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Review

Transthyretin cardiomyopathy – diagnosis and therapeutic options

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ABSTRACT

Transthyretin amyloid cardiomyopathy (ATTR-CM) is a rare but increasingly recognized cause of heart failure. ATTR-CM results from the deposition of misfolded transthyretin (TTR) protein fibrils in the extracellular matrix. Two main forms of ATTR are distinguished: hereditary (hATTR) and wild-type (wtATTR). The diagnostic gold standard has shifted from invasive biopsy toward a non-invasive algorithm, which includes laboratory tests, echocardiography, cardiac magnetic resonance, and scintigraphy. Contemporary disease-modifying therapeutic strategies – transthyretis stabilizers (tafamidis, acoramidis) and gene-silencing drugs (vutrisiran, patisiran) significantly improve the prognosis and functional capacity of patients with ATTR-CM.

KEYWORDS

transthyretin amyloid cardiomyopathy, bone scintigraphy, transthyretin stabilizers

Introduction

Transthyretin amyloid cardiomyopathy (ATTR-CM) is a rare but increasingly recognized cause of heart failure, particularly in elderly patients [1,2]. ATTR-CM results from the deposition of misfolded transthyretin (TTR) protein fibrils in the extracellular matrix.

Advances in imaging techniques, including radioisotope studies and cardiac magnetic resonance (CMR), have enabled rapid and non-invasive diagnostics [3,4], while the introduction of TTR stabilizers and gene therapies has revolutionized patient prognosis [5,6,7]. The unfavorable prognosis in ATTR has significantly improved due to the possibility of early initiation of specific treatments that inhibit amyloid deposition in organs. This article summarizes the pathophysiology, diagnostic algorithms, and modern therapeutic strategies for ATTR-CM.

Pathophysiology

The disease process in a patient with ATTR-CM proceeds through several key stages [2,8]:

- tetramer dissociation – this is the critical point. Due to genetic reasons or aging, the stable tetramer dissociates into individual monomers
- misfolding – the released monomers are unstable and change their spatial configuration, adopting a structure rich in beta-sheets
- aggregation – the altered monomers begin to associate, forming small oligomers, then protofibrils, and finally insoluble amyloid fibrils
- tissue deposition – these fibrils deposit in the interstitial space of various organs, most commonly the heart and the nervous system.

The accumulation of amyloid fibrils leads to stiffening of the heart walls, diastolic dysfunction, and subsequently, restrictive cardiomyopathy [1,8]. In advanced stages, patients present with biventricular systolic failure and microcirculatory disorders. Physiologically, transthyretin (TTR), synthesized in the liver and also known as prealbumin, serves as a transporter for thyroxine and retinol. The misfolding of TTR leads to amyloidogenesis.

Types of amyloidosis

Although over 30 precursor proteins have been identified, two types account for 95% of amyloidosis cases [1,9]:

1. Light chain amyloidosis (AL) – associated with plasma cell dyscrasia, characterized by an aggressive course (median survival without treatment <6 months) [10,11].
2. Transthyretin amyloidosis (ATTR) – results from the instability of the transthyretin (TTR) tetramer - a thyroxine and retinol transport protein produced mainly in the liver.

We distinguish two forms of ATTR [2,12]:

1. Hereditary (hATTR) – caused by a mutation in the TTR gene.
2. Wild-type (wtATTR) – acquired, age-related, occurring primarily in men over 65 years of age.

Hereditary Transthyretin Amyloidosis (hATTR) This is a rare disease caused by a mutation in the TTR gene. Its frequency depends on the geographical region. It is estimated that approximately 50,000 people worldwide live with hATTR [2]. In Poland, it is an ultra-rare disease. The exact number of patients is unknown, but it is estimated to be several hundred people [12]. In certain regions, such as northern Portugal, Sweden, Brazil, and Japan, the prevalence is significantly higher.

Wild-type Transthyretin Amyloidosis (wtATTR) known as senile amyloidosis, it is much more common than previously thought and mainly affects the elderly. It is estimated that amyloid protein is present in the hearts of up to 25% of individuals over 80 years of age, though it does not cause clinical symptoms in everyone [2,11].

Diagnosis

ATTR-CM often “hides” under the guise of other conditions. Diagnostic vigilance is crucial in high-risk groups:

- heart failure with preserved ejection fraction (HFpEF) – affects about 13% of this population [11]
- aortic valve stenosis – it is estimated that up to 16% of patients qualifying for TAVI may have concomitant ATTR-CM [13]
- extracardiac symptoms – may precede cardiomyopathy by many years [2,14]. These include: bilateral carpal tunnel syndrome (5–10 years earlier), spinal canal stenosis, and spontaneous rupture of the biceps brachii tendon.

Modern algorithms allow for a diagnosis without the need for invasive myocardial biopsy [3,15], provided specific criteria are met:

1. Exclusion of AL amyloidosis – should be the first step in ATTR diagnostics. This involves serum free light chain (FLC) assays and serum/urine protein immunofixation [1,3].

2. ECG – often shows low voltage (despite thickened heart walls) or conduction disturbances (blocks) [9,12].

3. Echocardiography (TTE) – the appearance in amyloidosis is very characteristic [8,12] and often allows for a preliminary diagnosis:

- thickening of heart walls – the most typical feature. It affects both the left (LV) and right (RV) ventricles, as well as the interventricular septum. Crucially, this thickening results from amyloid infiltration rather than cardiomyocyte hypertrophy (as seen in hypertension)

- myocardial structure ("Sparkling appearance") – classically described as "granular"

- thickening of other structures – as amyloid deposits everywhere, TTE also shows: thickening of valve leaflets, interatrial septum hypertrophy, right ventricular free wall hypertrophy

- atrial enlargement – results from high ventricular filling pressures. Significant biatrial enlargement is often seen alongside relatively small (or normal) ventricular cavities

- LV diastolic dysfunction – the earliest sign. The stiff myocardium is characterized by impaired relaxation. The next stage is the development of restrictive filling. Ejection fraction (LVEF) may remain normal for a long time (HFpEF) despite clinical symptoms, only declining in advanced stages of ATTR-CM

- pericardial effusion – a small to moderate amount of fluid in the pericardial sac is frequently observed.

The most sensitive and specific TTE parameter for amyloidosis is Global Longitudinal Strain (GLS). In amyloidosis, a characteristic “cherry on top” pattern (apical sparing) occurs [8,12]:

- strain (deformation) is significantly impaired in the basal and mid-segments of the heart
- strain in the apical segments remains normal or is significantly better than in the rest of the heart (“apical sparing”)
- on a “bull’s eye” map, this presents as a red center surrounded by lighter colors.

A vital diagnostic aspect is differentiating myocardial thickening caused by hypertensive heart disease from that caused by amyloidosis:

- in hypertension, thickening mainly affects the LV; the RV and interatrial septum usually remain normal
- in amyloidosis, practically the entire myocardium is thickened, including the valves. A rigid interatrial septum is characteristic
- in hypertension, thick LV walls on echocardiography correlate with high QRS voltages on ECG. In amyloidosis, there is a disproportion—LV walls are very thick, but ECG voltages are low (so-called low voltage).

Echocardiographic parameters differentiating patients with hypertensive heart disease and cardiac amyloidosis are presented in Table I.

Table I. Differential diagnosis: hypertension vs. cardiac amyloidosis

Parameter	Hypertension	Cardiac amyloidosis
Right ventricle	Usually not thickened	Frequently thickened
Interatrial septum	Thin (normal)	Thickened
Valves	Normal	Thickened
ECG (QRS)	High voltage	Low voltage
Strain pattern	Global decrease	Apical sparing
Pericardial effusion	Rare	Frequently present (small amount)

The interpretation of the parameters presented in Table I requires caution in patients with concomitant aortic stenosis (AS) and ATTR-CM. Latent amyloidosis is present in approximately

16% of patients undergoing transcatheter aortic valve implantation (TAVI) [13]. In this group, the classic “apical sparing” pattern in GLS (global longitudinal strain) imaging may be masked by non-specific strain abnormalities resulting from left ventricular pressure overload.

Furthermore, low QRS voltage - a classic feature of amyloidosis - occurs in only about 25–30% of patients with ATTR-CM. In many patients, the voltage may appear normal, which often leads to a misdiagnosis of hypertrophy (LVM) instead of protein infiltration. Therefore, critical assessment should not rely on voltage alone, but rather on the voltage-to-mass ratio. The disproportion between moderate voltage and massive wall thickening on echocardiography is a stronger predictor of amyloidosis than isolated low-voltage criteria.

4. Cardiac Magnetic Resonance (CMR) – currently considered the most accurate non-invasive imaging modality for diagnosing amyloidosis [3,4,14]. It allows not only for anatomical visualization (similar to echocardiography) but, more importantly, for tissue characterization, which is crucial for differentiating amyloidosis from other diseases. The patient receives a contrast agent (gadolinium), which washes out quickly from a healthy heart but remains longer in diseased tissue (e.g., affected by amyloid). This phenomenon is known as Late Gadolinium Enhancement (LGE).
In amyloidosis, enhancement is typically diffuse. Circumferential subendocardial enhancement (just below the inner layer of the muscle) is frequently observed. In advanced stages, amyloid involves the entire wall thickness (transmural enhancement), resulting in a very bright image of the entire myocardium. Modern CMR allows for mathematical quantification of tissue changes (mapping), which is particularly helpful in the early stages.

- Native T1 Mapping: Measures the longitudinal relaxation time of tissues without contrast. In amyloidosis, T1 values are very high (significantly higher than in hypertensive hypertrophy or hypertrophic cardiomyopathy). A native T1 mapping in an excellent non-invasive tool for detecting amyloid deposits in the heart, allowing for diagnosis even when other CMR parameters remain inconclusive.

- ECV (Extracellular Volume): This is the most important quantitative parameter. It measures the volume of the extracellular space. While the norm is approximately 25%, in amyloidosis, the ECV often exceeds 40–50%, meaning that half of the heart's volume is occupied by amyloid and fibrosis rather than muscle cells [3,4,14].

CMR confirms echocardiographic findings with greater precision:

- concentric thickening of the left and right ventricular walls.
- thickening of the interatrial septum.
- bi-atrial enlargement.
- frequent presence of pericardial and pleural effusions.

CMR has a very high negative predictive value. If the CMR image is normal (especially T1 and ECV parameters), cardiac amyloidosis is unlikely. Conversely, characteristic LGE combined with wall thickening almost confirms the diagnosis.

In the case of CMR, although parameters such as are revolutionary for the quantitative assessment of infiltration, their interpretation can be challenging in patients with chronic kidney disease (frequent in this population) due to the risk of nephrogenic systemic fibrosis following gadolinium administration. In such cases, the importance of Native T1 mapping parameters – which do not require contrast – increases, although their values may be masked by coexisting myocardial edema of a different etiology [4,16].

5. Bone Scintigraphy (using technetium-labeled phosphates): This is a key diagnostic tool for ATTR. These tracers have a specific affinity for transthyretin (TTR) deposits [3,13,17] in the heart, even though they were originally designed for skeletal imaging. Scintigraphy is evaluated using the Perugini Scale, which compares the cardiac signal intensity to the rib signal:

- Grade 0: No cardiac uptake (excludes ATTR).
- Grade 1: Mild cardiac uptake (less than bone uptake).
- Grade 2: Cardiac uptake equal to bone uptake (strong suspicion of ATTR).
- Grade 3: Cardiac uptake stronger than bone uptake, with the bone signal being barely visible or absent (the “vanishing skeleton” sign).

Before scintigraphy became widespread, the only way to definitively diagnose amyloidosis was through endomyocardial biopsy. Currently, if scintigraphy shows Grade 2 or 3 and blood/urine tests exclude AL amyloidosis, a diagnosis of ATTR can be made without a biopsy [3,13,17,18]. New diagnostic thresholds introduced in 2025 allow for even earlier detection of cardiac involvement (ATTR-CM), which is critical for prognosis. Moreover, the 2025 update confirms the algorithm based on bone scintigraphy and free light chain assays as the diagnostic gold standard [18].

Despite the high sensitivity of technetium pyrophosphate scintigraphy, its significant limitations must be emphasized. False-negative results may occur in patients with rare mutations (e.g.,

Phe64Leu), where the tracer's affinity for amyloid deposits is reduced [18]. Conversely, false-positive results (Perugini Grade 1) frequently appear in advanced AL amyloidosis, highlighting the necessity of concurrent hematological testing. It is vital to distinguish between the two main types of amyloidosis, as their treatments are entirely different (see Table II).

Table II. Comparison of ATTR and AL

Type	Cause	Bone Scintigraphy	Treatment
ATTR	Protein produced in the liver	Strongly positive	Protein-stabilizing drugs (e.g., Tafamidis)
AL	Hematologic malignancy	Usually negative	Chemotherapy

Diagnostics for cardiac amyloidosis are presented in Table III.

Table III. Diagnostic algorithm for cardiac amyloidosis

Immunofixation Result (Blood/Urine)	Scintigraphy Result (Perugini Scale)	Interpretation and Next Steps
NORMAL (No monoclonal protein)	**Grade 2 or 3** (Cardiac uptake)	**ATTR diagnosis** (no biopsy needed). Perform TTR genetic testing.
ABNORMAL (Monoclonal protein present)	**Grade 2 or 3**	Suspicion of AL or ATTR. **Heart biopsy** with Congo Red staining required.
NORMAL (No protein)	**Grade 0 or 1**	ATTR unlikely. If symptoms are severe – perform Cardiac CMR.
ABNORMAL (Protein present)	**Grade 0 or 1**	High suspicion of AL. Urgent hematological consultation and biopsy.

Genetic Testing

Once the presence of transthyretin deposits is confirmed, a genetic test (TTR gene sequencing) is essential. This allows for the differentiation between ATTRwt and ATTRm) [1,18,19].

Arrhythmias and conduction disorders in ATTR-CM

Structural changes in the heart (fibrosis and infiltration) serve as a substrate for numerous arrhythmias:

1. Supraventricular arrhythmias

- atrial fibrillation (AF) – This is the most common arrhythmia in ATTR-CM. It results from amyloid infiltration of the atrial walls, leading to stiffness, enlargement, and fibrosis. In an ATTR heart exhibiting diastolic dysfunction, atrial contraction accounts for a significant portion of ventricular filling. When AF occurs, cardiac output may suddenly drop by 25–30%; this condition can rapidly destabilize the patient and trigger signs of acute left ventricular heart failure, such as pulmonary oedema.

AF occurs in 44–69% of ATTR patients [11] and requires anticoagulation according to the CHA_2DS_2-VASc score [1,11]. Even in sinus rhythm, "stiff" atria may not contract effectively, promoting thrombus formation. Consequently, anticoagulation is often recommended regardless of the CHA_2DS_2-VASc score. Electrical cardioversion for AF often results in recurrence.

2. Conduction disorders

In ATTR-CM, involvement of the conduction system is progressive and often irreversible [12,19]. The most common conduction disorders include:

- sinus node dysfunction – May manifest as sinus bradycardia or tachycardia-bradycardia syndrome.

- atrioventricular (AV) blocks – Progression from first-degree block to complete heart block (third-degree) is frequently observed.

- intraventricular conduction disturbances – Widening of QRS complexes, left bundle branch block (LBBB), or multiscicular blocks are highly characteristic.

Pharmacological treatment of heart failure (CHF) in ATTR-CM

- beta-blockers – Routinely used in CHF; however, due to the fixed stroke volume of the "stiff" left ventricle, the heart rate of an ATTR patient must be strictly monitored.
- calcium channel blockers (verapamil, diltiazem) – These are contraindicated as they bind to amyloid, which can lead to advanced heart blocks [1,19].

In the treatment of ATTR-CM the use of loop diuretics and angiotensin receptor blockers (ARBs) requires great caution and an individualized approach.

- loop diuretics – These are the cornerstone of symptomatic treatment in ATTR-CM patients where heart failure with preserved ejection fraction (HFpEF) predominates. They help manage fluid overload symptoms (oedema, dyspnea, ascites). However, excessive doses can abruptly reduce cardiac output, leading to orthostatic hypotension, dizziness, and worsening renal function [1,6]. Higher doses than in standard heart failure are often necessary, but require strict monitoring of blood pressure and renal function.
- angiotensin receptor blockers (ARBs) – Unlike classical heart failure where ARBs are first-line drugs, their role in ATTR is often limited. Patients often have baseline hypotension and coexisting dysautonomia. ARB administration may trigger severe hypotension [1,12]. Furthermore, there is no strong clinical evidence that ARBs (or ACE inhibitors) inhibit the progression of amyloidosis or improve survival in this specific group. They may only be considered in patients with coexisting hypertension if well-tolerated.

Modern disease-modifying therapeutic strategies

Targeted therapies represent a breakthrough in ATTR-CM treatment [1,9,12], categorized as:

- TTR Stabilizers (tafamidis, acoramidis) – These bind to the TTR tetramer, preventing its dissociation. The ATTR-ACT study showed that tafamidis reduces mortality by 30% and hospitalizations by 32% [5]. Tafamidis has been granted the highest level of recommendation (ESC Class I) [13,20].

  Tafamidis treatment is currently a specific therapy with proven efficacy in reducing mortality and the risk of hospitalization frequency due to HF exacerbation among patients with ATTR-CM. The drug is a benzoxazole derivative that binds to tetrameric TTR, preventing the dissociation process into monomers. According to ESC guidelines and the position of the ESC Working Group on Myocardial and Pericardial Diseases, tafamidis is recommended as first-line treatment for both ATTRm and ATTRwt amyloidosis in patients with ATTR-CM, regardless of the co-occurrence of polyneuropathy. This position was confirmed in the 2021 ESC guidelines for the diagnosis and treatment of CHF, where tafamidis has a Class I recommendation with Level of Evidence B for patients with both ATTRm and ATTRwt amyloidosis and CHF in NYHA functional class I and II, as well as in the 2023 ESC guidelines on cardiomyopathies [5,20,21].

  The efficacy of tafamidis in ATTR-CM was established based on the results of an international, multicenter, randomized, placebo-controlled clinical trial (ATTR-ACT),

which enrolled 441 patients with ATTR-CM and followed them for 30 months. The group of patients receiving tafamidis demonstrated a statistically significant reduction in mortality and the number of urgent hospitalizations due to disease exacerbations, better physical performance, and improved quality of life. The main results of the study were published in 2018. The long-term extension phase of the ATTR-ACT study confirmed the efficacy of tafamidis treatment in reducing mortality during continuous treatment for up to 58 months and additionally showed a prognostic benefit in those patients who received placebo in the first phase of the study and only initiated tafamidis from the 30th month. Further analyses of the ATTR-ACT trial results also confirmed a statistically significant improvement in the clinical status of patients treated with tafamidis compared to those receiving placebo [5,20,21].

Acoramidis is a modern transthyretin (TTR) stabilizer used for the treatment of ATTR-CM. The most significant and groundbreaking research program for this drug is the ATTRibute-CM project. Acoramidis achieved near-total TTR stabilization (>90% in the majority of patients). It demonstrated a 42% reduction in the risk of all-cause mortality and cardiovascular-related hospitalizations compared to placebo. Patients treated with acoramidis reported significantly better quality of life (KCCQ score) and better physical capacity (6-minute walk test) than the placebo group. A significant decrease in NT-proBNP levels was observed, indicating reduced cardiac stress [21].

- gene silencers (vutrisiran, patisiran) – These utilize RNA interference (siRNA) to inhibit TTR production in the liver. The efficacy of vutisiran in ATTR-CM was confirmed in clinical trials [7,22]. Vutisiran's efficacy was demonstrated in the HELIOS-B trial [7,22]. Vutrisiran, administered subcutaneously every 3 months, is an effective option, particularly in forms involving polyneuropathy.

  Patisiran is a groundbreaking medication, being the first-ever approved therapy based on the RNA interference (siRNA) mechanism. Its primary function is to "silence" the production of the transthyretin (TTR) protein in the liver.

  APOLLO study demonstrated that patisiran not only slows the disease but, in many patients, reverses neurological symptoms. The study demonstrated that patisiran significantly improved functional capacity (measured by the 6-minute walk test) and quality of life compared to the placebo at 12 months [6,23].

  It confirms that "silencing" TTR production in the liver benefits cardiac patients.

  - gene therapies (CRISPR-Cas9 clinical tials) – a modern approach based on in vivo gene editing is showing promising results in early-phase clinical trials. In a small cohort

of patients with ATTR polyneuropathy, a single intravenous dose led to a dose-dependent reduction in serum TTR levels (up to 87%–96% at higher doses). This established the safety and potential for a “one-and-done” curative approach [22,23,24].

Currently, the main challenge lies in selecting the optimal timing and type of therapy.

TTR stabilizers (tafamidis, acoramidis) demonstrate the highest efficacy in the early stages of the disease (NYHA I/II), suggesting that their role is primarily to inhibit further progression rather than reduce existing deposits. In contrast, gene-silencing drugs (vutrisiran, patisiran) – by achieving nearly complete suppression of TTR synthesis in the liver (>80–90%) – theoretically enable amyloid regression through natural proteolytic mechanisms [6,25].

There are currently no head-to-head studies comparing these two groups. Although the APOLLO (patisiran) and HELIOS-B (vutrisiran) trials suggest cardiovascular benefits, tafamidis remains the only drug with robust evidence for reducing mortality in long-term follow-up [5,20].

The choice between stabilizers and gene silencers currently depends not only on the clinical status but also on the stage of disease progression. While tafamidis has the strongest evidence base (ATTR-ACT trial), analysis has shown that its benefits are significantly lower in patients in NYHA class III [5,24]. This implies that protein stabilization alone cannot overcome advanced heart failure.

Given the above, new therapies (e.g., vutrisiran, acoramidis) are being evaluated for their ability to more rapidly lower circulating TTR levels. Acoramidis, characterized by a higher degree of tetramer stabilization (>90%) than tafamidis, could theoretically provide better protection; however, the long-term effects of near-total inhibition of TTR production still require monitoring regarding thyroid hormone and retinol metabolism [22,23].

Sudden cardiac death

Ventricular arrhythmias in ATTR-CM, although less frequent than supraventricular ones, are highly dangerous and can lead to sudden cardiac death (SCD). Ventricular tachycardias (VT) result from areas of fibrosis and infiltration, which create the substrate for the reentry mechanism. SCD accounts for nearly half of the deaths in this group [11].

The decision to implant an implantable cardioverter-defibrillator (ICD) for the primary prevention of SCD should be based on current guidelines; nevertheless, every decision regarding ICD implantation must be considered individually. ICD implantation should be considered in patients with ATTR-CA who present with sustained ventricular tachycardia and have an expected survival

of >1 year [1,9,11,13,26]. There are insufficient data to formulate recommendations for the primary prevention of sudden cardiac death. An assessment proposed by the Stanford Amyloid Center, offering an algorithm for ICD qualification, is available in the literature. In that study, ICD intervention was effective in 80% of patients in the event of life-threatening ventricular arrhythmias. However, the high rate of appropriate shocks did not translate into improved prognosis.

Unfortunately, a large proportion of SCD occurs via the PFA mechanism – in this case, ICD implantation will not protect the patient from SCD [8].

Future perspectives

Despite significant progress in the diagnosis and treatment of ATTR-CM, several fundamental issues remain unresolved:

- combination therapy: will the simultaneous use of a stabilizer and a gene-silencing drug yield a synergistic effect? Even if studies demonstrate the benefit of combination therapy, its cost may be prohibitively high.
- amyloid regression: a new approach to treating ATTR-CM involves monoclonal antibodies targeted directly at existing deposits in the heart. This could be a breakthrough for patients in advanced stages of the disease, for whom tetramer stabilization alone is insufficient [25].
- early diagnostics: the use of artificial intelligence (AI) in ECG and echocardiography analysis may allow for the identification of ATTR-CM patients at the preclinical stage, before irreversible myocardial damage occurs [14].

Summary

Early recognition of ATTR-CM is critical [1,2,22,27] because currently available disease-modifying therapies can slow down the progression of changes but do not reverse existing damage. A diagnostic algorithm based on scintigraphy and the exclusion of monoclonal protein should be the standard for every patient with unexplained left ventricular hypertrophy and HFpEF [3,23,28]. Modern genetic medicine and pharmacology now offer a real chance to extend life and improve its quality for patients with ATTR and CHF, who can currently be offered effective therapeutic options.

Rapid exclusion of the AL type and implementation of targeted TTR-stabilizing treatment (tafamidis) significantly improve prognosis and functional capacity in patients [4,13,19,29]. It is important to remember that elevated light chain levels do not always indicate AL amyloidosis. In

patients with coexisting chronic kidney disease (CKD), light chain clearance is impaired, which shifts the reference ranges. For this reason, it is crucial to assess the kappa/lambda ratio rather than just absolute values [8].

NT-proBNP levels (elevated disproportionately to the severity of heart failure) and troponin levels in cardiac amyloidosis are typically persistently above the normal range, resulting from the direct toxic effect of fibrils on myocytes. These biomarkers serve not only for diagnosis but, above all, for assessing disease progression and response to treatment [1,3,7,29].

Authors' contribution

Study design – A. Pawlus, K. Kolebacz, B. Średniawa
Data collection – K. Kolebacz, A. Pawlus, B. Średniawa
Manuscript preparation – A. Pawlus, K. Kolebacz, B. Średniawa
Literature research – B. Średniawa, K. Kolebacz, A. Pawlus
Final approval of the version to be published – B. Średniawa, K. Kolebacz, A. Pawlus

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