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EDITORIAL COMMENT

Can Machines Find the Sweet Spot in End-Stage Heart Failure?*

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Medical therapies and structural interventions for heart failure (HF) have advanced rapidly in the last decade[1-3]; however, a large number of patients will still progress to end-stage (stage D) HF.[4] Patients with stage D HF may benefit from advanced therapies such as left ventricular assist device implantation or cardiac transplantation.[4] However, not all physicians agree on how end-stage HF should be defined.[5,6] Furthermore, the task of identifying the right patients is complicated by the fact that offering therapies, such as left ventricular assist device implantation, to patients with a less-advanced disease may not improve outcomes.[7] There is also a societal need to reserve the finite number of donor hearts available for patients most in need.[8] At the same time, physicians cannot wait too long as many patients with stage D HF will develop contraindications for advanced therapies. For example, 15% to 65% of patients with HF have evidence of congestive hepatopathy which can progress to cirrhosis.[9] Pulmonary hypertension, worsening renal function, and cachexia are also frequent comorbidities which can influence candidacy for advanced therapies. Therefore, physicians need to identify patients with end-stage HF in the sweet spot: when they are sick enough to benefit from advanced therapies but not so sick that comorbidities preclude them from candidacy.

Most centers rely on physicians to identify patients with advanced HF during routine clinical care. This approach inevitably leaves many patients falling through the cracks, with ~40% of patients being "too sick" at the time of referral for advanced therapies compared to 15% to 20% of patients being "too well."[10] Methods to automate this process could help identify these patients sooner, addressing an unmet clinical need. Dunlay et al[11] attempted to take on this issue by utilizing existing electronic health records to automate this process by combining International Classification of Diseases, 10th revision, codes to identify patients with stage D HF. However, the algorithms had a low positive predictive value, leaving physicians with a large number of potential patients to review manually.[11]

In this issue, Cheema et al[12] developed an ensemble machine learning (ML)-based workflow for categorizing patients from electronic health records. The model incorporated 2 tree-based ML algorithms and a feed-forward neural network, each voting on classification of no HF, stage C HF, or stage D HF. The ML model incorporated variables from established risk scores, with 14,846 patients for training and testing. During internal testing, the model had a sensitivity of 43% and a positive predictive value of 74% for identifying patients with stage D HF. Most importantly, the authors took on the monumental task of incorporating the ML model prospectively into a clinical workflow. The positive predictive value was unsurprisingly lower in this prospective test (50.3% for stage D HF), but there were 56 patients referred for advanced HF therapy evaluations which might not have occurred (or would be delayed) without this workflow.

Applying the latest artificial intelligence advances to this important clinical need is an intuitive and necessary advance for patients with HF. ML is particularly well-suited to this classification task because it can objectively integrate a vast array of information while accounting for nonlinear relationships and interactions between variables.[13]

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While ML has been applied to many different clinical problems, prospective implementation studies are few and far between. These studies are critical before clinical implementation to ensure that ML models perform adequately when applied to new patient data. This is particularly important when applying models to advanced HF populations which are constantly changing over time.[14] However, the performance of the proposed workflow should still be evaluated in an external population before broader implementation is pursued.

There are a few other potential barriers to clinical implementation which warrant further attention. Most apparent is the significant amount of clinical work generated by the ML workflow. With 416 patients identified for review in just over 8 months, dedicated, multidisciplinary support is needed. However, it is worth highlighting that the positive predictive value in the prospective testing is comparable to the proportion of patients accepted for advanced therapies referred through conventional pathways (~60%),[10] which could continue in parallel. Explainable ML models (which identify the most important features for a specific prediction)[14] could potentially simplify the review process. We recently demonstrated that explainable ML predictions could be used by physicians to improve their own interpretation accuracy when applied to myocardial perfusion imaging.[15]

One other potential barrier to clinical implementation of ML is the presence of missing values which are inevitable in data collected through routine clinical care. For example, in the present study, over 40% of values were missing for some variables. There are methods for handling this issue without sacrificing model performance,[16] including models with significantly reduced model features.[17] However, McGilvray et al[18] developed a deep-learning model to predict death or advanced HF therapies which incorporated up to 100 measurements over time for >100 variables. Their model had a c-statistic of 0.91 (during internal testing), highlighting the power of providing a large amount of information to the model.

Therefore, while the proposed workflow generates a new set of issues to consider, refinements in the approach could help address the most obvious concerns. Regardless, all health care workers will need to become more comfortable with artificial intelligence techniques as the number of potential clinical applications continues to grow.[19,20] In particular, it may be time to ask if computers can help us find the "sweet spot" in end-stage HF.

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