EDITORIAL

The Road to Early Diagnosis of Transthyretin Cardiac Amyloidosis in Argentina

El camino hacia un diagnóstico temprano de la amiloidosis cardíaca por transtiretina en Argentina

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Transthyretin cardiac amyloidosis (ATTR-CA) is a significant but underdiagnosed cause of heart failure in older adults. (1) In recent years, its diagnostic incidence has shown a considerable increase. This growth can be attributed to greater medical knowledge, the growing availability of noninvasive diagnostic tools such as bone scintigraphy with bisphosphonates, and the advent of new therapies modifying the course of the disease. (2) The concept of red flags aims to facilitate diagnosis by identifying combinations of clinical signs and symptoms yielding higher probability of cardiac amyloidosis detection. (2) Several of the red flags include clinical, electrocardiographic and echocardiographic elements, the most relevant being a history of bilateral carpal tunnel, wall thickening with low ECG voltages, altered ventricular filling, low tissue velocity or decreased global longitudinal strain (GLS) in the basal and medial segments, with apical preservation. (3) Nevertheless, the diagnosis of ATTR-CA continues to be made predominantly in elderly patients and in advanced stages, which limits therapeutic options and significantly reduces the positive prognostic impact that an early intervention could offer.

The importance of generating one's own knowledge

With this issue in mind, Gobbo et al. present the *deteCTTAR* score, a predictive model developed entirely from local data, (4) which ensures that the diagnostic tools are truly useful in our setting. Many predictive models developed in other regions do not necessarily reflect the characteristics of our populations, which can lead to diagnostic underestimation or implementation of ineffective strategies.

The model proposed by the authors is based on clinical, electrocardiographic and echocardiographic variables that are easily obtained in routine clinical practice and are considered red flags for the search of the disease in question. We believe that the inclusion of predictor variables such as history of bilateral carpal tunnel, interventricular septal thickness (≥16 mm) and pseudonormal or restrictive diastolic relaxation pattern makes it easily applicable, with information obtained simply from a correct anamnesis and a transthoracic Doppler echocardiogram, a widespread practice. On the other hand, the score showed remarkable sensitivity and specificity for the detection of cardiac amyloidosis (AUC 0.88), with better performance than other international scores already validated in different cohorts. These scores have been developed in larger multicenter studies for the diagnosis of ATTR-CA and light chain (AL) amyloidosis. Among these, one of the most important was that of Boldrini et al. who studied 1187 patients with suspected cardiac amyloidosis. In this study, 332 patients were diagnosed with AL amyloidosis and 339 with ATTR-CA. The parameters that were predictive for the diagnosis of AL amyloidosis were relative wall thickening, E/e' ratio, tricuspid annular plane systolic excursion (TAPSE) and GLS, while for ATTR-CA the apex-to-base systolic ratio was also added. (5) The study published in the Argentine Journal of Cardiology has the great value and originality of using local data.

Fitting the model: have we chosen the adequate septal thickness threshold?

One of the aspects that we believe is important to discuss is the choice of an interventricular septal thickness ≥16 mm as the cutoff point. This seems to be a solid criterion, but could limit the sensitivity of the model. In patients with earlier forms of the disease, a lower threshold, such as ≥12 mm, the cutoff point used in other international scores, could have better sensitivity, and thus potentially improve the model's ability to detect early-stage disease. In fact, in the

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study published by Gobbo et al, (4) 39% of patients diagnosed with ATTR-CA had septal thickness between 12 and 16 mm. This type of adjustment can be useful to ensure that we not only identify those who already have advanced disease, but also those in whom early intervention can make a difference.

The importance of red flags

The use of red flags as predictor variables in the model is one of the work's strengths. A history of bilateral carpal tunnel, for example, not only has a strong association with ATTR-CA, but also represents a unique opportunity to identify patients in subclinical stages. Incorporating this variable into clinical practice could foster greater diagnostic sensitivity among non-cardiologists, such as traumatologists and rheumatologists, expanding the opportunities for early diagnosis.

On the other hand, the pseudonormal or restrictive diastolic relaxation pattern, variables widely recognized in echocardiography, highlights the value of this method as an accessible and useful tool for the detection of ATTR-CA. Taken together, these variables reinforce the idea that the early diagnostic approach does not necessarily require complex technologies, but rather a correct identification of the key findings in the clinical and imaging evaluation.

Prospective validation, next steps and concluding remarks

Although the results of the *deteCTTAR* score are promising, its implementation in clinical practice will require prospective validation in independent cohorts. This step is crucial to confirm the robustness of the model and to adjust for possible biases derived from the population used in the initial analysis.

Its development marks a significant advance in the field of cardiac amyloidosis in our country. Beyond its figures and results, this work points to the importance of prioritizing local research and fostering a culture of knowledge generation adapted to our needs.

Today's medicine faces the challenge of being more accurate and earlier. In diseases such as ATTR-CA, where the time of diagnosis is a critical factor for the future prognosis of the compromised patient, tools such as the *deteCTTAR* score not only represent an opportunity to improve the diagnosis of cardiac amyloidosis, but also to optimize the prognosis through early treatment.

Ethical considerations

Not applicable.

Conflicts of interest

None declared.

(See authors' conflict of interests forms on the web).

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