

The Need for a New Description of Red Flags in Cardiac Amyloidosis in Turkish Population

Türk Toplumunda Kardiyak Amiloidozda Kırmızı Bayrakların Yeni Bir Tanımına Olan İhtiyaç

Dear Editor,

We read the article by Yalvaç et al.¹ entitled "The Most Predictive Red Flags for Suspecting Cardiac Amyloidosis in Patients with Heart Failure with Preserved Ejection Fraction." We want to share our experiences with cardiac amyloidosis and also have some concerns about the study. We think that addressing these concerns will provide a better understanding of the study.

Cardiac amyloidosis has gained attraction among cardiologists after the introduction of tafamidis as a new therapeutic agent in recent years. The ATTR-ACT (the Transthyretin Amyloidosis Cardiomyopathy Clinical Trial) study² has shown that tafamidis increases the six-minute walking distance, improves quality of life, and extends life. After the approval of tafamidis as a new therapeutic in Türkiye in November 2021, cardiologists have become increasingly suspicious of cardiac amyloidosis in patients, especially in those with signs and symptoms of heart failure accompanied by left ventricular hypertrophy in our country. Accordingly, efforts to diagnose and understand this rare disease have increased.

The study by Yalvaç et al.¹ is a good example of such efforts. An important feature of this study is that data collection began prospectively approximately one year before tafamidis was approved. This suggests that the authors planned the study independently of the treatment, which is admirable.






However, we have some concerns about the study. Firstly, although the study, and therefore the methods and materials, was approved by the Ethics Committee in December 2020, the authors declare that "All patients were assessed for transthyretin cardiac amyloidosis (TTR-CA) red flag features, cardiac and extracardiac, as outlined in the 'Diagnosis and Treatment of Cardiac Amyloidosis: A Position Statement of the European Society of Cardiology.' This guideline³ was published in 2021. The authors' explanation of how they received Ethics Committee approval in 2020 based on an article published in 2021 raises an important question in the minds of the readers.

Secondly, the related guideline recommends screening only patients with left ventricular wall thickness ≥ 12 mm. However, according to Table 3, the interventricular septum (IVS) thickness is 12 mm or thicker in 75.4% of the patients. This means that the IVS was thinner than 12 mm in 24.6% of the patients. It would be useful for the authors to state why and according to what criteria they investigated cardiac amyloidosis in these patients.

Lastly, we want to share the red flags of the four patients we have diagnosed with cardiac amyloidosis. The red flags that we have observed in these patients were:

1. Heart failure >65 years, predominantly right-sided and normal or mildly reduced left ventricular ejection fraction (four patients)
2. Left ventricular hypertrophy (four patients)
3. Aortic stenosis (one patient)

LETTER TO THE EDITOR EDİTÖRE MEKTUP

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4. Decreased tissue Doppler annular velocities (<5 cm/sec) (four patients)
5. Atrial fibrillation (four patients)
6. Being hypotensive or normotensive in previously hypertensive patients (four patients).

We have seen that the red flags in our four patients are quite different from those of the patients in Yalvaç et al.'s study.¹ The most important difference is that all of our patients had atrial fibrillation, while atrial fibrillation was present in less than 50% of the patients in this study. Additionally, none of our patients exhibited a pseudoinfarct pattern. Red flags in our patients similar to Yalvaç et al.'s study¹ were as follows: (1) All our patients were 65 years of age or older; (2) Although not meeting full criteria, there were lower QRS voltages than expected; (3) Tissue Doppler velocities were low in all cases.

When we compared this study with our own limited data, we learned that red flags are important, but there may be different red flags in different patients, all of which need to be investigated meticulously, including extracardiac red flags. Screening of patients with suspected cardiac amyloidosis is performed by methods that are both expensive and involve more

or less radiation. In this sense, it is of great importance to use red flags and to understand which red flags are more prominent in Türkiye. In this context, we find the study of Yalvaç and his colleagues valuable and believe that it is important to increase such studies and even conduct them across the country. We think that diagnostic algorithms specific to Türkiye should be created by combining experiences.

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