Atherosclerosis 366 (2023) 40–41

Contents lists available at ScienceDirect

Atherosclerosis

journal homepage: www.elsevier.com/locate/atherosclerosis

Editorial

Artificial intelligence for high-risk plaque detection on carotid CT angiography

ARTICLE INFO

Keywords
Computed tomography angiography
Atherosclerosis
Histopathology
Artificial intelligence

Atherothrombotic events such as myocardial infarction and stroke most commonly arise from the disruption of plaques that pathologically exhibit a large lipid-rich core, thin fibrous cap, and outward remodeling [1,2]. These high-risk morphological 'vulnerable plaque' features can be identified early by invasive and non-invasive imaging modalities [3], and their presence portends an increased lesion-specific and patient-level risk of future cardiovascular events [4–7]. In this issue of *Atherosclerosis*, Buckler et al. [8] present an artificial intelligence (AI)-based approach for the detection of high-risk carotid atherosclerotic plaque on computed tomography angiography (CTA), referenced by histopathology.

CTA is widely used in clinical practice for the assessment of patients with known or suspected cardiovascular disease. Recent advancements in CT technologies now enable the quantification and characterization of atherosclerotic plaque in different vascular beds using dedicated image analysis software platforms. Volumetric measurements of coronary plaque burden and composition have been validated in many studies against the invasive reference standard of intravascular ultrasound [9,10]. Similarly, *in vivo* CTA-derived quantitative measures of carotid plaque tissue characteristics have shown strong correlation with histology [11,12].

AI is being increasingly applied to cardiovascular imaging for identifying new disease phenotypes, enhancing risk stratification, and guiding treatment strategies [13]. Through an expanding role in clinical pathways and the generation of large three-dimensional imaging datasets, cardiovascular CTA is well-primed for AI applications [14]. Deep learning (DL) is a specific form of AI which uses multilayered convolutional neural networks (CNNs) to make predictions directly from input image data. In the domain of coronary CTA, DL has enabled the rapid and accurate quantification of plaque components, validated with intravascular ultrasound [15]. To date, however, few studies have applied AI for the detection of high-risk plaque morphology on CTA with use of a histological reference standard.

In the present analysis, Buckler et al. [8] employ a DL model for the classification of atherosclerotic plaque stability phenotype on carotid CTA, using histologic specimens from carotid endarterectomy as ground truth. Following software-aided plaque segmentation on CTA images, 496 vessel cross-sections were input into a CNN which was trained to classify plaque as minimal, stable, or unstable, referenced by matched, pathologist-annotated histologic sections. The initial layers of the CNN detected CTA image features in the segmented tissue regions, while subsequent layers calculated the likelihood of each cross-section belonging to a particular plaque phenotype. Following training, the CNN was validated in an unseen dataset of 408 vessel cross-sections, demonstrating strong agreement with pathologist classification (kappa 0.82) and high discriminatory value for each plaque phenotype (area under the receiver operating characteristic curve 0.95–0.99). There was good agreement among 3 pathologists (kappa 0.68–0.84), with the final section classification based on consensus. Meanwhile, quantitative luminal diameter stenosis on CTA showed poor agreement with histology-defined plaque phenotype (kappa 0.25).

These findings represent an extension of the authors' prior work, in which quantification of carotid plaque tissue components on CTA using their semi-automated software was validated against histopathologic findings [12]. In this previous study, there was strong correlation between CTA and histology for cross-sectional area measurements of lipid-rich necrotic core, calcification, and fibrotic plaque. Moreover, in both studies, the software employed an image processing algorithm which mitigated blurring and calcium blooming artifacts to improve segmentation accuracy and repeatability.

The study by Buckler et al. [8] has several strengths. Although the study population comprised only 53 patients, both the derivation and validation datasets included two geographically distinct cohorts with different demographics. The authors applied a well-established histologic plaque phenotype classification scheme which has been progressively refined over the past two decades [1,2]. The use of histology increases the signal-to-noise ratio in the data being presented to a CNN classifier, in contrast to image-based ground truths, which are subject to greater variability in acquisition parameters and expert interpretation. Further, the ability of their software to align histologic sections with

https://doi.org/10.1016/j.atherosclerosis.2023.01.006
Received 12 December 2022; Received in revised form 26 December 2022; Accepted 11 January 2023
Available online 14 January 2023

corresponding locations in the CTA images could theoretically enable accurate assignment of each CT voxel to a specific tissue type (or, accounting for partial volume effects, a specific mixture of tissue types). Finally, the proposed DL model is embedded in the image analysis software and able to perform phenotype classification in less than 5 minutes following plaque segmentation.

Although these initial results are promising, the DL model requires external validation in large, diverse, real-world datasets. It also remains to be determined if such a model trained using carotid tissue specimens is generalizable to plaques in other vascular beds, particularly the coronary arteries. While atherosclerotic plaque development in both the carotid and coronary arteries share similar characteristics, differences exist in plaque biology and progression. Vulnerable carotid plaques tend to have a thicker fibrous cap, higher prevalence of intraplaque hemorrhage and calcified nodules, and lower prevalence of plaque erosion as compared with vulnerable coronary plaques [16,17]. Moreover, technical factors such as differences in vessel size and motion need to be considered when imaging the carotid versus coronary arteries. Futures studies will also need to evaluate the prognostic utility of the proposed plaque risk phenotype and its incremental value beyond current CTA-derived measures of lesion-specific risk including stenosis severity, qualitative high-risk plaque features, and quantitative plaque volumes.

The present study findings add to the growing body of literature on the use of AI in cardiovascular CTA for risk stratification [13]. Multiple commercial AI applications for stenosis estimation, plaque characterization, and functional assessments are permeating into daily cardiovascular care [14]. The ultimate goal of such AI systems is to increase efficiency in image analysis and interpretation and provide clinical decision support tools. To facilitate the widespread adoption of AI, it will be important to establish appropriate ground truth standards such as invasive imaging or histopathology to ensure accuracy, precision, and generalizability [18]. Careful vetting of AI technologies is required by regulatory bodies, as well as through peer-reviewed studies and professional societies. Finally, the effects of individualized therapies that are guided by the identification of AI-based high-risk plaque phenotypes will need to be examined in future prospective randomized clinical trials.

Declaration of competing interest

The author declares that he has no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

References

[1] H.C. Stary, A.B. Chandler, R.E. Dinsmore, et al., A definition of advanced types of atherosclerotic lesions and a histological classification of atherosclerosis, Circulation 92 (5) (1995/09/01 1995) 1355–1374, https://doi.org/10.1161/01.CIR.92.5.1355.

[2] R. Virmani, A.P. Burke, A. Farb, F.D. Kolodgie, Pathology of the vulnerable plaque, J. Am. Coll. Cardiol. 47 (8 Suppl) (Apr 18 2006) C13–C18, https://doi.org/10.1016/j.jacc.2005.10.065.

[3] P. Ibrahimi, F. Jashari, R. Nicoll, G. Bajraktari, P. Wester, M.Y. Henein, Coronary and carotid atherosclerosis: how useful is the imaging? Atherosclerosis 231 (2) (Dec 2013) 323–333, https://doi.org/10.1016/j.atherosclerosis.2013.09.035.

[4] G.W. Stone, A. Maehara, A.J. Lansky, et al., A prospective natural-history study of coronary atherosclerosis, N. Engl. J. Med. 364 (3) (2011/01/20 2011) 226–235, https://doi.org/10.1056/NEJMoa1002358.

[5] S. Motoyama, H. Ito, M. Sarai, et al., Plaque characterization by coronary computed tomography angiography and the likelihood of acute coronary events in mid-term follow-up, J. Am. Coll. Cardiol. 66 (4) (2015) 337–346, https://doi.org/10.1016/j.jacc.2015.05.069, 2015/07/28/.

[6] N. Takaya, C. Yuan, B. Chu, et al., Association between carotid plaque characteristics and subsequent ischemic cerebrovascular events, Stroke 37 (3) (2006) 818–823, https://doi.org/10.1161/01.STR.0000204638.91099.91.

[7] A.E. Zavodni, B.A. Wasserman, R.L. McClelland, et al., Carotid artery plaque morphology and composition in relation to incident cardiovascular events: the Multi-Ethnic Study of Atherosclerosis (MESA), Radiology 271 (2) (May 2014) 381–389, https://doi.org/10.1148/radiol.14131020.

[8] A.J. Buckler, Atherosclerosis risk classification with computed tomography angiography: a radiologic-pathologic validation study, Atherosclerosis (2022), https://doi.org/10.1016/j.atherosclerosis.2022.11.013 in press.

[9] S. Voros, S. Rinehart, Z. Qian, Coronary atherosclerosis imaging by coronary CT angiography: current status, correlation with intravascular interrogation and meta-analysis, JACC Cardiovasc. Imag. 4 (2011) 537.

[10] H. Matsumoto, S. Watanabe, E. Kyo, et al., Standardized volumetric plaque quantification and characterization from coronary CT angiography: a head-to-head comparison with invasive intravascular ultrasound, *Eur Radiol.* Nov 29 (11) (2019) 6129–6139, https://doi.org/10.1007/s00330-019-06219-3.

[11] T.T. de Weert, M. Ouhlous, E. Meijering, et al., In vivo characterization and quantification of atherosclerotic carotid plaque components with multidetector computed tomography and histopathological correlation, Arterioscler. Thromb. Vasc. Biol. 26 (10) (Oct 2006) 2366–2372, https://doi.org/10.1161/01.Atv.0000240518.90124.57.

[12] M. Sheahan, X. Ma, D. Paik, et al., Atherosclerotic plaque tissue: noninvasive quantitative assessment of characteristics with software-aided measurements from conventional CT angiography, Radiology 286 (2) (2017) 622–631, https://doi.org/10.1148/radiol.2017170127, 2018/02/01.

[13] A. Lin, M. Kolossváry, M. Motwani, et al., Artificial intelligence in cardiovascular imaging for risk stratification in coronary artery disease, Radiology: Cardiothorac. Imag. 3 (1) (2021), e200512, https://doi.org/10.1148/ryct.2021200512, 2021/02/01.

[14] A. Lin, M. Kolossváry, M. Motwani, et al., Artificial intelligence in cardiovascular CT: current status and future implications, J. Cardiovasc. Comput. Tomogr. 15 (6) (Nov-Dec 2021) 462–469, https://doi.org/10.1016/j.jcct.2021.03.006.

[15] A. Lin, N. Manral, P. McElhinney, et al., Deep learning-enabled coronary CT angiography for plaque and stenosis quantification and cardiac risk prediction: an international multicentre study, Lancet Digit. Health 4 (4) (2022) e256–e265, https://doi.org/10.1016/S2589-7500(22)00022-X.

[16] F. Jashari, P. Ibrahimi, R. Nicoll, G. Bajraktari, P. Wester, M.Y. Henein, Coronary and carotid atherosclerosis: similarities and differences, Atherosclerosis 227 (2) (2013) 193–200, https://doi.org/10.1016/j.atherosclerosis.2012.11.008, 2013/04/01.

[17] F. Sigala, E. Oikonomou, A.S. Antonopoulos, G. Galyfos, D. Tousoulis, Coronary versus carotid artery plaques. Similarities and differences regarding biomarkers morphology and prognosis, Curr. Opin. Pharmacol. 39 (2018) 9–18, https://doi.org/10.1016/j.coph.2017.11.010, 2018/04/01/.

[18] P.P. Sengupta, S. Shrestha, B. Berthon, et al., Proposed requirements for cardiovascular imaging-related machine learning evaluation (prime): a checklist: reviewed by the American college of cardiology healthcare innovation council, JACC Cardiovasc. Imag. 13 (9) (Sep 2020) 2017–2035, https://doi.org/10.1016/j.jcmg.2020.07.015.

Andrew Lin*

Monash Victorian Heart Institute, Monash University and MonashHeart, Monash Health, Melbourne, Victoria, Australia

Biomedical Imaging Research Institute, Cedars-Sinai Medical Center, Los Angeles, CA, USA

* Corresponding author. Monash Victorian Heart Institute, Monash University and MonashHeart, Monash Health, Melbourne, Victoria, Australia.

E-mail address: andrew.lin@monash.edu.