Converging on the distribution profile of coronary artery disease
Juarez-Orozco, Luis Eduardo; Ruijsink, Bram; Knuuti, Juhani

Published in:
European Heart Journal - Cardiovascular Imaging

DOI:
10.1093/ehjci/jeac060

IMPORTANT NOTE: You are advised to consult the publisher's version (publisher's PDF) if you wish to cite from it. Please check the document version below.

Document Version
Publisher's PDF, also known as Version of record

Publication date:
2022

Link to publication in University of Groningen/UMCG research database

Citation for published version (APA):

Copyright
Other than for strictly personal use, it is not permitted to download or to forward/distribute the text or part of it without the consent of the author(s) and/or copyright holder(s), unless the work is under an open content license (like Creative Commons).

The publication may also be distributed here under the terms of Article 25fa of the Dutch Copyright Act, indicated by the “Taverne” license. More information can be found on the University of Groningen website: https://www.rug.nl/library/open-access/self-archiving-pure/taverne-amendment.

Take-down policy
If you believe that this document breaches copyright please contact us providing details, and we will remove access to the work immediately and investigate your claim.

Downloaded from the University of Groningen/UMCG research database (Pure): http://www.rug.nl/research/portal. For technical reasons the number of authors shown on this cover page is limited to 10 maximum.

Download date: 16-09-2023
Converging on the distribution profile of coronary artery disease

Luis Eduardo Juarez-Orozco 1,2,3*, Bram Ruijsink 1,4, and Juhani Knuuti 2

1Division Heart & Lungs, Department of Cardiology, University Medical Center Utrecht, Utrecht University, Heidelberglaan 100, 3508, GA, Utrecht, The Netherlands; 2Turku PET Centre, University of Turku and Turku University Hospital, Kiramyllykatu 4-8, 20520 Turku, Finland; 3Department of Cardiology, University of Groningen, University Medical Center Groningen, Hanzeplein 1, 9700RB Groningen, The Netherlands; and 4Division of Imaging Sciences and Biomedical Engineering, King’s College London, St Thomas’ Hospital, King’s College London Strand, London, WC2R 2LS, UK.

This editorial refers to ‘Vessel-specific plaque features on coronary computed tomography angiography among patients of varying atherosclerotic cardiovascular disease risk’, by A.M. Bax et al. doi: 10.1093/ehjci/jeac029.

It is often the case out of practical convention that intuitions on the distribution and progression of a disease in a specific system are adopted, while exhaustive statistical characterization may be bypassed due to lack of data and the assumption that our experiential notions about it suffice. This has been the case in atherosclerotic coronary artery disease (CAD) and its vessel-specific [left anterior descending (LAD), left circumflex (LCx), and right coronary artery (RCA)] burden. Case in point, long has clinicians recognized CAD in the LAD coronary artery as causing the largest proportion of acute coronary syndromes. And in fact, the ‘widow maker’ has been a classic term denoting obstructive CAD in the proximal LAD, exemplifying the concern physicians have attached to its clinical relevance.

Convergence is the evolutionary biology term for the tendency of independent species to evolve similarly under equal environmental conditions. This concept is germane when studying the heart as it is an independent species to evolve similarly under equal environmental conditions. Notably, even though the interest in the role of evolutionary biology on health and disease has increased, much less is known about the genetics and evolution of the coronary artery tree and its anomalies. It is logical, however, to assume that such network also represents the result of a long evolutionary process to optimize myocardial perfusion delivering a two-ostia (left and right) and three-main-branch system that seems preserved amongst reptiles, birds, and mammals. It is also likely that such system may not have optimized for coronary ‘health’ or longevity given that both the reproductive and life span of human beings considerably diverge.

So, how is CAD specifically distributed among the coronaries in stable and progressive disease? Does this distribution translate into different risk of cardiovascular events? And more essentially, why should it have a specific distribution?

Previously, Maxim Bax and colleagues have addressed the first question. Their characterization of CAD distribution across the coronaries showed that in average the LCx artery has the lowest burden of atherosclerosis in terms of total plaque volume (10 vs. 33 in the RCA and 59 mm3 in the LAD), the lowest prevalence of high-risk plaque features and more often calcified, all irrespective of vessel volume. The second question is approached as the authors deliver an interesting and timely analysis of the such differential CAD distribution along with its anatomical and compositional quantification across different levels of ASCVD risk.

This study makes clever use of the unique advantages offered by the sizeable PARADIGM (coronary computed tomography angiography) data, which evaluated non-invasively the presence, location, and burden of atherosclerosis throughout the coronary artery tree of 1340 patients with varying levels of cardiovascular risk. As expectedly, CAD burden increased with the ASCVD risk score. And interestingly, atherosclerotic plaque was most commonly found in the LAD territory in the substantial proportion of cases that demonstrated single-vessel disease, irrespective of the ASCVD risk group. While confirming that plaque burden in the LCx artery is lower with respect to LAD and RCA, their results also demonstrate that this distribution is practically sustained across low-, intermediate-, and high-ASCVD risk. In the latter subgroup, however, atherosclerotic plaque prevalence was comparable in the LCx and RCA (~55%), while clearly higher in the LAD artery (~85%). What this suggests is open to debate, but one intuitive possibility is that the coronary artery tree may be prone to sequential CAD development in the LAD, RCA, and LCx. And that in very high-risk conditions (i.e. with accumulated effect from systemic factors promoting plaque progression, such as endothelial dysfunction, lipid deposition, and inflammatory
phenomena), there may be some catch-up phenomenon in the LCx coronary. However, this triggers the natural question of whether such an effect would not rather equalize plaque burden at the top tier of the ASCVD risk. And since this was not observed in the current report, the notion of some special degree of predisposition to disease in the LAD remains.

Furthermore, quantitative plaque evaluation was concordant with the aforementioned tendencies with the lowest plaque volume and percentages of necrotic core and fibrofatty composition in the LCx artery across all levels of ASCVD risk. Nevertheless, the proportion of calcified plaque was comparable between LCx and RCA in the low-risk end and between LCx and LAD at the high-risk end. This finding probably links to the simultaneous importance of calcium globally as a risk biomarker in CAD and locally as a possible sign of plaque stability. Although not discussed in this study, the reported findings open the door to expand the differential study of calcification across the coronary artery tree in individual subjects. Such level of personalization is highly desired and will become increasingly possible through the analysis of existing large registries and with the implementation of modern analytics.

Overall, Bax and colleagues make the case for attributing a lower vulnerability of the LCx artery to CAD (with the lowest plaque burden and with a more stable composition as compared to RCA and LAD) with varying levels of (treated) cardiovascular risk. Whether these results will also translate to hard endpoints in this registry poses an interesting query to follow-up on.

Evidence on suspected influences that could explain this disease behaviour (such as tortuosity and angulations) is independently emerging with concepts such as shear stress and could potentially be answered using applied fluid dynamics.7 And although little is known about the driving forces of coronary artery evolution, we could speculate how the metabolic necessities of the left ventricle may have warranted a dual-branching system where LCx may in fact function as a pragmatic ‘backup’ in crucial circumstances such as acute obstruction and thrombosis. In the era of artificial intelligence implementations, this statistical characterization of the differential affection of the coronary arteries by atherosclerotic disease provides a much-needed base for the generation and fine-tuning of complex risk evaluations both at the diagnostic and prognostic fronts in the search for highly personalized medicine.

**Conflict of interest:** none declared.

**References**