Using artificial intelligence to switch from accident to sagacity in the serendipitous detection of uncommon diseases

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Among the acknowledged advantages of artificial intelligence (AI) applications in diagnostic imaging, there is the capability to register apparently hidden features in complex images and to connect them for identifying specific disease patterns. This approach has been effectively applied to established techniques for both diagnostic and prognostic purposes.[1] However, the task becomes substantially more demanding if the involved method makes the recognition of subtle changes particularly difficult and its use is mainly finalised to identify coarse abnormalities related to urgent clinical indications. This is the case for point-of-care ultrasonography (POCUS), especially if used in emergency departments.[2] There are many diseases that are probably underrecognised and would benefit from an early diagnosis in otherwise unsuspected individuals, who are submitted to imaging investigations for unrelated indications. Two of these conditions are hypertrophic cardiomyopathy and transthyretin amyloid cardiomyopathy. The prevalence of hypertrophic cardiomyopathy is approximately 0·2% in the general population, but the absence of symptoms in most people makes the diagnosis difficult; sudden death is its most feared complication, particularly in young patients (ie, those aged <45 years).[3] Similarly, transthyretin amyloid cardiomyopathy is becoming an increasingly recognised cause of heart failure in the older population (ie, those aged >70 years) and its mortality can be reduced by earlier detection.[4] AI has already been effectively used in both settings to improve disease recognition. For instance, the analysis of electrocardiography with convolutional neural networks allows the diagnosis of hypertrophic cardiomyopathy with good accuracy.[5] For transthyretin amyloid cardiomyopathy, deep learning has been used to improve the detection of cardiac involvement with bone scintigraphy.[6] Another use has been to track the preclinical evolution of transthyretin amyloid cardiomyopathy taking advantage of the AI analysis applied to electrocardiography and echocardiography.[7]

In this issue of the *Lancet Digital Health*, Evangelos K Oikonomou and colleagues present a new study put together with most of the above-mentioned points, presenting remarkable findings.[8] Applying a rigorous analysis to a large cohort of echocardiograms to identify the features that signal the presence of either hypertrophic cardiomyopathy or transthyretin amyloid cardiomyopathy, the authors were able to derive a POCUS-adapted detection model that they then used to interpret an even larger POCUS dataset. Their main result was a reliable accuracy for both conditions; moreover, they were able to show that the diagnosis provided by the model on POCUS preceded of approximately two years the confirmatory one with standard techniques, with possible favourable implications for more timely interventions. Finally, in control patients without known disease the occurrence of higher probabilities of hypertrophic cardiomyopathy or transthyretin amyloid cardiomyopathy phenotypes was associated with worse long-term survival, suggesting widespread under-diagnosis. Beyond all these results, an intrinsic advantage of focusing on a method that can be widely used even in low-resource settings is to expand the number of potentially marginalised patients in whom an early diagnosis becomes possible.[9]

These are certainly noteworthy achievements, which confirm the validity of the chosen method. However, there are some limitations that deserve attention. As for all methods applied to large patient cohorts in which the disease prevalence is very low, the positive predictive values remain minimal. Accordingly, there will always be the problem of unconfirmed diagnoses, with ensuing additional costs and unwanted patient anxiety. While in this scenario the psychological pressure could be lower than in oncological screening programmes, imagining a reasonable and manageable workflow to reach the final disease certainty would be necessary. Another point, connected to the first, is the explainability of the individual patient classification. This is a general need in AI models applied to the clinical setting but would be probably even more relevant when the suggested diagnosis and all the following steps concern a completely unexpected condition. The saliency maps shown in the study are unfortunately quite ineffective in conveying convincing evidence to the patient and to the managing physician. Finally, as for many other proposed models, independent of their accuracy, there is the problem of the exportability to the final user, who, in this case, could have limited possibilities for implementing it in their devices. Regarding this, the reported effectiveness of this approach could be hoped to convince some software or hardware vendors to develop it for a commercial use. If not, similar to many other promising algorithms, even this could remain a mere scientific achievement but not become a useful clinical improvement. Nevertheless, this study shows that a clever use of AI can make sagacity prevail over accident in the detection of what is present but not searched.

I declare no competing interests.

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