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Right ventricular systolic function predicts survival in patients with cardiac amyloidosis

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Cardiac amyloidosis is a condition characterized by the deposition of amyloid fibrils in the heart tissue, leading to restrictive cardiomyopathy and heart failure. The two main types of amyloidosis affecting the heart are immunoglobulin light chain (AL) amyloidosis and transthyretin (TTR) amyloidosis. AL amyloidosis is caused by the deposition of light chains produced by plasma cells, while TTR amyloidosis is due to mutations or misfolding of the transthyretin protein. These amyloid deposits disrupt the normal structure and function of the heart, resulting in symptoms of heart failure. Cardiac amyloidosis is often diagnosed at an advanced stage, contributing to its generally poor prognosis (1,2).

This study aims to assess selected echocardiographic parameters in patients with cardiac amyloidosis. We also seek to analyze biochemical markers and clinical signs of right ventricular dysfunction. Additionally, the study investigates the impact of these factors on patient survival. By understanding these correlations, we hope to identify key prognostic indicators in cardiac amyloidosis.

We retrospectively analysed medical records of 27 patients with cardiac amyloidosis. Mean age was 65.3 ± 10.5 years, with gender distribution men/women 19/8 patients. There were two types of cardiac amyloidosis: immunoglobulin light chain (AL, n=20) and transthyretine amyloidosis (TTR, n=7). Mean left ventricular ejection fraction (LVEF) was 46.5 ± 16.7%. Selected laboratory parameters are shown in **Table 1**. Median time of survival (time from definitive diagnosis to death) was 133 days (IQR 37-283). Posterior wall thickness significantly positively correlated with elevated levels of serum troponine concentrations (r=0.56, p=0.002), also with serum creatinine concentrations (r=0.40, p=0.03). Right wall thickness strongly positively correlated with increased levels of serum troponine concentrations (r=0.68, p=0.001) and serum creatinine concentrations (r=0.69, p=0.02). Tricuspid annular plane systolic excursion positively correlated with survival time (r=0.79, p<0.0001), but not with serum bilirubin concentrations, inferior vena cava diameter and spontaneous prothrombin time. There was no correlation between survival time and NTproBNP, nor selected ECG parameters (QRS amplitude, PR interval and corrected QT interval).

Elevated natriuretic peptides and troponin positivity are among the readily available laboratory markers that signal myocardial involvement. The level of natriuretic peptides also has a stratification and prognostic character, and their normal value practically excludes amyloid cardiomyopathy (1,2,3,4). In the entire monitored group, there was no patient who showed physiological values of troponin, and the values of natriuretic peptides were also highly elevated, which ultimately correlated with the fact that the patients arrived at an advanced

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Table 1 Selected characteristics

Parameter	(n=27 patients)
Urea [mmol/L]	11 [6.4-12.8]
Creatinine [umol/L]	127 ± 62
NTproBNP [pg/mL]	13065 ± 10959
Troponine [ng/mL]	143 ± 99
Bilirubin [umol/L]	23 ± 6
Hemoglobin [g/L]	134 ± 13
LVEF [%]	46,5 ± 16,7
Posterior wall thickness [mm]	16,4 ± 3,1
Right ventricle thickness [mm]	7,4 ± 1,5
TAPSE [mm]	11±3
Vena cava inferior [mm]	22 ±4

Unless otherwise specified the data are presented as means ± SD
LVEF – left ventricular systolic function, NTproBNP – N terminal pro b-type natriuretic peptide, TAPSE – tricuspid annular plane systolic excursion

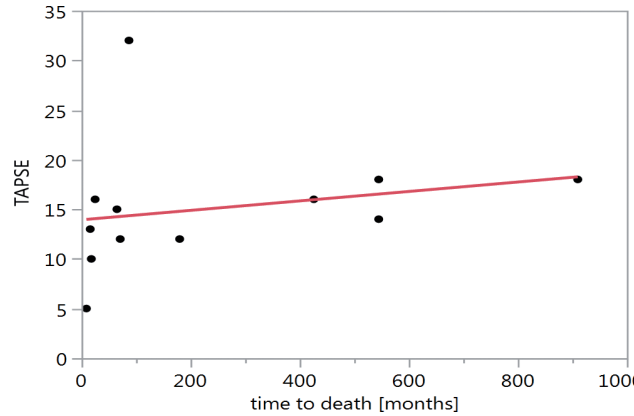

Figure 1 TAPSE and survival time correlation

stage of the disease and almost 78% of them died during the follow-up. The majority of patients were hospitalized in NYHA functional class III or IV (up to 89% in total). According to current recommendations for the treatment of acute and chronic heart failure, this fact limits the use of specific treatment, both in AL and TTR amyloidosis (2). In analyses of echocardiographic parameters of the cohort, TAPSE was very strongly correlated with time from diagnosis to death (**Figure 1**). Of course, it is not the only parameter for assessing the function of the right ventricle, but several studies have been published in which the TAPSE value could be a simple prognostic marker for patients with amyloid cardiomyopathy (5). There are several hypotheses that attempt to explain the prognostic role of right ventricular dysfunction in amyloid cardiomyopathy. The key determinants of TAPSE reduction are low right ventricular preload and high afterload per se. Atrial fibrillation, which was common in the patients in our group (more than half), affects the filling of the right ventricle and may contribute to the reduction of TAPSE. Concomitant left ventricular dysfunction with high filling pressures leads to increased wedge pressure and right ventricular overload. Thus, right ventricular dysfunction is the result of complex mechanisms, not only the presence of amyloid deposits. Right ventricular dysfunction occurs later compared to deposits in the left ventricle, which also explains why it dramatically worsens the prognosis of patients (6). It can be assumed that TAPSE could be a simple prognostic marker that reflects both right ventricular and secondary left ventricular dysfunction (5,6).

Patients in the cohort who died, regardless of the type of amyloid cardiomyopathy, had a median survival time from diagnosis to death of 133 days (IQR 37-283). This is partly due to the high percentage of patients with AL amyloidosis, who, despite treatment, have a significantly worse prognosis compared to TTR amyloidosis (7). For patients with TTR amyloidosis, in the subgroup of deaths, the median survival was close to 233 days (IQR 125-718). This indicates that the patients were diagnosed at advances stages of the disease. The estimated survival for this type of amyloidosis is typically 43-67 months (7). This raises the question of early diagnosis and treatment availability once again.

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