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Editorial

Artificial intelligence for plaque characterization: A scientific exercise looking for a clinical application

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In this issue of *Atherosclerosis*, Kang and colleagues [1] describe their attempt to utilize machine learning in the identification of the vulnerable plaque using invasive imaging. The authors included a total of 517 coronary lesions and the study patients were randomized 4:1 into the training and testing samples, respectively. Each patient underwent OCT and IVUS, and every OCT frame with a 0.4-mm interval was co-registered with its comparable IVUS frame by using anatomical landmarks such as vessel shape, side branches, calcium, perivascular structures, and distance from the ostium. Each IVUS frame was labeled according to the presence *vs.* absence of OCT-derived TCFA. Following that, hundreds of different plaque features were measured and evaluated in each image. These quantitative features are broadly classified into four categories: intensity, structure, texture/gradient, and wavelet, based on the types of plaque characteristics they capture [2]. However, the authors do describe in details what are these features and what groups they represent. Later, these extracted plaque features were studied in 3 different ML models. The 17 non-overlapping plaque features were selected to be entered in a machine learning algorithm to predict the presence of vulnerable plaque. Different models using different machine learning techniques were derived and validated using support vector machine (SVM) and artificial neural network (ANN). The overall prediction accuracy for OCT-TFCA feature was over 80%. However, the differences between the IVUS images with *versus* without TCFA, in this specific study, were relatively subtle.

The study is an experiment that may lead to some clinical applications in the future. However, it is still far from clinical adoption. Its main importance come from its investigation of the high risk plaque. The search for the vulnerable plaque that is associated with incident acute coronary syndrome and thrombosis has been the subject of multiple investigations utilizing different invasive and noninvasive imaging modalities [3,4]. New imaging tools, like coronary computed tomography angiography (CCTA) and magnetic resonance imaging, have been at the cornerstone of these investigations non-invasively [5,6]. On the other hand, invasive imaging, including intravascular ultrasound (IVUS) and optical coherence tomography (OCT), is considered the gold standard for this purpose. Both modalities have suggested that compared to histology, thin-cap fibroatheroma (TCFA) characterized by a large necrotic core, a thin-fibrous cap, and infiltration of numerous macrophages are the main morphological phenotypes of vulnerable plaque [7].

However, several histological and technical features limit the identification of TCFA, including the spatial resolution of invasive imaging as well as spatial and temporal resolution in noninvasive imaging. In addition, an overwhelming number of artifacts and technical limitations may hamper the overall applicability and generalizability [8]. On the other hand, the prevalence of TCFA plaque is low. Similarly, the absolute event rate among patients with high risk plaques is relatively low, as has been shown by multiple studies [4]. In a study of more than 3000 patients who underwent CCTA, high risk plaques were seen in 294 patients of which 16% had an acute coronary syndrome during follow-up compared to 3% among patients without high risk plaques. The low prevalence of high-risk plaques would potentially lead to a high false positive identification of these plaques. While OCT and IVUS have a higher spatial resolution than noninvasive imaging tools, it is unclear if this translates into better identification of patients who might develop future events.

In the past few years, artificial intelligence and machine learning techniques started to be increasingly adopted in the clinical arena. Some of these applications are applied to categorized data collected on spreadsheets while others are applied to the images, either in Digital Imaging and Communications in Medicine (DICOM) or JPEG/TIFF formats [9-11]. The latter approach would allow for more data and feature extraction from the images. These applications have been used to help in clinical decision making in some fields [12–15], while they are not widely adopted in other domains. The experiment described in this paper requires advanced and extensive computing hardware (often referred to as supper computers) as well as special support from skilled staff (specifically computer scientists and bioinformatics). Thus, this approach need to be simplified before making it to the clinical arena. Moreover, this study did not use direct image based deep learning techniques. A deep leaning model using convolutional neural networks or other supervised or unsupervised computer science tools may have

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been more appropriate and could limit the number of analytical steps. These steps are not easy to understand and are often referred to as black box steps.

On the other hand, the gold standard used in this study is an IVUS-OCT hybrid catheter, which is not readily available and is associated with additional cost. It is also an invasive procedure, which cannot be used clinically for routine screening. Recent data suggest that CCTA may be able to assess plaque characteristics and predict its rupture potential. Whether using a noninvasive imaging approach routinely to accurately identify vulnerable plaques at risk of rupture is pending investigations.

Looking at this from a different perspective, one would realize that the real clinical need is to identify those patients who are at risk of having or developing a vulnerable plaque. Using artificial intelligence, machine and deep learning to achieve this goal would add significantly to the current prevention schemes and identify those patients whose first presentation of coronary artery disease may be sudden cardiac death. If that is a far-reaching goal, then at least standardization of the identification of high-risk plaques on noninvasive imaging could be a lower hanging fruit. Several recent studies attempted to evaluate the plaques on CCTA using machine learning. This group of investigators previously evaluated 727 cross-sections co-registered by both CCTA and OCT. Although the investigators identified low attenuated plaque (odds ratio [OR] = 4.05) and napkin ring sign (OR = 2.47) as the independent predictors of an OCT-TCFA, the relatively low resolution of CCTA still limited the accurate diagnosis of TCFA [16].

The current study should be interpreted within the limitations of the approach and imaging modalities used. In addition, there have been some recent doubts about the high-risk plaque outcome predictivity. Data from the PROspective Multicenter Imaging Study for Evaluation of chest pain (PROMISE) trial and The Scottish COmputed Tomography of the HEART (SCOT-HEART) study showed that high risk plaque may be associated with worse long-term outcomes. In PROMISE, 676 patients had high-risk plaques, and these plaques were independently associated with higher event rates (6.4% *vs.* 2.4%; hazard ratio, 2.73; 95% CI, 1.89–3.93) [17]. The association between high risk plaques and worse long term outcomes was also seen in the SCOT HEART trial, but the prognostic value of high risk plaque features became non-significant after adjustment for coronary artery calcium score [18]. This may imply that a simple measure of coronary atherosclerosis (coronary artery calcium score) may have a similar predictive value of future events. Calcium score is reproducible, has much less variability and can be readily available with minimal risk [19,20].

In summary, an application that will help identify high risk vulnerable patients and plaques is welcome. However, such an application should have the prerequisites to make it into the clinical arena. That includes good accuracy, reproducibility as well as time efficiency and incremental diagnostic and prognostic value.

Conflict of interest

The authors declared they do not have anything to disclose regarding conflict of interest with respect to this manuscript.

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