of aortic calcification seen on chest x-ray was predictive of cardiovascular death,[6] but in the Multi-Ethic Study of Atherosclerosis (MESA), thoracic aortic calcium, as measured by CT, was an independent risk factor for coronary events only in women.[7] In a recent study by Wong et al, in a healthy asymptomatic population of >2300 subjects (notably only 7% diabetic), there was no relationship between CT-measured thoracic aortic calcium and cardiovascular disease.[8] Lack of consistent findings may relate to differences in measurement and quantification of thoracic aortic calcium or to the use of healthy populations with overall low rates of cardiovascular disease. In addition, many prior studies considered all thoracic aortic calcium as one anatomic entity, and it is possible that differences in pathophysiology and disease risk may exist depending on the location of the calcification.

In particular, ascending thoracic aortic calcium involving the aortic root and ascending aorta may relate differently to cardiovascular risk as compared to descending thoracic aortic calcification. The ascending and descending sections of the aorta are subject to different hemodynamic stresses and differ in their embryologic origins, which appear to affect susceptibility to calcification,[9] and they are known to calcify at different rates.[10] In addition, 2 distinct pathophysiological processes of arterial calcification exist—calcification of the arterial intima, which is viewed primarily as part of atherosclerotic plaque development, and calcification of the medial layer, which is particularly prominent in diabetes and other metabolic disorders—and it is possible these occur differentially in different sections of the vessel.[11]

We therefore decided to quantify thoracic aortic calcium by cardiac CT in a large diabetic sample and ask whether important differences exist between calcification of the ascending and descending thoracic aorta with respect to traditional cardiovascular risk factors, the presence of subclinical coronary atherosclerosis as measured by coronary artery calcium, and the presence of peripheral arterial disease.

2. Methods

2.1. Study participants

Details of the Penn Diabetes Heart Study recruitment have been described previously.[12] Briefly, this was a single-center cross-sectional study of atherosclerotic and vascular risk factors in subjects with T2DM without clinical coronary disease or significant renal disease (as defined by serum creatinine ≥2.5 mg/dL). Subjects were recruited from 2001 to 2011 from clinics at or affiliated with the Hospital of the University of Pennsylvania and the Philadelphia Veterans Affairs Medical Center. Inclusion and exclusion criteria were as previously described; all subjects were aged 35 to 75 years had a diagnosis of T2DM and serum creatinine <2.5 mg/dL and weighed <300 pounds.[12] The University of Pennsylvania Institutional Review Board approved the study protocol, and all participants gave informed consent.

All subjects who had a baseline electron beam CT scan and complete covariate data were included in this study, with the final sample including 1739 of 2032 eligible recruited subjects. Subjects excluded because of missing covariate or CT data were similar to included subjects with regard to age and gender but were disproportionately African American (39% vs 33%; $P = .03$).

2.2. Evaluated parameters

All subjects were evaluated at the University of Pennsylvania's Clinical and Translational Research Center after a 12-hour fast. All subjects underwent a detailed medical questionnaire and had standard anthropometric measurements. Standard lipid panels were measured in real time in Penn's Centers for Disease Control–certified lipid laboratory using enzymatic assays (Hitachi 912; Roche Diagnostic Systems Inc., Branchburg, NJ) in lipoprotein fractions after ultracentrifugation (β-quantification technique). Fasting low-density lipoprotein cholesterol (LDL-C) was measured