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CASE REPORT

INTERMEDIATE

CLINICAL CASE

Percutaneous Repair of Atrial Functional Tricuspid Regurgitation in Cardiac Amyloidosis

Combining Linear With Lateral Thinking

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ABSTRACT

Restrictive physiology, such as cardiac amyloidosis, compromises atrial and ventricular performance, often leading to "atrial" functional valvular regurgitation. While focusing on atrial functional tricuspid regurgitation we aimed at summarizing the pathophysiological characteristics of, and therapeutic options in, cardiac amyloidosis. (**Level of Difficulty: Intermediate.**) (J Am Coll Cardiol Case Rep 2023;5:101685) © 2023 The Authors. Published by Elsevier on behalf of the American College of Cardiology Foundation. This is an open access article under the CC BY-NC-ND license (http://creativecommons.org/licenses/by-nc-nd/4.0/).

A 79-year-old retired dentist was admitted to the cardiology unit for shortness of breath and fatigue (NYHA functional class III-IV). Physical examination revealed a near-normal blood pressure, a crescendo-decrescendo systolic murmur, and an irregular pulse. Jugular vein distention and peripheral lower-leg edema were consistent with overt right heart failure.

LEARNING OBJECTIVES

- To be able to correctly interpret clinical and imaging data looking for an appropriate diagnosis of CA, which still represents an underdiagnosed disorder.
- To identify new therapeutic opportunities, such as percutaneous tricuspid repair in carefully selected patients, where the traditional pharmacological practice for heart failure is less effective and poorly tolerated.

MEDICAL HISTORY

The risk factors for coronary artery disease include hypertension, dyslipidemia, and former smoking. The patient's medical history was remarkable for persistent atrial fibrillation (AF), aortic stenosis, and previous percutaneous revascularization of the left anterior descending coronary artery. Comorbidities included renal failure (glomerular filtration rate 45 mL/min/1.73 m^2) and coxarthrosis.

DIFFERENTIAL DIAGNOSIS

The differential diagnosis included right heart failure, atrial fibrillation, hypertensive cardiomyopathy, aortic stenosis, tachycardia-induced cardiomyopathy, cardiac amyloidosis.

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The authors attest they are in compliance with human studies committees and animal welfare regulations of the authors' institutions and Food and Drug Administration guidelines, including patient consent where appropriate. For more information, visit the Author Center.

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ABBREVIATIONS AND ACRONYMS

AF = atrial fibrillation

aFTR = atrial functional tricuspid regurgitation

CA = cardiac amyloidosis

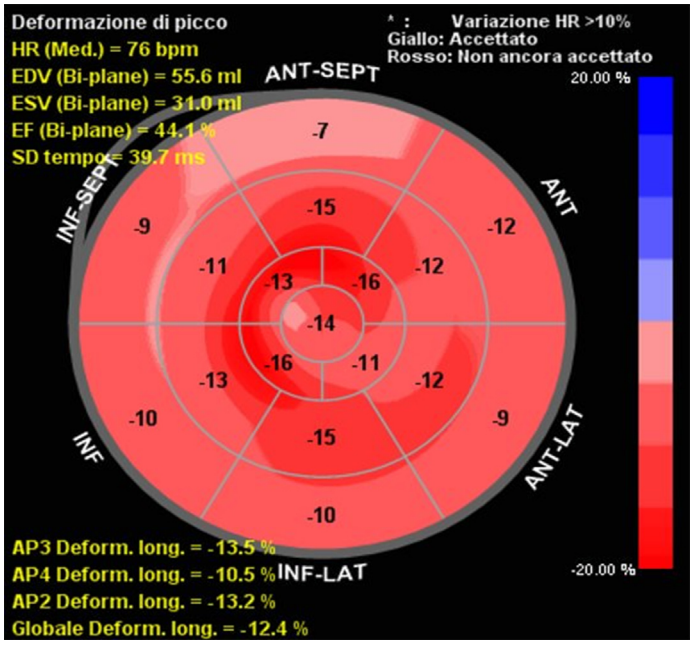
ECG = electrocardiogram

INVESTIGATIONS

The electrocardiogram (ECG) showed low voltages, AF (98 beats/min), and left bundle branch block. Transthoracic echocardiography displayed increased biventricular thickness, with a granular and sparkling pattern and a low to normal left ventricular ejection fraction (55%) (Video 1). Two-dimensional speckle tracking indicated an apical sparing pattern of longitudinal strain (**Figure 1**). Bi-atrial enlargement was consistent with elevated ventricular filling pressures and persistent atrial fibrillation. Thickening and calcification of the left-side valves led to moderate aortic stenosis and mild mitral regurgitation. The increase in tricuspid annular dimension accompanying right atrial enlargement produced severe atrial functional tricuspid regurgitation (aFTR): the vena contract width was 0.7 cm, the effective regurgitant orifice was 0.4 cm^2, and the calculated regurgitant volume was 45 mL (Video 2). Transesophageal echocardiography showed thickened tricuspid leaflets consistent with amyloidosis infiltration and confirmed severe aFTR due to significant enlargement of the annulus (45 mm), with a main coaptation gap between the septal and the anterior leaflets (**Figure 2**).

As a whole, the patient's medical history and the clinical, ECG, and echocardiographic findings were consistent with cardiac amyloidosis. The ^{99m}Tc-hydroxymethylene diphosphonate confirmed a significant cardiac uptake (Grade 3) (**Figure 3**). Serum and urine electrophoresis and immunofixation and serum-free light chain measurement ruled out a clonal disease. The absence of genetic mutations eventually allowed the diagnosis of wild-type transthyretin cardiac amyloidosis.

FIGURE 1 2-Dimensional Speckle-Tracking Echocardiography Showing the Apical Sparing Pattern



MANAGEMENT

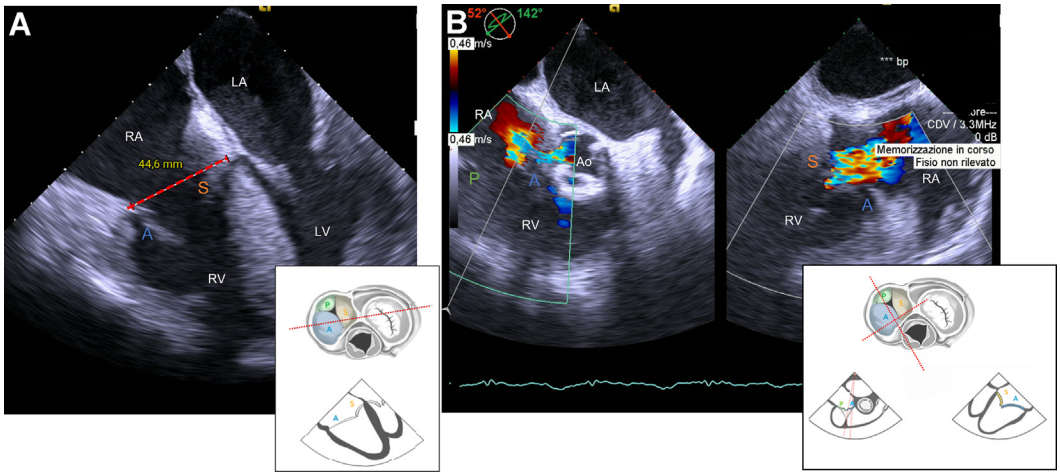
The patient was already treated at home with a high dosage of furosemide (175 mg/day), in the presence of kidney disease, and therefore aFTR was thought to play a significant role in the ongoing episode of right heart failure and on the risk of future recurrences.

Owing to a notable risk of conventional surgery, we planned a percutaneous tricuspid valve repair. Preprocedural dedicated computed tomography confirmed severe dilatation of the tricuspid valve annulus with a central coaptation gap. Right cardiac catheterization performed immediately before tricuspid valve intervention, under a maximal diuretics dosage to facilitate grasping the leaflets, still showed elevated mean atrial, end-diastolic right ventricular, and mean pulmonary artery pressures (10, 11, and 35 mm Hg, respectively). The percutaneous procedure was performed by placing a first TriClip XT between the septal and the anterior leaflets and an additional clip between the septal and the posterior leaflets (triple orifice technique). The residual regurgitation was mild, with a mean pressure gradient forward the valve of 1.8 mm Hg (**Figure 4**).

DISCUSSION

Cardiac amyloidosis is characterized by the progressive extracellular deposition of misfolded proteins, resulting in a phenotype mimicking other frequent cardiovascular diseases, such as aortic stenosis or hypertensive cardiomyopathy (**Figure 5**).[1] Although underdiagnosed, recent data suggest that cardiac amyloidosis is responsible for a notable proportion of heart failure cases with preserved ejection fraction.[2]

FIGURE 2 **Transesophageal Echocardiography Evaluation of Tricuspid Annulus and Regurgitation**



(A) Measurement of the septolateral diameter of the tricuspid valve annulus in mid-esophageal 4-chamber view (0°-20°). **(B)** Mid-esophageal right ventricle inflow/outflow with multiplane view (60°-100°) showing the main origin of the jet between the anterior and septal leaflets. A = anterior leaflet; Ao = aorta; LA = left atrium; LV = left ventricle; P = posterior leaflet; RA = right atrium; RV = right ventricle; S = septal leaflet.

Of note, wild-type transthyretin cardiac amyloidosis represents the most common cause of restrictive cardiomyopathy in older adults.[1]

Once the diagnosis of transthyretin cardiac amyloidosis is suspected and eventually confirmed, targeted pharmacological approaches, more effective in the early stages of the disease, are now becoming available at tertiary centers.[1,3] Nevertheless, most CA patients still mainly rely on the management of cardiovascular complications. Diuretics for fluid control represent a therapeutic cornerstone, but their effectiveness is limited because of the onset of diuretic resistance and the development of renal insufficiency. Moreover, despite a normal systolic function, the restrictive physiology impairs ventricular filling and forward stroke volume, which can be additionally reduced by the use of diuretics. Similarly, inasmuch as cardiac output in CA is maintained through an adequately high heart rate, β-blockers can be detrimental. Angiotensin-converting enzyme inhibitors, angiotensin II receptor blockers, and angiotensin receptor II blocker/neprilysin inhibitors are effective in patients with heart failure, but their use in CA remains uncertain.[4,5]

Concerning valvular heart disease, both functional and organic lesions occur in CA. Myocardial infiltration causes atrial enlargement by increasing ventricular filling pressures and eventually atrial functional tricuspid insufficiency.[6] On the other hand, atrial enlargement can also lead to AF, as reported in our

FIGURE 3 **^{99m}Tc-Hydroxymethylene Diphosphonate Scintigraphy Showing Significant Cardiac Uptake**

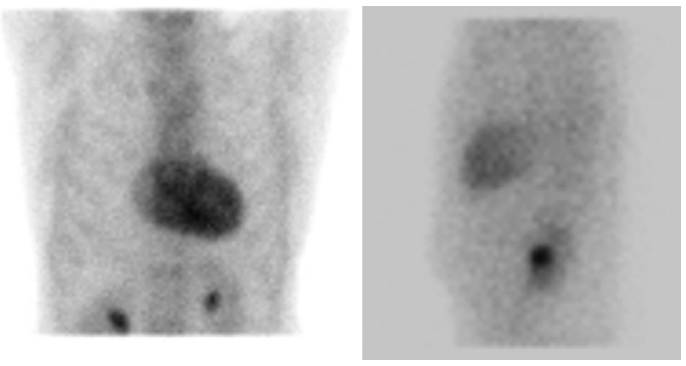
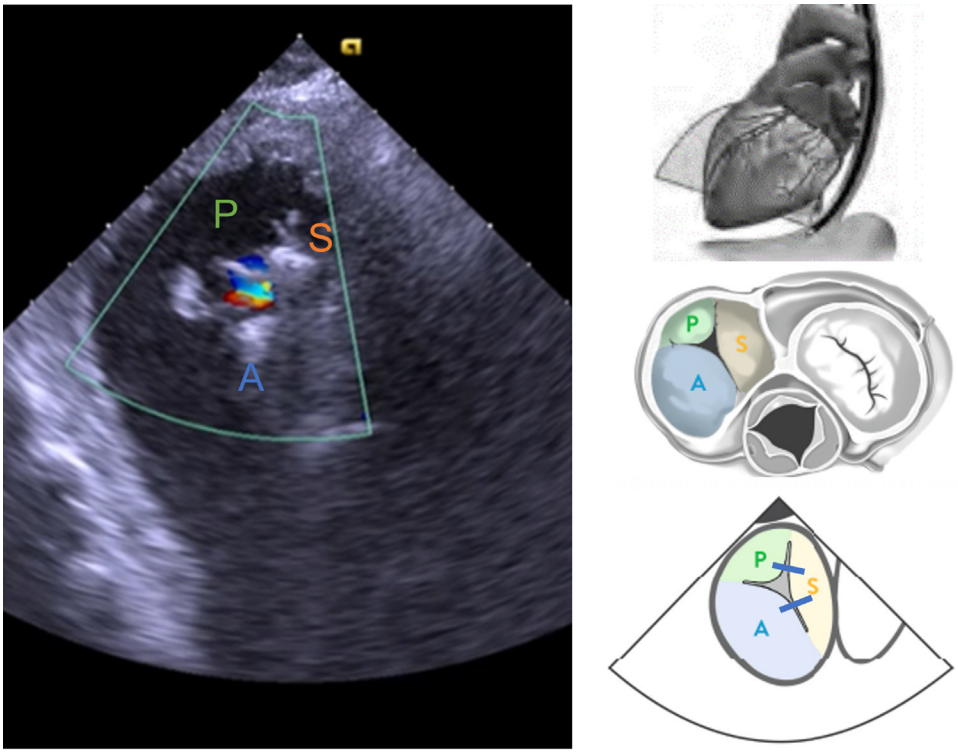


FIGURE 4 Postprocedural Transesophageal Echocardiography Evaluation of Tricuspid Regurgitation



Transesophageal transgastric short-axis view (20°-50°) focusing on the leaflets' tip after grasping the septal and anterior leaflet and septal and posterior leaflet with mild residual regurgitation. A = anterior leaflet; P = posterior leaflet; S = septal leaflet.

patient. Once established, AF might concur to atrial remodeling and further progression of annular enlargement.[7]

Finally, amyloid may directly deposit on atrial walls, increasing atrial stiffness, and on valve leaflets, eventually combining an organic cause with the functional component of the tricuspid regurgitation.[8]

Given that the clinical picture in our patient was dominated by right heart failure and the medical therapy was already maximized, we decided to tackle aFTR. Notably, the subtype of TTR amyloidosis, as in our patient, has been associated with increased involvement of the right side when compared with AL amyloidosis.[9] The percutaneous correction of aFTR significantly improved clinical conditions. The potential benefits of aFTR correction may lie in several factors. First, the reduced right atrial pressure may improve backward signs and symptoms characterizing right heart failure driven by congestion. Second, we hypothesize that aFTR correction may contribute to increasing forward stroke volume. In the setting of a reduced forward stroke volume due to the restrictive physiology, as in cardiac amyloid, the increased forward cardiac output may be relevant.[10] Although aFTR treatment may represent a therapeutic opportunity, it is worth remembering not to underestimate any therapeutic options in this challenging group of CA patients (**Figure 6**).

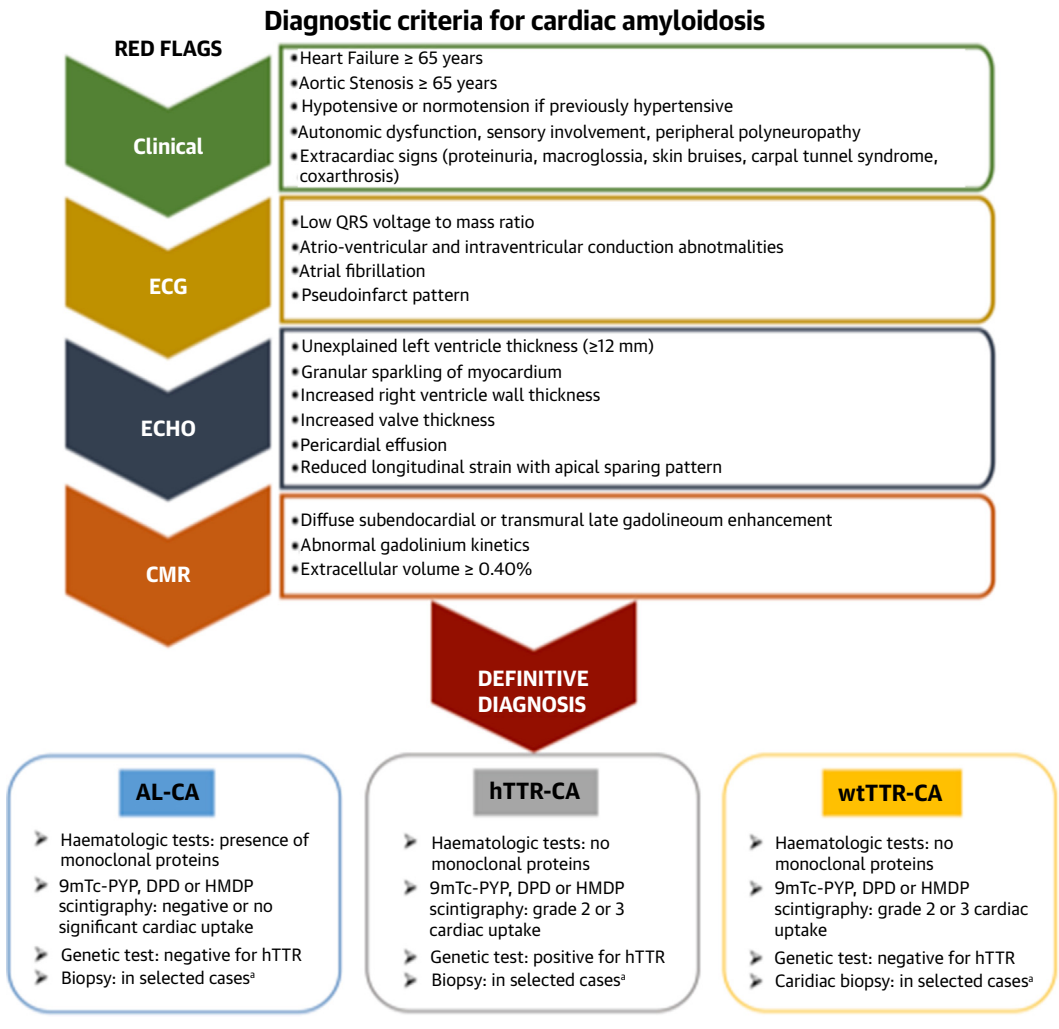
FOLLOW-UP

At 30 days, the patient experienced a significant improvement in symptoms and functional status (NYHA functional class I-II). The echocardiogram performed during the follow-up visit confirmed the short-term procedural success, defined as stability of the implanted devices and mild residual regurgitation (Video 3). A reduction in diuretic drugs was achieved.

CONCLUSIONS

In selected patients with right heart failure due to cardiac amyloid and aFTR, percutaneous edge-

FIGURE 5 Diagnostic Work-Up of Cardiac Amyloidosis



Cardiac or extracardiac biopsy is needed in the following cases: no cardiac scintigraphy uptake and negative monoclonal proteins, but very high clinical suspicion; grade 1 cardiac uptake and negative monoclonal proteins; scintigraphy showing cardiac uptake and at least 1 of the monoclonal protein tests is abnormal (cardiac biopsy). ECG = electrocardiogram; ECHO = echocardiography; CMR = cardiac magnetic resonance; AL-CA = light chain cardiac amyloidosis; hTTR-CA = hereditary transthyretin cardiac amyloidosis; wtTTR-CA= wild-type transthyretin cardiac amyloidosis; Tc = technetium; PYP = pyrophosphate; DPD = diphosphono-propanodicarboxylic acid; HMDP = hydroxymethylene diphosphonate.

to edge tricuspid valve repair might represent a new and promising therapeutic approach.

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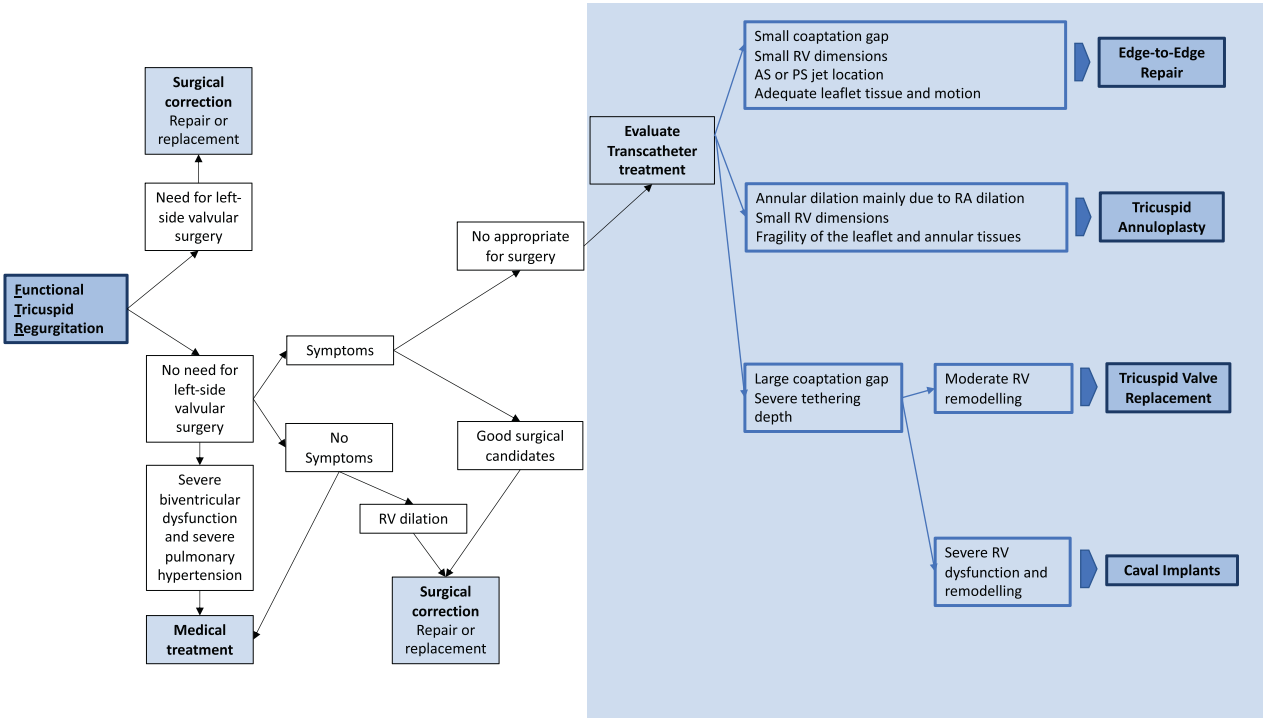
FIGURE 6 Therapeutic Approach to Functional Tricuspid Regurgitation



AS = anteroseptal; PS = posterior-septal; RA = right atrium; RV = right ventricle.

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KEY WORDS cardiac amyloidosis, restrictive physiology, atrial functional tricuspid regurgitation, tricuspid percutaneous repair

APPENDIX For supplemental videos, please see the online version of this paper.