folia medica

Folia Medica 66(5):608-617
DOI: 10.3897/folmed.66.e135893

Original Article

Clinical and Echocardiographic Characteristics of Patients with Atrial Cardiomyopathy and their Impact on Prognosis

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Received: 29 August 2024 ♦ **Accepted:** 6 October 2024 ♦ **Published:** 31 October 2024

Citation: Ilieva R, Kinova E, Slavchev B, Kalaydzhiev P, Somleva D, Goudev A. Clinical and echocardiographic characteristics of patients with atrial cardiomyopathy and their impact on prognosis. Folia Med (Plovdiv) 2024;66(5):608-617. doi: 10.3897/folmed.66.e135893.

Abstract

Introduction: Patients with diverse demographic and clinical characteristics and comorbidities are included in the category of atrial cardiomyopathy (ACM).

Aim: Our study aims to evaluate the demographic, clinical, laboratory, and echocardiographic parameters of patients with ACM and to assess their impact on prognosis.

Materials and methods: Only 200 of the 724 consecutively evaluated patients with dilated left atrium who met the criteria for advanced ACM were included in the analysis. Forty age- and sex-matched controls with normal left atrial volume were also included. On enrollment, all patients received a detailed echocardiography with volumetric and speckle tracking analysis, and they were followed for 36 months for cardiovascular outcomes, including mortality.

Results: The mean age of the ACM population was 73.91±9.74 years, with 58% being women. Hypertension was found in 93% of them, 79% had atrial fibrillation, 60% had heart failure, 37% were obese, and 26% had diabetes. Over a median follow-up of 20.6 months, 35 deaths were registered in the ACM group compared to 1 death in the control group (17.5% vs. 2%, p=0.011). The presence of heart failure (HR 5.2, p=0.004), cancer (HR 3.7, p=0.007), severe tricuspid regurgitation (TR) (HR 5.4, p<0.001), high NT-proBNP (HR 1.4, p<0.001), and low right ventricular free wall strain (RVFWLS) (HR 1.2, p=0.006) were predictors of poor outcome.

Conclusion: In patients with ACM, the most prevalent comorbidities are hypertension, atrial fibrillation, heart failure, obesity, and diabetes. ACM is associated with high mortality with the best echocardiographic predictors – the presence of severe TR and RVFWLS >–17 %.

Keywords

atrial cardiomyopathy, atrial fibrillation, heart failure, NT-proBNP, right ventricular strain

INTRODUCTION

Though the relationship between atrial dilation and atrial arrhythmias has been known for a long time, atrial cardiomyopathy (ACM) has been introduced as a new term in recent years due to the wider use of the new imaging modalities in cardiology – strain echocardiography and cardiac magnetic resonance. Several definitions have been proposed for atrial cardiomyopathy[1-4], but unified criteria for its diagnosis are lacking. Additionally, the relationship between morphological and functional changes and clinical manifestations is not well understood. Generally, ACM is characterized by structural and functional changes in the atria that lead to arrhythmia and/or heart failure, in the absence of significant valvular or ventricular dysfunction. Atrial cardiomyopathy is a heterogeneous entity, which includes patients with atrial arrythmias or conduction disorders, atrial functional mitral and tricuspid regurgitation. Patients with ACM are at a higher risk of heart failure, stroke, peripheral emboli, and death.

The etiological factors of ACM are not entirely clarified. Still, the following comorbidities are essential in remodeling the atria: atrial fibrillation (AF), arterial hypertension, diabetes mellitus, obesity, obstructive sleep apnea, and aging. Structural and functional changes in the atria result also from congestive heart failure, valvular diseases, cardiac amyloidosis, genetic diseases, myocarditis, and other conditions.[4] An association between ACM and cancer is considered as well.

AIM

ACM includes patients with heterogenous demographic and clinical characteristics and comorbidities. Our study aims to evaluate the demographic, clinical, laboratory and echocardiographic parameters of patients with atrial cardiomyopathy and to assess their impact on prognosis.

MATERIALS AND METHODS

Study population

Consecutive patients with advanced atrial cardiomyopathy who were hospitalized in the Cardiology Department of our hospital between September 2020 and May 2023 were included in the study. We defined advanced atrial cardiomyopathy as a severely dilated left atrium with volume index (LAVI) ≥48 ml/m^2, preserved left ventricular (LV) systolic function – ejection fraction (EF) ≥50%, without a primary valvular or ventricular disease. Exclusion criteria were the presence of ventricular cardiomyopathy (dilated, hypertrophic or infiltrative), moderate or severe left ventricular hypertrophy (interventricular septum and posterior wall thickness of LV >13 mm), presence of primary valvular diseases (mitral stenosis, mitral or tricuspid regurgitation, aortic stenosis), acute coronary syndrome or pulmonary embolism, congenital heart disease, and constrictive pericarditis. Patients with pacemakers and cancer who did not fulfil the exclusion criteria were included in the study.

The study also included 40 control patients with normal left atrial volume (LAVI <34 ml/m^2). The patients from the control group were age- and sex-matched to the patients with atrial cardiomyopathy but with structurally normal hearts. They were recruited from the patients to our hospital's outpatient clinic.

All demographic and clinical data of the study group and the controls were collected from the hospital database (GlobalHis) and included age, sex, blood pressure and heart rate, smoking status, body mass index (BMI), the presence of comorbidities such as atrial fibrillation, heart failure (HF), arterial hypertension, diabetes mellitus, obesity, obstructive sleep apnea (OSA), coronary artery disease (CAD), sinoatrial (SA) or atrio-ventricular (AV) block, a pacemaker, stroke, and cancer, and the current medication. Collected laboratory data included hemoglobin and creatinine level, N-terminal pro-B-type natriuretic peptide (NT-proBNP), and C-reactive protein (CRP). The estimated glomerular filtration rate (eGFR) was calculated using the 2021 CKD-EPI Creatinine formula.

All patients (study group and controls) underwent detailed two-dimensional echocardiography on a Philips Epiq 7 machine with Matrix X5-1 transducer, including volumetric and speckle tracking analysis performed by a single operator. For the analysis, 32 echocardiographic parameters were used including strain of the left and right atrium, left and right ventricle. All measurements were performed according to the recommendations for cardiac chamber quantification of the European Association of Cardiovascular Imaging.[5] Strain analysis was performed offline on Tom Tec (Minnesota, USA 2021) software.

Outcome and follow-up

The primary outcome of the study was all-cause death. Cardiovascular death was defined as death directly related to cardiovascular diseases, mainly congestive heart failure, sudden death, or an embolic event. The patients from the study group and the controls were followed for a median of 20.6 months by a visit to the clinic or a telephone call for the occurrence of the primary outcome. When contact with the patient was impossible, information was gathered from his relatives, or his vital status was verified from the National Health Institute records of Bulgaria.

Ethics approval

The study was approved by the Research Ethics Committee of the Medical University of Sofia. All patients signed informed consent before inclusion.

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Statistical analysis

Continuous variables, expressed as means and standard deviation, and the differences between the groups were assessed using the one-way analysis of variance (ANOVA) and Kruskal-Wallis one-way ANOVA, respectively. Categorical variables were expressed as counts and percentages, and differences between the groups were assessed using the chi-squared test (or Fisher exact test, when appropriate).

Differences in terms of mortality by group membership were evaluated using a log-rank test and drafted according to Kaplan-Meier curves. Stepwise proportional Cox regression analysis was used to determine the predictors of mortality.

In our main analysis, when evaluating predictors of mortality, NT-proBNP and right ventricular free wall longitudinal strain (RVFWLS) were separately assessed as the best predictors of mortality. Using these continuous variables, the accuracy of their prediction of outcomes was assessed by generating receiver-operating characteristic curves (ROC) and reporting the area under the curve (AUC) using parametric methods, and reporting sensitivity and specificity. Recognizing a lack of accepted cutoff(s) for RV strain for assessing RV dysfunction or predicting outcome, we determined the RV strain threshold that maximized the index: sensitivity + specificity – 1 for classifying all-cause mortality in our cohort.

All analyses were performed using IBM SPSS v. 29.0. All statistical significance levels were two-sided, and significant differences were expressed as $p<0.05$.

RESULTS

Demographic and clinical characteristics

Of 724 consecutive patients with dilated left atrium, only 200 met the inclusion criteria for advanced atrial cardiomyopathy. The population under study, comprising 58% women, had a mean age of 73.9±9.7 years (46–100). Hypertension was found in 93% of them, diabetes in 26%, 79% had AF, 60% of them had heart failure, 20% had cancer, and 24% had SA or AV block. The mean BMI was 27.5±5.3, and 37% of them were obese.

The ACM group, compared to the control group, had significantly higher rates of hypertension (93% vs. 75%, $p=0.001$), congestive heart failure (60% vs. 0%, $p<0.001$), diabetes (26% vs. 8%, $p=0.013$, OSA (11% vs. 0%, $p=0.032$), SA or AV block (24% vs. 0%, $p=0.001$), and implanted pacemakers (15% vs. 0%, $p=005$). The ACM patients also had a significantly higher prevalence of coronary artery disease (9% vs. 0%, $p=0.049$), stroke (17% vs. 3%, $p=0.020$) and AF (79% vs. 5%, $p<0.001$).

In terms of laboratory parameters, the ACM patients, compared to the control group, had lower eGFR (67.4±21.4 vs. 78.6±18.7 ml/min/1.73 m^2, $p=0.010$) and higher levels of NT-proBNP (1674.8±2053.4 vs. 88±32.7 pg/ml, $p<0.001$). Baseline demographic, clinical and laboratory characteristics are presented in **Table 1**.

Treatment

Fifty-eight percent of ACM patients were treated with diuretics, 65% with angiotensin-converting enzyme inhibitors (ACE) or angiotensin receptor blockers (ARB), 79% with beta-blockers, 34% with mineralocorticoid receptor antagonists (MRA), and 14% with sodium-glucose cotransporter-2 inhibitors (SGLT2i). Eighteen percent of ACM patients received digoxin, 35% antiarrhythmic drugs, and 72% – anticoagulation agents. Compared to the control group, ACM patients had significantly higher rates of diuretic, beta-blocker, MRA, SGLT2i, digoxin, antiarrhythmic, and anticoagulant treatment **(Table 2)**.

Echocardiographic characteristics

The mean ejection fraction of the LV of ACM patients was 56.1±4.9%, the mean LAVI was 54.7±8.5 ml/m^2, and mean RAVI was 36.0±15.9 ml/m^2. Their global longitudinal strain of LV was 16.0±4.9%, right ventricular free wall strain - −20.1±5.9%, reservoir strain of LA – 17.1±9.4%, and of RA – 18.8±9.7%. There was a significant difference in all studied echocardiographic parameters between the ACM and control group **(Table 3)**. Patients with ACM had significantly more mitral and tricuspid regurgitation as well.

Mortality risk

Over a median follow-up of 20.6±9.6 (1-39) months, 35 deaths were registered in the ACM group compared to 1 death in the control group (17.5% vs. 2%, $p=0.011$). Most deaths (21) in the ACM group were of cardiovascular origin, mainly due to heart failure. The causes of death of ACM patients are presented in **Table 4**. The cause of death for the individual in the control group was not cardiovascular. Kaplan-Meier curves with the difference in the incidence of mortality between the two groups are presented in **Fig. 1**.

Multivariable stepwise Cox proportional regression analysis was employed to identify predictors of mortality. The model included the following clinical variables: sex, age, atrial fibrillation, arterial hypertension, diabetes mellitus, heart failure, obesity, obstructive sleep apnea, cancer, coronary artery disease, SA or AV block, implanted pacemakers, stroke, BMI, smoking, and systolic and diastolic blood pressure, as well as heart rate **(Table 5)**. The analysis revealed that the clinical factors that were most strongly associated with mortality were the presence of heart failure (HR 5.2, CI 1.7÷16.3, $p=0.004$) and cancer (HR 3.7, CI 1.4÷9.5, $p=0.007$).

The same analysis was applied to the following laboratory parameters: hemoglobin, creatinine, eGFR, CRP, and NT-proBNP. Among these, NT-proBNP (HR 1.4, CI 1.2÷1.6, $p<0.001$) emerged as the strongest predictor of mortality **(Table 6)**.

From all studied echocardiographic parameters, the

Table 1. Demographic, clinical and laboratory parameters of ACM patients and controls

	Atrial cardiomyopathy n=200	Controls n=40	*p*-value
Age (years)	73.9±9.7	72.9±7.5	0.907
Female sex (%)	58	59	0.936
Hypertension (%)	93	75	0.001
Diabetes mellitus (%)	26	8	0.013
CHF (%)	60	0	<0.001
Obesity (%)	37	25	0.148
OSA (%)	11	0	0.032
Cancer (%)	20	8	0.060
CAD (%)	9	0	0.049
SA or AV block (%)	24	0	0.001
Pacemaker (%)	15	0	0.005
Stroke (%)	17	3	0.020
AF (%)	79	5	<0.001
Paroxysmal AF (%)	29	5	0.063
Persistent/permanent AF (%)	51	0	<0.001
BMI (kg/m^2)	27.5±5.3	27.1±4.0	0.700
Smoking (%)	32	21	0.169
SBP mmHg	129±18	127±13	0.576
DBP mmHg	79±11	80±9	0.543
HR	75±16	71±11	0.239
CRP (mg/dl)	1.5±2.1	0.9±0.9	0.177
Hemoglobin (g/l)	131.6±20.0	135.6±12.4	0.320
Creatinine (mcmol/l)	94.1±38.2	77.4±18.1	0.027
eGRF (ml/min/1.73 m^2)	67.4±21.4	78.6±18.7	0.010
NT-proBNP (pg/ml)	1 674.8±2053.4	88±32.7	<0.001

AF: atrial fibrillation; AV: atrio-ventricular; CAD: coronary artery disease; CHF: congestive heart failure; CRP: C-reactive protein; NT-proBNP: N-terminal pro-B-type natriuretic peptide; OSA: obstructive sleep apnea, SA block: sinoatrial block

Table 2. Treatment of ACM and control patients

	Atrial cardiomyopathy (n= 200)	Controls (n= 40)	*p*-value
Diuretics (%)	58	0	<0.001
ACEi/ARB (%)	65	63	0.764
Beta blockers (%)	79	38	<0.001
Statin (%)	34	38	0.628
MRA (%)	34	3	<0.001
SGLT2i (%)	14	3	0.036
Digoxin (%)	18	0	0.004
Antiarrhythmic drug (%)	35	3	<0.001
Anticoagulation agents (%)	72	3	<0.001
Anticoagulation – DOAC (%)	61	3	<0.001
Anticoagulation – Vitamin K antagonist (%)	11	0	0.032

ACEi/ARB: angiotensin-converting enzyme inhibitors/angiotensin receptor blockers; DOAC: direct oral anticoagulants; MRA: mineralocorticoid receptor antagonists; SGLT2i: sodium-glucose cotransporter-2 inhibitor

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Table 3. Echocardiographic parameters of the ACM and control patients

	Atrial cardiomyopathy n= 200	Controls n= 40	*p*-value
LV EF (%)	56.1±4.9	59.8±4.7	<0.001
GLS LV (%)	−16.0±3.9	−19.4±3.2	<0.001
E/e′ m	14.3±4.9	10.1±2.6	<0.001
E/e′ l	11.5±3.8	8.3±2.4	<0.001
RVFWLS (%)	−20.1±5.9	−24.6±5.9	<0.001
RVGLS (%)	−16.9±5.8	−19.1±8.3	0.044
LAVI ml/m^2	54.7±8.5	25.9±5.9	<0.001
LASr (%)	17.1±9.4	39.7±11.2	<0.001
LAScd (%)	−11.7±5.5	−22.3±6.4	<0.001
LASct (%)	−5.2±5.4	−17.4±7.8	<0.001
RAVI ml/m^2	36.0±15.9	18.7±6.0	<0.001
RASr (%)	18.8±9.7	35.7±10.2	<0.001
RAScd (%)	−12.6±7.1	−22.7±8.2	<0.001
RASct (%)	−5.4±5.2	−13.4±5.7	<0.001
PASP mmHg	40.1±13.4	27.7±6.4	<0.001
MR >mild (%)	35	8	<0.001
Severe MR (%)	3.5	0	0.232
TR >mild (%)	46	8	<0.001
Severe TR (%)	20	0	0.002

E/e′ m: E/e′ ratio of medial mitral annulus; E/e′ l: E/e′ ratio of lateral mitral annulus; GLS LV: global longitudinal strain of left ventricle; LAVI: left atrium volume index; LASr: left atrial reservoir strain; LAScd: left atrial conduit strain; LASct: left atrial contractile strain; LV EF: left ventricular ejection fraction; MR: mitral regurgitation; PASP: pulmonary artery systolic pressure; RAVI: right atrium volume index; RASr: right atrial reservoir strain; RAScd: right atrial conduit strain; RASct: right atrial contractile strain; RVFWLS: right ventricular free wall longitudinal strain; RVGLS: right ventricular global longitudinal strain; TR: tricuspid regurgitation.

Table 4. Causes of death in ACM patients

Causes of death in ACM	Number of patients
Cardiovascular death	21
Heart failure	16
Thromboembolism	3
Sudden cardiac death	2
Noncardiovascular death	12
Cancer	5
Bleeding	1
Infection	4
Other	2
Unknown	2

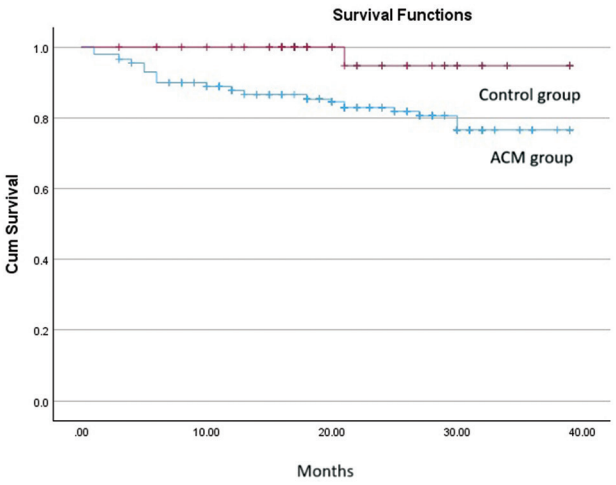

Figure 1. Kaplan-Meier curves showing the difference in the mid-term mortality between ACM patients and the control group.

following variables were included in the proportional Cox regression analysis to identify predictors of mortality: ejection fraction and global longitudinal strain of the left ventricle, E/e′ of the medial and lateral mitral annulus, free wall global longitudinal strain and global strain of the right ventricle, indexed left and right atrial volume, the three components of left and right atrial strain (reservoir, conduit, and contractile), pulmonary artery systolic pressure, and the presence of more than mild, and severe mitral and tricuspid regurgitation **(Table 7)**. The analysis showed that

Table 5. Multivariable Cox proportional hazards regression analysis of the clinical variables

Variable	Hazard ratio	95% Confidence interval	*p*-value
Age	1.03	0.98÷1.09	0.243
Sex, female	2.25	0.77÷6.61	0.140
Arterial hypertension	2.39	0.41÷13.89	0.332
Atrial fibrillation	1.46	0.76÷3.08	0.178
Diabetes mellitus	1.12	0.96÷1.39	0.216
Heart failure	5.2	1.67÷16.32	0.004
Obesity	0.83	0.69÷1.95	0.274
OCA	2.98	0.99÷9.36	0.056
Cancer	3.69	1.43÷9.49	0.007
CAD	1.39	0.35÷5.60	0.636
SA or AV block	1.06	0.18÷6.37	0.952
Pacemakers	0.98	0.12÷8.08	0.983
Stroke	1.02	0.78÷1.53	0.253
BMI	1.05	0.92÷1.19	0.485
Smoking	3.07	0.99÷11.39	0.060
Systolic blood pressure	0.99	0.96÷1.02	0.533
Diastolic blood pressure	0.97	0.93÷1.02	0.241
Heart rate	1.02	0.98÷1.04	0.282

Table 6. Multivariable Cox proportional hazards regression analysis of the laboratory parameters

Variable	Hazard ratio	95% Confidence interval	*p*-value
CRP	1.11	0.93÷1.35	0.239
Hemoglobin	0.98	0.95÷1.00	0.121
Creatinine	1.01	0.99÷1.02	0.745
eGRF	0.96	0.91÷1.01	0.159
NT-proBNP	1.40	1.20÷1.60	<0.001

the right ventricular free wall strain (RVFWLS) (HR 1.2, CI 1.05÷1.37, p=006) and the presence of severe tricuspid regurgitation (HR 5.4, CI 2.6÷11.3, p<0.001) were the strongest predictors of mortality.

Since NT-proBNP and right ventricular free wall strain (RVFWLS) were identified as the best predictors of mortality, we selected them for ROC analysis to calculate the area under the curve (AUC). NT-proBNP correctly classified death with an AUC value of 0.812 (p<0.001). NT-proBNP value of 1200 pg/ml was determined to discriminate best mortality with 82% sensitivity and 71% specificity **(Fig. 2)**. RVFWLS properly classified death with an AUC value of 0.738 (p<0.001). The RVFWLS value of –17% discriminated the best mortality with 79% sensitivity and 62% specificity **(Fig. 3)**.

DISCUSSION

In our study, we assessed the clinical and echocardiographic characteristics of a cohort of patients with advanced atrial cardiomyopathy and explored their impact on prognosis. These are the four major findings: Firstly, the most common comorbidities of ACM patients were hypertension, atrial fibrillation, congestive heart failure, obesity, and diabetes. Secondly, patients with ACM had relatively high levels of NT-proBNP and were treated mainly with beta-blockers, ACEi/ARB, anticoagulants, and diuretics. Third, ACM is characterized by unfavorable echocardiographic parameters. Finally, ACM is an entity with a high mortality rate, and there are distinct clinical, laboratory, and echocardiographic characteristics that are associated with poor outcome.

Our findings of the most common comorbidities of ACM patients are in line with the literature that high-incidence pathologies like congestive heart failure[6], AF[7], hypertension[8], diabetes mellitus[9], and some other conditions, including aging, obesity[10], obstructive sleep apnea[11] are well-established causes of atrial remodeling – the hallmark of atrial cardiomyopathy[12]. Recent studies have shown that inflammation and excess production of reactive species of oxygen seem to play a principal role in atrial remodeling.[13] Even mild systemic inflammation can be associated with increased cardiovascular risk, and this proinflammatory status is found in many pathologies, such as hypertension, CHF, coronary artery disease, obesity, or diabetes mellitus.[14]

The second important finding in our study is the pres-

Table 7. Multivariable Cox proportional hazards regression analysis of the echocardiographic parameters

Variable	Hazard ratio	95% Confidence interval	*p*-value
LV EF	0.97	0.88÷1.06	0.485
GLS LV	1.09	0.75÷1.07	0.246
E/e′ m	1.25	0.91÷2.02	0.073
E/e′ l	1.35	0.98÷2.05	0.055
RVFWLS	1.20	1.05÷1.37	0.006
RVGLS	1.10	1.02÷1.39	0.019
LAVI	1.05	0.99÷1.01	0.057
LASr	1.10	1.01÷1.19	0.018
LAScd	1.04	0.91÷1.14	0.171
LASct	1.04	0.96÷1.12	0.353
RAVI	1.09	0.95÷1.05	0.880
RASr	1.08	1.03÷1.14	0.010
RAScd	1.04	1.00÷1.09	0.052
RASct	1.09	0.98÷1.20	0.106
PASP	1.02	0.98÷1.06	0.459
MR >mild	1.23	0.56÷2.70	0.613
Severe MR	2.9	0.64÷13.37	0.167
TR >mild	1.96	0.93÷4.19	0.082
Severe TR	5.4	2.63÷11.31	<0.001

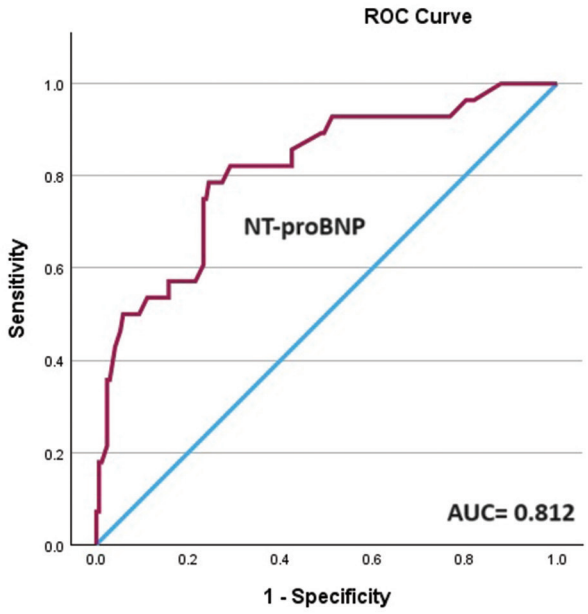

Figure 2. Receiver operating characteristic for NT-proBNP as a predictor of mortality in ACM patients.

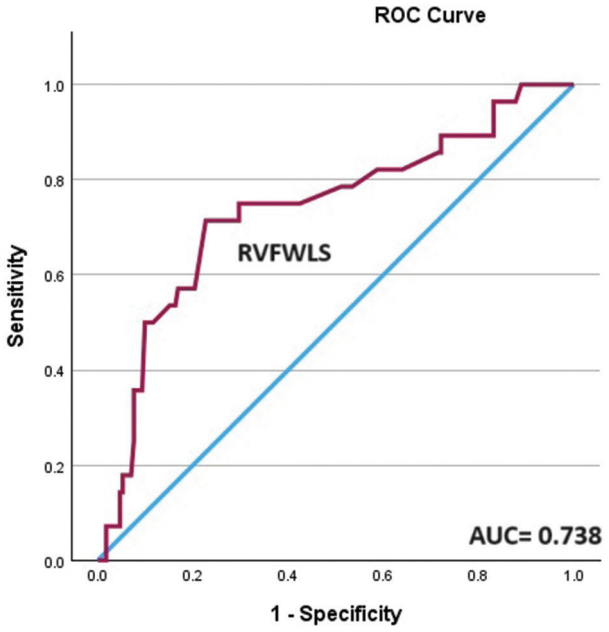

Figure 3. Receiver operating characteristic for RVFWLS as a predictor of mortality in ACM patients.

ence of elevated levels of NT-proBNP in patients with ACM. Increased NT-proBNP levels serve as an important diagnostic and prognostic biomarker. They show a significant correlation with echocardiographic parameters related to AF remodeling and dysfunction and are associated with the burden of AF.[15] A reverse relationship is observed between high levels of NT-proBNP and low reservoir and contractile strain of the left atrium, suggesting that left atrial myopathy is associated with persistent congestion.[16]

Regarding the treatment of ACM patients, we found that most patients were treated with beta-blockers, anticoagulants, diuretics, and ACE inhibitors or ARB. The recommended strategies for the pharmacological management of ACM are based on stroke prevention, cardiac rhythm therapy, and rate control.[17] Many studies have demonstrated that the most effective treatment is the rhythm control

strategy, especially AF catheter ablation. Unfortunately, our patients had advanced ACM and substantial atrial fibrosis; the majority of them had long-standing AF and were not good candidates for rhythm control therapy. Only a small group of them (younger, obese with paroxysmal atrial fibrillation) were on antiarrhythmic medications, and a few underwent catheter ablation. Anticoagulation is the mainstay of ACM treatment due to the high risk of stroke in this population. The high percentage of diuretic therapy in our study could be explained by the high prevalence of HF.

Taking into account the important roles of angiotensin II, aldosterone, and inflammation in the pathophysiology of ACM, therapy with ACE inhibitors (ACEi) or angiotensin receptor blockers (ARB) shows promising results in reducing the incidence of AF in patients with cardiovascular diseases. Additionally, ACEi/ARB therapy has an additive effect when combined with spironolactone and statins.[12] In this regard, 66% of our ACM patients were treated with ACEi/ARB, while 34% received mineralocorticoid receptor antagonists (MRA) and statins.

Some recent reports on the pleiotropic, cardiovascular protective effects of sodium-glucose cotransporter-2 (SGLT2) inhibitors show promising results on atrial remodeling.[18,19] Due to financial reasons (not reimbursed in Bulgaria for the treatment of HF with preserved ejection fraction until 01.2023) only a small group of our patients were treated with SGLT2 inhibitors, most of them with diabetes.

Our study included a comprehensive evaluation of the echocardiographic characteristics of the ACM patients with 32 parameters studied. We also used advanced echocardiographic methods – a two-dimensional strain of the left and right atrium, and of the left and right ventricle. The most extensively studied echocardiographic parameters in ACM are LA size and volume and, recently, LA strain. It is established that low LA reservoir strain values predict recurrences of AF, especially after pulmonary vein isolation, stroke and other embolic events, heart failure, and poor outcome.[20,21] Right heart chambers geometry and function in ACM patients have been studied so far only in those with atrial functional tricuspid regurgitation.[22] Although patients with significant primary valvular disease were excluded from our study, 3.5% of our ACM patients presented with severe mitral regurgitation, and 20% with severe tricuspid regurgitation. These valvular lesions are classified as atrial functional regurgitation and represent important clinical manifestations of ACM.

The poor prognosis of advanced atrial cardiomyopathy that we established is confirmed in a large study by Masuda et al.[23] They demonstrated a composite endpoint rate of 7.1% over a follow-up of 5 years. Composite endpoints were defined as death, heart failure, and stroke, and developed more frequently in the group with extensive left atrial fibrosis (19.1%), which is very similar to our cohort of patients. The authors of the same study found that other independent predictors of composite endpoints were concomitant diabetes mellitus, history of heart failure, low estimated glomerular filtration rate, large left atrial diameter, and AF recurrence.

Regarding the predictors of outcome, most studies so far have been performed on AF patients and only a few in ACM. AF is the most important etiological factor of ACM, therefore, results from AF studies are extrapolated on ACM. In our study, we demonstrated that the strongest predictors of poor outcome are the presence of heart failure, cancer, high NT-proBNP values, RVFWLS >−17% and severe tricuspid regurgitation. The high proportion of patients with heart failure in our cohort confirms the pivotal role of this comorbidity as the leading cause of death in patients with AF, even more important than ischemic stroke.[24] It is known that cancer is an important risk factor for mortality in the AF population.[25]

Though the prognostic significance of NT-proBNP is widely studied in patients with heart failure, to our knowledge, this issue has not been previously explored in the ACM population. It has been established that a value of NT-proBNP >1000 pg/ml predicts an increased risk of mortality and hospitalizations in patients with chronic stable heart failure.[26] Our study demonstrates that NT-proBNP >1200 pg/ml (AUC=0.812) has the best predictive value.

Although the prognostic role of RV strain in atrial cardiomyopathy is not yet established, it is known to be an important predictor of mortality in heart failure, pulmonary hypertension, and valvular heart disease.[27] RVFWLS value of >−17 was determined to discriminate best mid-term mortality with 70% sensitivity and 63% specificity. Regarding the prognostic significance of tricuspid regurgitation, it is demonstrated that significant tricuspid regurgitation portends a worse survival in patients with AF.[28]

Limitations

Our study has several limitations, and our results should be interpreted with caution. One is the small sample size we studied. Secondly, patients in our study were with advanced form of ACM and were from hospital setting – older with more comorbidities, thus, our results may not be valid for younger and healthier outpatient population with more subtle forms of atrial cardiomyopathy. Thirdly, our conclusions apply only to the Bulgarian population. Further studies are warranted to analyze and better understand the heterogeneity of atrial cardiomyopathy.

CONCLUSION

In patients with atrial cardiomyopathy, we identified that the most prevalent comorbidities are hypertension, atrial fibrillation, heart failure, obesity, and diabetes. These patients are characterized by unfavorable echocardiographic parameters and high mortality rates. The presence of heart failure, cancer, severe tricuspid regurgitation, NT-proBNP >1200 pg/ml, and RVFWLS >−17% are associated with worse outcome.

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Our results provide new insights into the clinical complexity of atrial cardiomyopathy and its outcome.

Acknowledgements

The authors have no support to report.

Funding

The authors have no funding to report.

Competing Interests

The authors have declared that no competing interests exist.

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Клинические и эхокардиографические характеристики пациентов с предсердной кардиомиопатией и их влияние на прогноз

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Дата получения: 29 августа 2024 г. ♦ **Дата приемки:** 6 октября 2024 г. ♦ **Дата публикации:** 31 октября 2024 г.

Образец цитирования: Ilieva R, Kinova E, Slavchev B, Kalaydzhiev P, Somleva D, Goudev A. Clinical and echocardiographic characteristics of patients with atrial cardiomyopathy and their impact on prognosis. Folia Med (Plovdiv) 2024;66(5):608-617. doi: 10.3897/folmed.66.e135893.

Резюме

Введение: Пациенты с различными демографическими и клиническими характеристиками и сопутствующими заболеваниями включены в категорию предсердной кардиомиопатии (ПКМ). Наше исследование направлено на оценку демографических, клинических, лабораторных и эхокардиографических параметров пациентов с ПКМ и оценку их влияния на прогноз.

Материалы и методы: Только 200 из 724 последовательно обследованных пациентов с расширенным левым предсердием, которые соответствовали критериям развитой ПКМ, были включены в анализ. Также были включены сорок соответствующих по возрасту и полу контрольных лиц с нормальным объёмом левого предсердия. При зачислении все пациенты прошли подробную эхокардиографию с волюметрическим и спекл-трекинговым анализом (volumetric and speckle tracking analysis), и они наблюдались в течение 36 месяцев на предмет сердечно-сосудистых исходов, включая смертность.

Результаты: Средний возраст популяции с ПКМ составил 73.91 ± 9.74 года, причём 58% были женщинами. У 93% из них была обнаружена гипертония, у 79% была мерцательная аритмия, у 60% была сердечная недостаточность, у 37% было ожирение и у 26% был диабет. За период медианного наблюдения в 20.6 месяцев было зарегистрировано 35 смертей в группе ПСМ по сравнению с 1 смертью в контрольной группе (17.5% против 2%, p=0.011). Наличие сердечной недостаточности (HR 5.2, p=0.004), рака (HR 3.7, p=0.007), тяжёлой трикуспидальной регургитации (ТР) (HR 5.4, p<0.001), высокого NT-proBNP (HR 1.4, p<0.001) и низкой деформации свободной стенки правого желудочка (RVFWLS) (HR 1.2, p=0.006) были предикторами неблагоприятного исхода.

Заключение: У пациентов с ПКМ наиболее распространёнными сопутствующими заболеваниями являются гипертония, мерцательная аритмия, сердечная недостаточность, ожирение и диабет. ПКМ ассоциируется с высокой смертностью при лучших эхокардиографических предикторах – наличии тяжелой ТР и RVFWLS >−17 %.

Ключевые слова

предсердная кардиомиопатия, мерцательная аритмия, сердечная недостаточность, NT-proBNP, деформация правого желудочка