Echocardiography in Diabetic Cardiomyopathy

El ecocardiograma en la miocardiopatía diabética

MARÍA EUGENIA DELLE DONNE[1]

Diabetic cardiomyopathy is defined as structural and functional myocardial impairment secondary to diabetes mellitus, in the absence of coronary artery disease, hypertension, or other causes of heart disease. (1) Its prevalence is uncertain, but it is estimated that approximately 12–22% of diabetic patients develop diabetic cardiomyopathy after 10 years of disease duration. (1) Therefore, it is essential to identify clinical, laboratory, and imaging markers that enable early diagnosis, allowing timely initiation of appropriate treatment and preventing disease progression.

Pathophysiologically, hyperglycemia, insulin resistance, and lipotoxicity induce oxidative stress, inflammation, cardiomyocyte apoptosis, and interstitial fibrosis, initially resulting in impaired ventricular relaxation, followed by left ventricular hypertrophy and, in advanced stages, impaired systolic function. (2)

Consequently, echocardiography is a useful, accessible, and reproducible imaging technique. It enables the identification of patients with diastolic dysfunction, an early marker of diabetic cardiomyopathy, (1) as well as patients with reduced global longitudinal strain before changes in ejection fraction occur, an early marker of systolic dysfunction. (3)

In the study entitled "*Differences in Diastolic Function and Global Longitudinal Strain on Stress Echocardiography between Elderly Diabetic and Non-diabetic Patients*" by Kufert et al., 176 diabetic patients and 771 non-diabetic patients underwent stress echocardiography. The researchers found that the group with diabetes had a higher prevalence of significant diastolic dysfunction, both at rest and during exercise, and that although left ventricular ejection fraction was normal and similar between the two groups, global longitudinal strain was significantly lower in diabetic patients. (4)

The study's strengths include the number of patients enrolled, the systematic exclusion of coronary artery disease as a potential confounder, the incorporation of conventional echocardiographic parameters alongside global longitudinal strain, and the assessment of impaired diastolic reserve during exercise, thereby unmasking an abnormality that is often not apparent at rest.

As a limitation, considering this was a cross-sectional study, the true prognostic impact of the observed abnormalities cannot be established. Although the association of diabetes with diastolic dysfunction and reduced global longitudinal strain is consistent, this does not address whether these findings identify patients at higher risk of developing heart failure with preserved ejection fraction. In this context, it would have been of interest to examine variables related to the course of diabetes, particularly whether patients were receiving SGLT2 inhibitors or GLP-1 receptor agonists, given that these therapies have been shown to modify the risk of heart failure and could influence echocardiographic parameters. (2;3)

As suggested by this study, diabetes mellitus is independently associated with a higher prevalence of diastolic dysfunction and reduced global longitudinal strain, even in the presence of preserved ejection fraction, reinforcing the concept of subclinical myocardial involvement. Awareness of these findings allows the echocardiographer to focus the examination on assessing these parameters and provides the clinical cardiologist with a broader perspective when initiating or modifying treatment in this population, rather than focusing solely on coronary or peripheral vascular disease.

Ethical considerations

Not applicable.

Conflicts of interest

None declared.

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AUTHORS' REPLY

Dear Dr. María Eugenia Delle Donne:

We appreciate your interest in our publication and agree that understanding the prognosis of this condition, asymptomatic diabetic diastolic cardiomyopathy, is important for determining the most appropriate therapeutic approach. We are continuing our work in this area and hope to share our results with you soon.

Sincerely.

Alejandro Simón Kufert
Cardiologist, Hospital Cesar Milstein

Are There Really Sex-Related Differences in Transthyretin Amyloidosis?

¿Existen realmente diferencias de sexo en la cardiopatía amiloidótica por transtiretina?

JOSEFINA PARODI[1]

We read with great interest the study "Clinical, imaging, and disease progression sex-related differences in transthyretin cardiac amyloidosis" by Decotto et al. The authors present one of the first national registries specifically addressing this topic and report findings consistent with international experience: women represent a minority of diagnosed patients, are diagnosed at older ages, and have lower wall thickness and better-preserved ventricular function at the time of diagnosis, with no significant differences in clinical course during follow-up. (1) Far from settling the debate, these results prompt us to reconsider several questions regarding the true impact of sex on this disease.

The first question is whether the marked epidemiological difference reflects a lower true prevalence or, at least in part, underdiagnosis in women. International registries such as THAOS and other contemporary cohorts show a clear male predominance, although the magnitude of this difference varies across studies. (2–4) The SCAN-MP study, which used an active screening strategy with nuclear scintigraphy in minority populations, found that women accounted for 31.3% of the active ascertainment cohort, compared with 13.3% of referral clinical cohorts. (5) Suspicion of transthyretin cardiac amyloidosis (ATTR-CA) continues to rely heavily on increased wall thickness, with absolute cutoffs derived from predominantly male populations. In this context, it is particularly interesting that, in the cohort presented, differences in wall thickness disappear after indexing these measurements to body surface area, and that a significant proportion of women have a septal thickness <12 mm at the time of diagnosis. These findings support the need to reassess whether current echocardiographic criteria might delay clinical suspicion and, consequently, access to confirmatory testing such as scintigraphy.

However, diagnostic bias likely does not fully account for the observed difference. In hereditary ATTR-CA, penetrance is clearly influenced by sex, with lower clinical expression and later disease onset in women carrying several pathogenic variants. This difference in penetrance suggests that biological mechanisms—possibly related to hormonal factors and transthyretin tetramer stability—also contribute to the natural history of the disease. The lower representation of women is likely the result of an interaction between these biological differences and lower clinical recognition.

Another relevant aspect is prognosis. Although some early series suggested a more unfavorable course in men, contemporary analyses adjusted for disease stage, including THAOS and other recent registries, have not demonstrated consistent differences in mor-

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tality or heart failure hospitalizations, in line with the results reported by the authors. (2,3) This suggests that the differences observed at the time of diagnosis do not necessarily translate into differences in disease course once the disease is established.

Finally, these observations should be interpreted in light of a persistent limitation in clinical research: the underrepresentation of women in pivotal ATTR-CA trials. Studies such as ATTR-ACT (6) and more recent trials of transthyretin-stabilizing or -silencing therapies included a markedly lower proportion of women, limiting the ability to perform sex-specific analyses. In this context, clinical practice registries are particularly valuable, as they provide a more precise understanding of the actual disease burden in women and help identify opportunities to optimize diagnostic and therapeutic strategies.

The study by Decotto et al. represents a valuable contribution to the regional literature. Rather than confirming that women present a different form of the disease, their findings prompt us to ask whether we are using diagnostic tools that are sufficiently sensitive to recognize a presentation that is likely to be different as well.

Ethical considerations
Not applicable.

Conflicts of interest
None declared.

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

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AUTHORS' REPLY

We thank Dr. Parodi for her interest in our article, "Clinical, Imaging, and Disease Progression Sex-Related Differences in Transthyretin Cardiac Amyloidosis," and for the accompanying editorial.

We agree with the hypotheses put forward and, in particular, with her concluding reflection, which prompts us to ask whether the diagnostic tools we currently use are sufficiently sensitive to recognize a clinical presentation that likely differs in women as well.

As Dr. Parodi points out, the challenge is no longer merely to demonstrate that differences exist between men and women with transthyretin cardiac-amyloidosis, but rather to develop diagnostic strategies capable of promptly identifying these differences and ensuring earlier access to diagnosis and treatment.

Santiago Decotto and team

Specialized Heart Failure Units

Unidades especializadas de insuficiencia cardíaca

MARIANGEL SANCHEZ[1]

Heart failure (HF) units have been established to systematize the diagnosis, treatment, and clinical follow-up of patients with HF, incorporating multidisciplinary teams, standardized protocols, and structured follow-up. In developed countries, their main benefit is the reduction of hospitalizations and the op-

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timization of guideline-based treatment. (1) In Latin America, where health care systems exhibit greater heterogeneity and structural restrictions, their implementation remains limited.

In the research study published by the Argentine Journal of Cardiology, "Impact of a Specialized Heart Failure Unit on Patients Hospitalized for Acute Heart Failure: Analysis of a Decade of Experience," 3368 hospitalizations for acute HF over a ten-year period were analyzed at a high-complexity center in Argentina, comparing an initial phase (2014–2019) with a consolidation phase (2020–2024) of the program. The most significant finding was a sustained reduction in the length of hospital stay, from 9.3 to 2.8 days, without an increase in in-hospital mortality or 30-day rehospitalization. (2) This result is clinically significant, as prolonged hospital stays for acute HF are associated with higher costs, complications, and a poorer prognosis. (3)

Although this study provides local evidence and suggests a consistent positive impact of HF units, it should be noted that the model was developed at a high-complexity, referral center. Its implementation required a considerable set of resources, such as staff specialized in HF, access to a day hospital, and telemonitoring, among others. Unfortunately, this level of resources is not typically available in most public centers or in a significant number of private centers in the region. This reality is evident in the ARGEN-IC registry, (4) a multicenter study with heterogeneous complexity, which reported longer hospital stays and reduced access to early outpatient follow-up, illustrating the gap between what has been demonstrated and what is replicable.

However, it is likely that not all components of the program have an equal impact on the observed outcomes; therefore, the real challenge for the future appears to be identifying which components are indispensable and which could be adapted for centers with fewer resources. An interesting contribution of this study was the use of the coefficient of variation (CV) as an indicator of care stability. In this regard, this methodological tool could also be applied to evaluate adapted versions of the model and thus generate local evidence to guide its gradual implementation in our setting. (5)

The study's findings encourage reconsidering the design of HF units in versions adapted to available resources, identifying those components of greater clinical impact, with the goal of expanding access to a population with increasing prevalence, as patients with HF.

Ethical considerations
Not applicable.

Conflicts of interest
None declared.

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

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AUTHORS' REPLY

We thank the author for her careful reading and comment, which provides a valuable perspective on the implementation of HF units in heterogeneous healthcare systems. We agree that the gap between what has been demonstrated and what is replicable in the region is real, and that the ARGEN-HF registry clearly illustrates this disparity. However, we believe it is necessary to clarify one point: the commentary groups components of quite different nature under the notion of "resources," and that distinction is, in our view, central to considering the replicability of the model.

Staff specialized in HF, day hospital, and telemonitoring do indeed require institutional investment, whether in dedicated training, physical space, or technology. But a significant portion of our program's components do not depend on that type of investment: management based on critical pathways, structured discharge checklist, education with written guidelines, administrative coordination of appointments and follow-up, and multidisciplinary case conferences for complex decision-making are not merely ancillary elements of the program; rather, the available evidence suggests that they account for a significant portion of its clinical effect, and their implementation depends on systematization and organizational discipline, not on the facility's level of complexity.

This is consistent with the meta-analysis by McAlister et al., which showed that multidisciplinary strategies involving active follow-up by trained staff and access to specialized consultations reduce all-cause mortality and hospitalizations, whereas models of scheduled consultations without structured follow-up show a considerably smaller benefit. (1) Similarly, the meta-analysis by Feltner et al. on transitional care in

HF showed that programs focused on discharge education, follow-up coordination and early post-discharge contact—rather than isolated technological interventions—were the ones that significantly reduced readmissions. (2)

Something similar can be said regarding the day hospital. Its rationale does not lie in the availability of a dedicated space, but preferably in a protocol for intensive outpatient treatment and follow-up that helps prevent avoidable hospitalizations in selected low-risk patients. Strictly speaking, it is a way of working—involving explicit selection criteria, a standardized diuretic regimen, and closely spaced follow-up appointments—rather than a physical structure. In our own experience, the day hospital operated for many years using general inpatient beds, without a dedicated physical space, and it was not until 2023—toward the end of the consolidation period analyzed—that a dedicated area became available. This reinforces the fact that the protocolized approach preceded, and largely explains, the observed benefit, regardless of the infrastructure available at any given time.

It should also be noted that, within our own cohort, components such as telemonitoring were gradually incorporated only in the final years of the consolidation period, whereas the most pronounced decline in length of stay was already evident in earlier stages, limiting the ability of these technological components alone to explain the sustained improvement observed throughout the decade. This point is significant when considering local historical evidence: the DIAL study, conducted in Argentina two decades ago, showed that an intervention as simple as structured telephone follow-up by trained nurses—without any technological support—significantly reduced mortality and hospitalizations due to HF in outpatients. (3) The fact that a low-cost strategy without a technological component has demonstrated a benefit of this magnitude reinforces the idea that the critical factor is the consistency and quality of contact with the patient—and not necessarily the sophistication of the tool used to achieve it.

In short, we agree with the author that identifying the relative importance of each component is the central challenge in the future, and that the proposed coefficient of variation could be a useful tool for that assessment.

Our interpretation of the evidence suggests that these results are based on organizational components and structured follow-up—which do not require a high-complexity center for implementation—rather than on the incorporation of technology. Ultimately, we believe that a HF unit is not a matter of technological sophistication or exceptional resources, but rather of maintaining a systematic, patient-centered approach to care. It is, above all, an institutional decision: a project that relies on widely available or low-cost resources, whose true challenge lies not in availability but in sustainability—consistently applying these protocols with a care team whose goal is the continuous improvement of the quality of care for patients with HF. Standardizing care—rather than any specific resource—is what explains the observed results and what expands, instead of restricting, the real possibilities for adapting the model to other centers in the region.

The Authors

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