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EDITORIAL COMMENT

Revival and Revision of Right Ventricular Assessment by Machine Learning*

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Complexities and conundrums posed by heart failure arise from its phenotypic heterogeneity in addition to its high prevalence and substantial burden to patients, providers, and health systems. Disease heterogeneity, in particular, is considered a major reason for the ongoing challenges around heart failure prognostication. To this end, increasing efforts have been made to leverage advanced computational methods for predicting heart failure outcomes, especially for those at the greatest risk for severe adverse events and in whom conventional risk prediction models tend to fall short, such as patients with nonischemic cardiomyopathy (NICM).

Machine learning approaches are now well-suited for complex clinical challenges, particularly if they involve opportunities to analyze medical imaging data, given that great strides have already been made in tackling complex nonmedical computer vision tasks ranging from self-driving cars to facial recognition. Applying recent advances in computational techniques to address unmet medical needs is also very timely, given the exponentially greater magnitude of computational power that is now available for pushing the boundaries of new insights that can be gleaned from readily accessible and rapidly growing stores of medical imaging data.

Recognizing the importance and the opportunity, in this issue of *JACC: Cardiovascular Imaging*, Fahmy et al[1] used XGBoost, a gradient tree boosting-based classifier, on a combination of imaging and clinical parameters with the goal of improving prognostication for patients with NICM. The authors studied 2 populations of patients with NICM who underwent cardiac magnetic resonance imaging (CMR) and then went on to either develop or not develop the primary outcome defined as a composite endpoint of cardiovascular hospitalizations or death. They found that XGBoost was able to robustly predict the composite outcome based on input features including reported CMR measures of size, function, and gadolinium enhancement. On a held-out test cohort, XGBoost had an area under the curve (AUC) of 0.71 in predicting the composite outcome, and the performance was similar in a cohort of patients from a second institution whose data were not seen during algorithm training. Using Shapley value-based methods to weigh the importance of input features, the authors showed that pulmonary artery pressure and right ventricular end-diastolic volume were the 2 most important predictive variables, consistent with metrics of right ventricular size being significantly larger for patients with versus without occurrence of the primary outcome.

Right-heart integrity as a key differentiator of risk in left-heart failure is not a new concept, and yet this article's findings are noteworthy based on their emergence from a well-designed study involving a comprehensive model. Importance of the right ventricle first came to the forefront when the cardiac effects of pulmonary embolism and pulmonary hypertension were made evident. Since then, a revival of attention to the right ventricle emerged from the growing recognition that, beyond a simple reservoir function, the right ventricle can serve as an etiologic driver of morbidity across many types of conditions,[2,3] including various presentations of heart failure.[4] Notwithstanding the plethora of

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cardiac imaging metrics (often focused on the left ventricle) and comorbidities associated with heart failure outcomes,[5] the current study's findings reaffirm prior reports of right ventricular dilation and dysfunction being among the most important predictors of cardiovascular hospitalization and death in patients with NICM. Notably, the current study further demonstrates that right ventricular features predict NICM outcomes in a manner that appears to generalize across institutions and notwithstanding differences in imaging protocols, scanner types, and data analysis platforms.

A few additional factors are worth considering for context. The current study focused on patients who underwent CMR imaging and, importantly, it was the CMR-derived measures that were used to inform the machine learning algorithm. In real-world clinical practice, a large proportion of patients with NICM do not undergo CMR imaging; thus, referral patterns and selection bias must be considered when interpreting the possible generalizability of study results to all patients with NICM. It is also notable that, in the training cohort, the patients with hospitalization or death were younger than patients who did not develop the outcome of interest, which translated to model interpretation methods highlighting older age as a putative protective factor. Although possibly a true effect, it is more likely that patients who survived to an advanced age benefited from associated protective attributes, such that age itself was not the primary determinant of improved patient outcomes. Thus, although demonstrating the potential yield of a comprehensive new model, the study also signals caution to clinicians who might consider applying results for risk stratification, given the helpful reminder that all modeling techniques can be susceptible to identifying artifacts of cohort selection.

Another noteworthy aspect of the study is that XGBoost was applied to premade imaging measurements rather than to imaging features that could have been derived from computer vision analyses of raw CMR imaging data. Human assessments of the right ventricle, even when conducted using high-resolution CMR images, are still subject to the usual limitations that contribute to human inter- and intrareader variability. In fact, human measurement variation is known to be the primary factor limiting measurement accuracy, even in the context of superior signal-to-noise ratio offered by CMR when compared with all other cardiovascular imaging modalities.[6,7] Human biases in measurement, particularly when there are visual cues present, such as an enlarged right ventricle, may also confound downstream analyses when using machine learning. Incidentally, performance of XGBoost model in the external validation cohort was only slightly better than logistic regression (AUC: 0.69 vs 0.67), and this result could have been related to the limits of precision and reproducibility of measurements included as part of the model input.

Overall, this study nicely demonstrates how advanced computational methods can be leveraged to advance our usual approach to existing data and derive new insights, or renew attention to key concepts, as part of efforts to improve prognostication for a complex disease condition. The study results also offer promise for continued progress in applying computer vision-derived measures to standardize assessments and further improve the precision of downstream analyses and prgnostication.[8] The authors' parallel work with automating measurements in CMR,[9] in addition to concurrent work being done by others in computed tomography,[10] echocardiography,[11] and adjunctive medical imaging modalities, show the enormous potential of facilitating otherwise tedious measurements in ways that are likely to augment precision beyond even clinician intrareader variation. Given the rich information now available in medical imaging, including data acquired by high image fidelity techniques such as CMR, automated measurements conducted via machine learning will allow for even greater precision phenotyping, further clarification of the historically difficult-to-image right ventricle, and identification of opportunities to intervene and ultimately improve outcomes for patients with complex conditions such as heart failure.

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 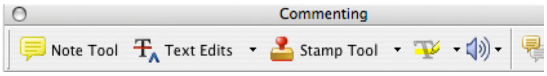

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 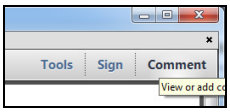

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 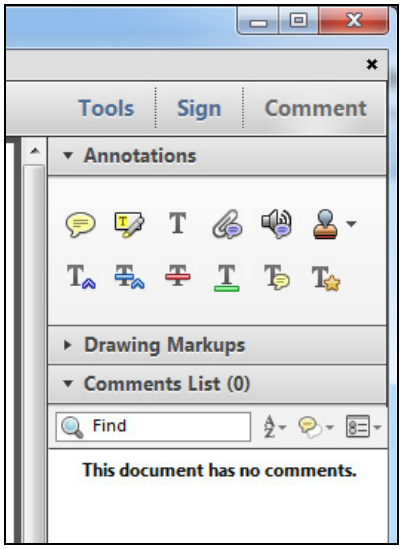
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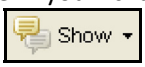
Review	To review your changes, click on the 'Show' button  on the Commenting tool bar. Choose 'Show Comments List'. Navigate by clicking on a correction in the list. Alternatively, double click on any mark-up to open the commenting box.	Your changes will appear automatically in a list below the Comment tool bar. Navigate by clicking on a correction in the list. Alternatively, double click on any mark-up to open the commenting box.
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