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https://doi.org/10.1016/j.recesp.2023.11.012

Diagnosing transthyretin amyloidosis in patients with known genetic cardiomyopathies – opportunities and open questions. Response

Amiloidosis por transtirretina diagnosticada en pacientes con una miocardiopatía previa - oportunidades y preguntas abiertas. Respuesta

To the Editor,

We would like to thank Casian et al. for their interest in our article,[1] and we will try to address some of the issues raised.

Although the family study in the first 2 cases did not identify more carriers, the *TNNC1* p.Ala8Val and *MYL3* p.Met173Val variants have been reported in other families with hypertrophic cardiomyopathy and functional studies have been reported that support their pathogenicity.[2,3]

False positives of cardiac scintigraphy occur mostly in other types of amyloid cardiomyopathy, but also in recent myocardial infarction or hydroxychloroquine cardiotoxicity. Blood pool could be interpreted as a false positive, and consequently single photon emission computed tomography is recommended to confirm uptake.[4] We acknowledge that false positive cases have been reported in hypertrophic cardiomyopathy,[5] but unlike ours, those did not show the red flags or imaging findings expected in cardiac transthyretin amyloidosis, such as apical sparing in speckle-tracking or high T_1/extracellular volume.[4] Our first case had a chronic coronary syndrome but not recent myocardial infarction, and transthyretin amyloidosis deposits were confirmed in endomyocardial biopsy.[1] Currently, a noninvasive diagnosis of cardiac transthyretin amyloidosis is accepted when the clinical picture is compatible and there is grade $\geq$ 2 uptake in cardiac scintigraphy in the absence of monoclonal gammopathy.[4]

Finally, tafamidis 61 mg was initiated in the first and second cases. In the third case, it was not initiated because the patient refused to attempt histological confirmation.

FUNDING

No funding was received for this study.

SEE RELATED CONTENT:
https://doi.org/10.1016/j.rec.2023.11.012

STATEMENT ON THE USE OF ARTIFICIAL INTELLIGENCE

No artificial intelligence tools were used in this study.

AUTHORS' CONTRIBUTIONS

E. Martín-Álvarez, R. Barriales-Villa and J.M. Larrañaga-Moreira designed and wrote the manuscript. M.G. Crespo-Leiro critically reviewed the manuscript.

CONFLICTS OF INTEREST

J.M. Larrañaga-Moreira, M.G. Crespo Leiro, and R. Barriales-Villa report they received funding from Pfizer to attend conferences. M.G. Crespo-Leiro received funding from Pfizer at her institution to participate in a clinical trial. R. Barriales-Villa has performed consultancy work for Pfizer, Alnylam, and Akcea.

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Available online 16 January 2024

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https://doi.org/10.1016/j.recesp.2023.12.009

Circadian rhythm of heart rate in patients with heart failure

Patrón circadiano de la frecuencia cardiaca en pacientes con insuficiencia cardiaca

To the Editor,

After reading with interest the study published in *Revista Española de Cardiología* by de Juan Bagudá et al.,[1] we would like to make some observations that may be useful for readers.

Blood pressure (BP) and heart rate (HR) are 2 physiological variables showing a circadian rhythm with diurnal peaks and nocturnal valleys. These vital signs are crucial for optimizing pharmacological therapy in patients with heart failure (HF). However, in clinical practice, a single daily measurement is obtained from patients and no consideration is given to the likely circadian behavior of these variables. This may limit the value of the prescribed drugs that could be mitigated by using ambulatory blood pressure monitoring (ABPM). Studies have compared ABPM with in-office measurement to better stratify the cardiovascular risk, particularly when ABPM is used to assess systolic BP during sleep. Not only do patients with BP with a blunted sleep decrease show increased cardiovascular risk, but this risk is also elevated in patients with a HR with a blunted sleep decrease.[2,3]

In a study published by de Juan Bagudá et al.,[1] ABPM was conducted in patients with HF with a full spectrum of left ventricular ejection fraction (LVEF) values. The objective was to determine the prevalence and factors associated with the different phenotypes of diurnal hypertension and to elucidate the nocturnal BP patterns in patients with HF. The study selected 266 patients who did not show clinical decompensation and who were receiving optimal medical therapy for BP measurement in the office and via 24-hour ABPM. The authors classified the nocturnal patterns as dipper, extreme dipper, nondipper, and riser (reverse dipper). The patients' mean age was 71.8 ± 12 years; 177 (66.5%) were men and 210 (79%) had a previous diagnosis of hypertension. The most frequent nocturnal pattern was nondipper (42.9%), which was associated with worse functional class and a higher proportion of patients with HF and reduced LVEF. Notably, no differences were seen in nocturnal patterns according to LVEF. The authors highlighted 2 crucial facts. First, they detected a high prevalence of abnormal nocturnal BP patterns vs the general population or those with hypertension. According to these data, just 31% of patients with HF had a dipper pattern compared with 70% of the healthy population and those with hypertension. Second, patients with a nondipper pattern represented 42.9% of the sample, which is possibly related to the higher levels of catecholamines and circulating blood volume in the recumbent position.

The nocturnal nondipper pattern of BP and HR is little studied in HF. Some data suggest that HR with a blunted nocturnal drop may be associated with higher all-cause mortality vs BP with no nocturnal decrease.[3] Recently, Ogoyama et al.[4] demonstrated that patients with a nocturnal nondipper HR pattern who have elevated natriuretic peptide levels exhibit a higher risk of cardiovascular events. The study by de Juan Bagudá et al.[1] did not examine the importance of the HR-related parameters measured by ABPM in patients with stable HF. In addition, the authors found no differences in the baseline natriuretic peptide concentrations of their population according to BP phenotype. It would be interesting to know if the same happens with HR.

Accordingly, the circadian analysis of HR in patients with HF could help to facilitate the prognostic determination of patients with stable HF. Given that the nondipper pattern of BP is present in many patients with HF, similar findings to those of HR might be obtained. HR measurement does not require additional actions during ABPM, is easily obtained, and could provide the circadian pattern of HR in patients with HF for an optimal therapeutic approach and better discrimination of cardiovascular risk.

SEE RELATED CONTENT:
https://doi.org/10.1016/j.rec.2023.02.018

FUNDING

No funding received.

AUTHORS' CONTRIBUTIONS

All authors contributed equally to the drafting of this letter.

CONFLICTS OF INTEREST

None.

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Available online 12 January 2024

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