Echocardiographic assessment of the right heart in conditions with transient right ventricular pressure overload

PhD thesis

Ágnes Nógrádi MD

Supervisor: Réka Faludi MD, PhD

Head of the Doctoral School: Prof. Lajos Bogár MD, PhD, DSc

Head of the Doctoral Program: Prof. István Szokodi MD, PhD, DSc

University of Pécs, Medical School

Heart Institute

Pécs, 2023

1. Introduction

Elevated pulmonary arterial pressure, a condition with complex aetiology, results in an increased right ventricular (RV) afterload, which in turn triggers anatomical and biochemical responses, both adaptive and maladaptive. These processes lead in the end to the clinical syndrome of right heart failure, an important cause of morbidity and mortality.

Among conditions with right heart overload, chronic obstructive pulmonary disease (COPD) is significant as a growing global epidemic, one of the leading causes of death, as well as representing a large health care burden and being an important cause of disability.

Dyspnoea and reduced functional capacity are common consequences with a multifactorial aetiology including parameters of the resting pulmonary function such as forced expiratory volume in the first second (FEV1), dynamic lung hyperinflation, pulmonary hypertension (PH), alterations of the cardiac function as well as other factors such as depression and skeletal muscle weakness. Among the potential cardiac causes of exercise intolerance, RV systolic failure with low cardiac output is rare in patients with COPD, but they often develop RV diastolic dysfunction with stress induced or resting elevation of filling pressures. Left ventricular (LV) diastolic dysfunction is also reported to be common in the COPD population. Nevertheless, data are scarce regarding the effect of the RV and LV diastolic dysfunction on the functional capacity in COPD.

Systemic sclerosis (SSc), another condition associated with PH, is a connective tissue disease characterized by inflammation, microvascular damage, and generalized fibrosis of the skin and various internal organs. It has been proved that cardiac and pulmonary manifestations are present in a high proportion of patients and are recognized as powerful adverse prognostic factors. LV diastolic dysfunction is frequent in SSc and is often accompanied by impaired left atrial (LA) function. RV dysfunction was traditionally attributed to the development of pulmonary arterial hypertension (PAH) or pulmonary fibrosis. Subclinical RV dysfunction, however, was also proved in SSc patients without the resting elevation of the pulmonary pressure, by using tissue Doppler or speckle tracking measurements. Recent data suggest that right atrial (RA) size and mechanics correlate well with the functional capacity of the patients in conditions with known right heart involvement, such as in idiopathic PAH. In SSc, however,

little is known about the RA mechanics and about its correlation with the functional capacity and survival of the patients.

Functional impairment of RV and RA is difficult to measure, but the novel echocardiographic methods such as tissue Doppler imaging (TDI) and the even more recently developed speckle tracking echocardiography (STE) are appropriately sensitive to recognise even the subclinical dysfunction of the right heart.

2. Objectives

The aim of the present work was the echocardiographic assessment of the right heart – focusing on the parameters of RA size and mechanics – in conditions with transient RV pressure overload, such as COPD and SSc. TDI and 2-dimensional STE-derived strain techniques were used to investigate the correlation between echocardiographic parameters and the functional capacity of the patients. Prognostic value of the RA size and mechanics was also investigated in SSc patients without manifest PAH.

3. Methods

3.1. Correlation between echocardiographic parameters of LV and RV diastolic function and the functional capacity of the patients in COPD

65 patients with COPD (61±9 years) in stages GOLD II-IV were investigated. Functional capacity was measured with 6-minute walk test (6MWT). RA and left atrial (LA) area index were measured; collapsibility index inferior vena cava was calculated. Parameters of the mitral and tricuspid inflow (E, A) as well as annular systolic (S), early (e') and late (a') diastolic myocardial longitudinal velocities were measured. E/A, E/e' and e'/a' ratios were calculated. Data of 34 healthy volunteers without any cardiac disease were used as control.

3.2. Significance of RA size and mechanics in SSc: correlation with functional capacity and prognostic value

A total of 70 SSc patients (age: 57 ± 12 years) were investigated. Functional capacity was measured with 6MWT. At baseline, echocardiographic parameters of the RV systolic function (TAPSE, RVFAC), parameters of the tricuspid inflow (E, A), and tricuspid annular systolic (S), early- (e') and late- (a') diastolic myocardial velocities were measured. RV wall thickness was obtained. RA reservoir, conduit, and contractile strain were measured with 2D speckle tracking technique. RA stiffness was calculated as ratio of tricuspid E/e' to reservoir strain. Echocardiographic data were compared with an age- and gender-matched group of 25 healthy volunteers. Survival was assessed after 5 years. All-cause mortality was chosen as outcome. Sequential chi^2 analysis was used to evaluate the incremental prognostic benefit of adding RA volume, strain or stiffness to tricuspid S.

4. Results

4.1. Correlation between echocardiographic parameters of LV and RV diastolic function and the functional capacity of the patients in COPD

6MWT distance was 330 ± 76 m. LV diastolic dysfunction was found in 48 (74%) patients. LV and RV filling pressures were elevated in 28 (43%) and in 29 (45%) patients, respectively. In univariate analysis LA area index as well as various echocardiographic parameters of the right heart showed significant correlation with the functional capacity, as shown in **Table 1.** In stepwise multiple linear regression analysis tricuspid e'/a' (r = 0.611; p = 0.000), collapsibility index (r = 0.505; p = 0.000), RA area index (r = −0.445; p = 0.000) and body surface area (r = 0.314; p = 0.011) were independent predictors of 6MWT distance (**Figure 1**).

Table 1. Predictors of the 6MWD (m) in patients with COPD: univariate and multivariate regression analyses (Unstandardized (B) and standardized (β) regression coefficients).

	Univariate analysis			**Multivariate analysis**		
	B	**r**	**p**	**B**	**β**	**p**
Age (years)	-2.297	-0.273	**0.029**			
BSA (m^2)	91.399	0.314	**0.011**	96.914	0.359	**0.000**
LA area index (cm^2/m^2)	-15,515	-0.319	**0.011**			
RV basal diameter index (mm/m^2)	-10.627	-0.290	**0.021**			
RV longitudinal diameter index (mm/m^2)	-6.357	-0.271	**0.031**			
RA area index (cm^2/m^2)	-22.522	-0.445	**0.000**	-15.606	-0.304	**0.001**
Collapsibility index (%)	2.677	0.505	**0.000**	1.384	0.270	**0.005**
Tricuspid a' (cm/s)	-17.858	-0.525	**0.000**			
Tricuspid e'/a'	355.493	0.611	**0.000**	213.688	0.377	**0.000**

Statistically significant p-values are formatted in bold (p<0.05)

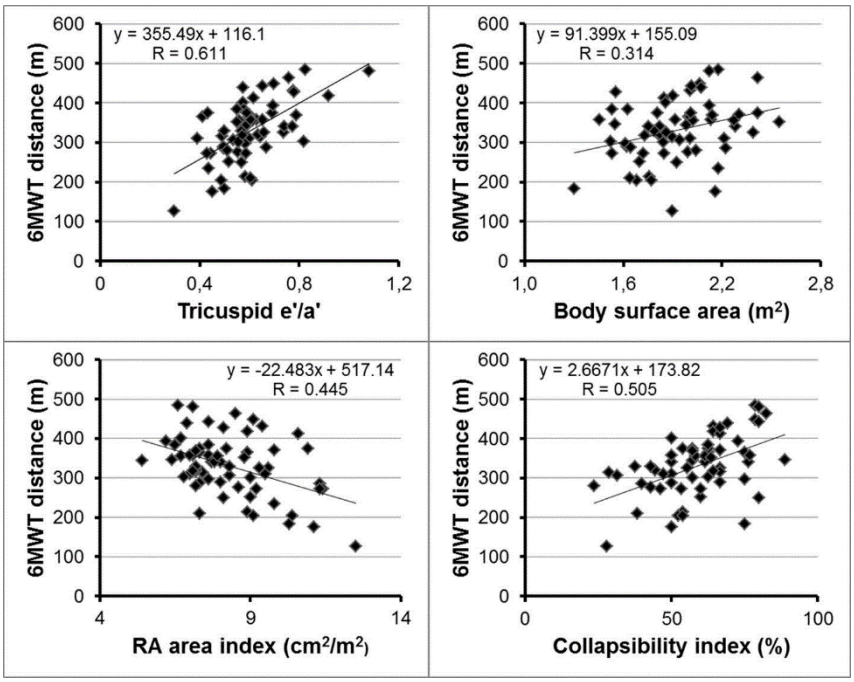


Figure 1. *Main predictors of the 6MWD in patients with COPD*

4.2. Significance of RA size and mechanics in SSc: correlation with functional capacity and prognostic value

RA reservoir strain (49.3 ± 10.7 vs 59.6 ± 9.9%, p = 0.000) and conduit strain (26.8 ± 8.1 vs 34.3 ± 7.3%, p = 0.000) were significantly lower in SSc patients. No significant difference was found in contractile strain (22.9 ± 5.8 vs 25.3 ± 5.7%, p = 0.082). RA stiffness was significantly increased in SSc patients (0.11 ± 0.04 vs 0.08 ± 0.02, p = 0.001). Echocardiographic parameters of SSc patients compared to healthy controls are shown in **Table 2**. 6MWT distance was 391 ± 95 m. In stepwise multiple linear regression analysis RV wall thickness (r = − 0.289, p = 0.030) and RA stiffness (r = − 0.418, p = 0.002) became independent predictors of 6MWT distance (**Figure 2**).

Table 2. Echocardiographic data of the SSc population and comparison with healthy subjects

Variable		**Systemic sclerosis (n=70)**	**Healthy subjects (n=25)**	**p**
Age (years)		57±12	54±7	0.239
BSA (m^2)		1.75±0.19	1.83±0.18	0.071
Female gender n (%)		63 (90%)	19 (76%)	0.082
LV ejection fraction (%)		60.8±4.5	63.3±2.5	**0.011**
LV diastolic function n (%)	Normal	20 (28.6)	25 (100)	**<0.001**
	Impaired relaxation	35 (50)		
	Pseudonormal	15 (21.4)		
Grade of tricuspid regurgitation n (%)	Mild	63 (90)	25 (100)	0.259
	Moderate	5 (7)		
	Severe	2 (3)		
PASP (mmHg)		26.2±5.7	25.8±2.9	0.724
RV basal diameter index (mm/m^2)		18.4±2.4	17.5±1.6	0.924
RV mid-cavity diameter index (mm/m^2)		13.5±2.1	13.0±1.5	0.175
RV longitudinal diameter index (mm/m^2)		31.7±3.6	32.3±2.8	0.392
IVC (mm)		14.0±3.8	14.8±4.7	0.469
Collapsibility index (%)		55.5±11.5	55.0±13.4	0.874
RV wall thickness (mm)		5.0±1.0	4.8±0.8	0.329
RVFAC (%)		47.5±7.2	54.1±6.6	**0.000**
TAPSE (mm)		21.1±2.6	23.6±1.6	**0.000**
Tricuspid E (cm/s)		47.5±9.2	54.3±8.9	**0.002**
Tricuspid A (cm/s)		39.5±8.8	39.0±5.6	0.771
Tricuspid e’ (cm/s)		9.5±2.3	11.7±2.8	**0.002**
Tricuspid a’ (cm/s)		13.2±2.6	13.6±3.3	0.533
Tricuspid S (cm/s)		12.4±2.3	13.6±2.3	**0.027**
Tricuspid E/e' ratio		5.3±1.5	4.9±1.4	0.278
RA Vmax index (ml/m^2)		19.4±5.5	19.5±5.9	0.943
RA reservoir strain (%)		49.3±10.7	59.6±9.9	**0.000**
RA contractile strain (%)		22.9±5.8	25.3±5.7	0.082
RA conduit strain (%)		26.8±8.1	34.3±7.3	**0.000**
RA stiffness		0.11±0.04	0.08±0.02	**0.001**

Statistically significant p-values are formatted in bold ($p<0.05$)

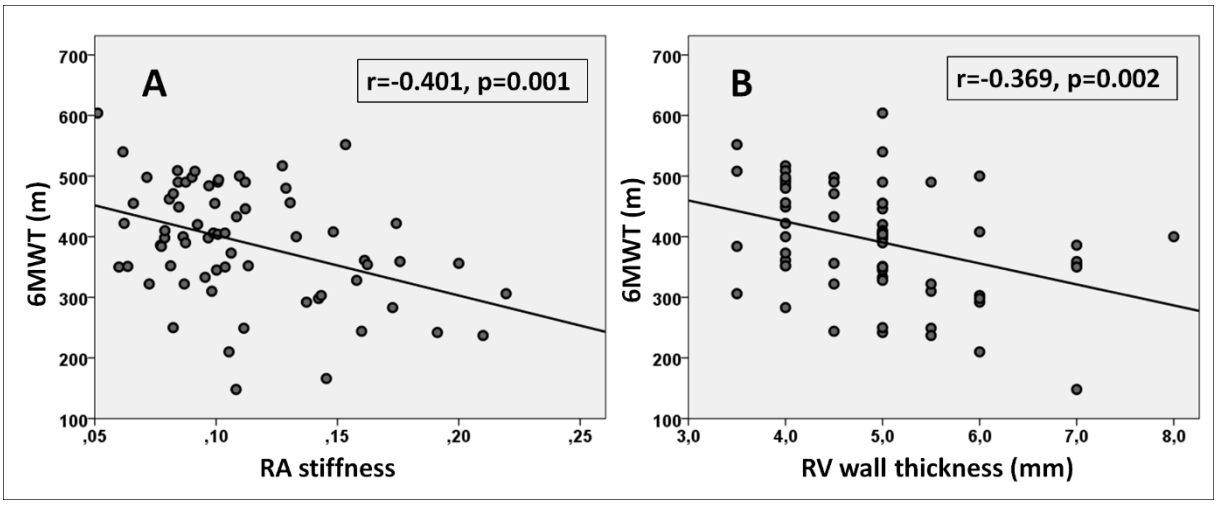


***Figure 2**. Main predictors of the 6MWD in patients with SSc are RA stiffness (A) and RV wall thickness (B).*

During the follow-up period of 4.7 ± 0.9 years, 6 patients (8.6%) died. When added to tricuspid S in sequential Cox model, RA stiffness significantly improved the diagnostic performance of the model (Δchi^2 = 3.950; p = 0.047) and remained independent predictor of the outcome (HR 2.460 (1.005-6.021); p = 0.049). Vmax index and strain parameters did not show incremental prognostic value over tricuspid S (**Table 3**). Using ROC analysis, RA stiffness ≥ 0.156 was the best predictor of mortality (sensitivity = 83.3%, specificity = 89.1%, AUC = 0.859) as shown on **Figure 3**.

When evaluated by comparing groups above and below the cut-off value (10 cm/s for tricuspid S and 0.156 for RA stiffness) for each parameter, patients with high tricuspid S AND low RA stiffness (n=55) showed the lowest mortality rate (1 event (1.8%)). Compared with this reference group, patients with low tricuspid S OR high RA stiffness (n=10) had significantly higher mortality rate (2 events (20%); log-rank p=0.008) whereas the highest mortality rate was observed in patients with low tricuspid S AND elevated RA stiffness (n=5, 3 events (60%), log-rank p<0.001) (**Figure 4**).

Table 3. Models of sequential Cox regression analysis for predicting outcome in SSc. *C-statistics represents the overall performance of the predictive model. Δchi² reflects the incremental prognostic value of the RA variables over tricuspid S, when added to the model.*

		Model 1	**Model 2**	**Model 3**
C-statistics	0.721	0.737	0.820	0.849
Δchi²		2.376; p=0.123	2.536; p=0.111	3.950; **p=0.047**
Variables in model	**HR (95%CI) p-value**	**HR (95%CI) p-value**	**HR (95%CI) p-value**	**HR (95%CI) p-value**
Tricuspid S (cm/s)	0.548 (0.355-0.848); **p=0.007**	0.687 (0.421-1.122); p=0.134	0.599 (0.399-0.901); **p=0.014**	0.768 (0.464-1.271); p=0.304
RA Vmax index (ml/m²)		1.114 (0.967-1.283); p=0.135		
RA contractile strain (%)			0.867 (0.716-1.049); p=0.141	
RA stiffness				2.460 (1.005-6.021); **p=0.049**

Statistically significant p-values (p < 0.05) are formatted in bold.

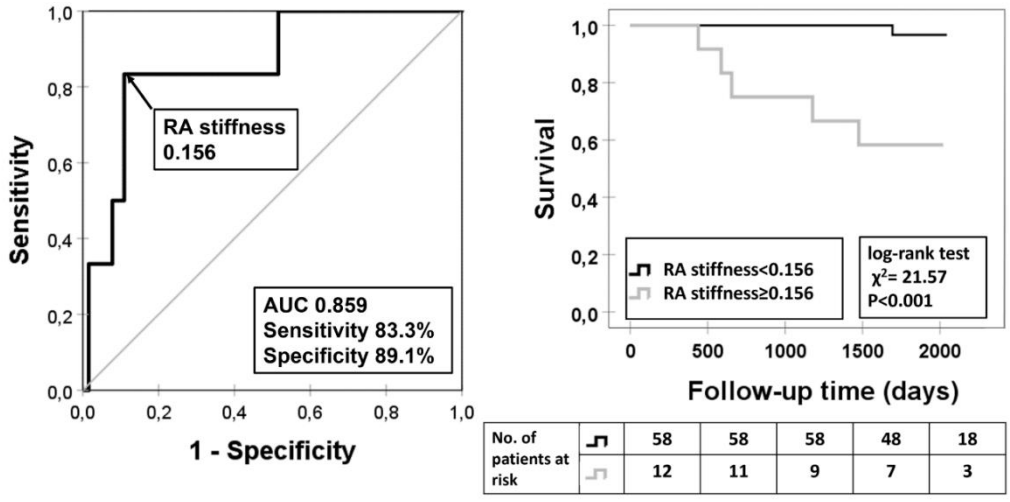
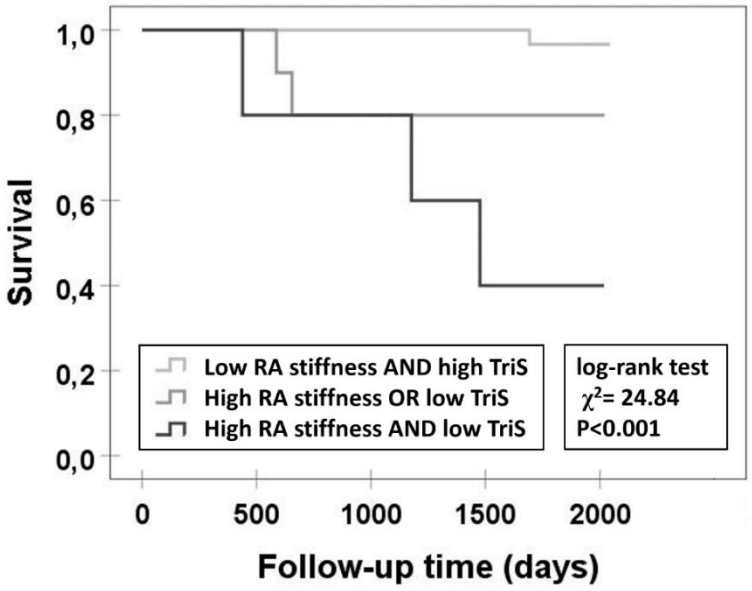


Figure 3. *ROC curve and Kaplan–Meier survival curve demonstrating the performance of RA stiffness in predicting all-cause mortality (χ^2: chi^2)*



No. of patients at risk	⌐¬	55	55	55	47	18
	⌐¬	10	10	8	6	1
	⌐¬	5	4	4	2	2

Figure 4. *Kaplan–Meier survival curve demonstrating the incremental prognostic value of RA stiffness when added to tricuspid S (TriS) in predicting all-cause mortality. The cohort was stratified by tricuspid S and RA stiffness profile of the patients. (χ^2: chi^2)*

5. Conclusion

In our work we proved that RV diastolic function and filling pressure have strong influence on the functional capacity in patients with COPD. Similarly, our results suggest that speckle tracking-derived RA stiffness is increased in SSc compared with healthy subjects and shows strong correlation with the functional capacity of the patients. Besides, RA stiffness is significantly associated with all-cause mortality in SSc patients without PAH independent of and incremental to the RV longitudinal systolic function.

A possible explanation to these results is the pathological increase of pulmonary arterial pressure on exercise, leading to transient pressure overload of the right heart, which in turn results in decreased functional capacity as well as a latent functional impairment of RV and RA, which may be identified with the modern, sensitive echocardiographic techniques applied in our studies.

Our results suggest that these relatively simple, resting echocardiographic parameters may be useful in screening high risk populations and identifying patients with potential exercise PH and worse prognosis.

6. Novel findings

- Echocardiographic parameters of the RV diastolic function and filling pressure show strong correlation with the functional capacity of COPD patients.
- Right atrial reservoir and conduit strain are impaired, whereas RA stiffness is increased in SSc compared with healthy subjects.
- Right atrial stiffness is one of the main determinants of the functional capacity in SSc patients.
- Right atrial stiffness is associated with all-cause mortality in SSc patients without PAH independent of and incremental to the RV longitudinal systolic function.

7. Publications of the author

Original papers and letters

In connection with the topic of the thesis

Nógrádi, Á.; Varga, Z.; Hajdu, M.; Czirják, L.; Komócsi, A.; Faludi, R. Prognostic value of right atrial stiffness in systemic sclerosis. CLINICAL AND EXPERIMENTAL RHEUMATOLOGY 40: 10 pp. 1977-1985. (2022)
Q1 IF≈ 4.862

Nógrádi, Á.; Porpáczy, A.; Porcsa, L.; Minier, T.; Czirják, L.; Komócsi, A.; Faludi, R. Relation of Right Atrial Mechanics to Functional Capacity in Patients With Systemic Sclerosis. AMERICAN JOURNAL OF CARDIOLOGY 122: 7 pp. 1249-1254. (2018)
Q1 IF 2.843

Faludi, R.; Hajdu, M.; Vértes, V.; **Nógrádi, Á.;** Varga, N.; Illés, M.B.; Sárosi, V.; Alexy, G.; Komócsi, A. Diastolic Dysfunction Is a Contributing Factor to Exercise Intolerance in COPD. COPD-JOURNAL OF CHRONIC OBSTRUCTIVE PULMONARY DISEASE 13: 3 pp. 345-351. (2016)
Q1 IF 2.576

Nógrádi, Á.; Faludi, R. A jobb pitvari méret és funkció noninvazív vizsgálatának módszerei és jelentőségük. CARDIOLOGIA HUNGARICA 50: 1 pp. 54-59. (2020).

Not in connection with the topic of the thesis

Vértes, V.; Porpáczy, A.; **Nógrádi, Á.;** Tőkés-Füzesi, M.; Hajdu, M.; Czirják, L.; Komócsi, A.; Faludi, R. Galectin-3 and sST2: associations to the echocardiographic markers of the myocardial mechanics in systemic sclerosis – a pilot study. CARDIOVASCULAR ULTRASOUND 20 : 1 Paper: 1. (2022)
Q2 IF 2.263

Ezer, P.; Kálmán, E.; **Nógrádi, Á.;** Vértes, V.; Cziráki, A.; Faludi, R. Chloroquin indukálta cardiomyopathia avagy a „pszeudo-Fabry-kór" fatális lefolyású esete. CARDIOLOGIA HUNGARICA 52: 1 pp. 38-44. (2022)

Hajdu, M.; Krämer, K.; Vértes, V.; **Nógrádi, Á.;** Varga, N.; Illés, M.B.; Sárosi, V.; Faludi, R. Krónikus obstruktív tüdőbetegségben a bal kamra diasztolés funkciózavara gyakori és rossz prognózissal társul. CARDIOLOGIA HUNGARICA 50 pp. 410-416. (2020)

Porpáczy, A.; **Nógrádi, Á.;** Vértes, V.; Tőkés-Füzesi, M.; Czirják, L.; Komócsi, A.; Faludi, R. Left atrial stiffness is superior to volume and strain parameters in predicting elevated NT-proBNP levels in systemic sclerosis patients. INTERNATIONAL JOURNAL OF CARDIOVASCULAR IMAGING 35: 10 pp. 1795-1802. (2019)
Q2 IF 1.969

Vértes, V.; **Nógrádi, Á.;** Porpáczy, A.; Minier, T.; Czirják, L.; Komócsi, A.; Faludi, R. A bal kamrai globális longitudinális strain károsodott szisztémás szklerózisban és korrelál a betegek funkcionális kapacitásával. CARDIOLOGIA HUNGARICA 49: 1 pp. 12-16. (2019)
Porpáczy, A.; **Nógrádi, Á.;** Kehl, D.; Strenner, M.; Minier, T.; Czirják, L.; Komócsi, A; Faludi, R. Impairment of the Left Atrial Mechanics is an Early Sign of the Myocardial Involvement in Systemic Sclerosis. JOURNAL OF CARDIAC FAILURE 24: 4 pp. 234-242. (2018)

Q1 IF 3.967

Cumulative impact factor: 18.480

Independent citations: 56

Citable abstracts

In connection with the topic of the thesis

Nógrádi , Á.; Varga, Zs.; Szebényi, D.; Porpáczy, A.; Vértes, V.; Czirják, L.; Komócsi, A.; Faludi, R. Prognostic role of right ventricular and atrial mechanics in systemic sclerosis. In: Kajos, Luca Fanni; Bali, Cintia; Preisz, Zsolt; Polgár, Petra; Glázer-Kniesz, Adrienn; Tislér, Ádám; Szabó, Rebeka (szerk.) 10th Jubilee Interdisciplinary Doctoral Conference: Book of Abstracts. Pécsi Tudományegyetem Doktorandusz Önkormányzat p. 25. (2021)

Nógrádi, Á.; Varga, Z.; Szebényi, D.; Porpáczy, A.; Vértes, V.; Czirják, L; Komócsi, A.; Faludi, R. Prognostic role of right ventricular and atrial mechanics in systemic sclerosis. EUROPEAN HEART JOURNAL 41: Suppl. 2 p. 106. (2020)

Nógrádi, Á.; Varga, Zs.; Szebényi, D.; Porpáczy, A.; Vértes, V.; Czirják, L.; Komócsi, A.; Faludi, R. A jobb kamra és pitvar funkcióját jellemző echokardiográfiás paraméterek prognosztikus szerepe sclerodermás populációban. CARDIOLOGIA HUNGARICA 50: Suppl. D pp. 158-159. (2020)

Nógrádi, Á.; Porpáczy, A.; Molnár, F.; Minier, T.; Czirják, L.; Komócsi, A.; Faludi, R. A speckle tracking alapú jobb pitvari strain paraméterek jól korrelálnak a fázisos pitvari volumen indexekkel systemás sclerosisos betegekben. CARDIOLOGIA HUNGARICA 48: Suppl. C p. C23 (2018)

Nógrádi, Á; Porpáczy, A.; Molnár, F.; Minier, T.; Czirják, L.; Komócsi, A.; Faludi, R. Speckle tracking derived right atrial strain parameters show strong correlation with phasic volume indices in systemic sclerosis patients. EUROPEAN HEART JOURNAL 38: Suppl. pp. 1092-1093. (2017)

Nógrádi, Á.; Porpáczy, A.; Molnár, F.; Minier, T.; Czirják, L.; Komócsi, A. Faludi, R. A jobb pitvari stiffness a funkcionális kapacitás meghatározója systemás sclerosisos betegekben. CARDIOLOGIA HUNGARICA 47: Suppl. C p. C3. (2017)

Nógrádi, Á.; Porcsa, L.; Minier, T.; Czirják, L.; Komócsi, A.; Faludi, R. Determinants of the right atrial mechanics in systemic sclerosis (P1436) EUROPEAN HEART JOURNAL 37: 1. Suppl. p. 258. (2016)

Nógrádi, Á.; Porpáczy, A.; Porcsa, L.; Minier, T.; Czirják, L.; Komócsi, A.; Faludi, R. Echocardiographic determinants of the functional capacity in systemic sclerosis: role of the right heart. EUROPEAN HEART JOURNAL-CARDIOVASCULAR IMAGING 17: Suppl. 2 p. ii279. (2016)

Nógrádi, Á.; Porcsa, L.; Minier, T.; Czirják, L.; Komócsi, A.; Faludi, R. A jobb pitvari funkció meghatározó tényezői szisztémás szklerózisos betegekben. CARDIOLOGIA HUNGARICA 46: Suppl. F p. 4. (2016)

Not in connection with the topic of the thesis

Vértes, V.; Porpáczy, A.; **Nógrádi, Á.;** Hajdu, M.; Czirják, L.; Komócsi, A.; Faludi, R. Echocardiographic markers of the myocardial involvement are related to the physical functioning dimension of SF-36 health survey in systemic sclerosis. EUROPEAN JOURNAL OF HEART FAILURE 24 pp. 76-77. (2022)

Vértes, V.; Tőkés-Fuzesi, M.; Porpáczy, A.; **Nógrádi, Á.;** Czirják, L.; Komócsi, A.; Faludi, R. Circulating biomarkers of cardiac fibrosis: do they correlate with the echocardiographic parameters of the myocardial mechanics in systemic sclerosis? EUROPEAN HEART JOURNAL-CARDIOVASCULAR IMAGING 22: Suppl. 1 p. i149 (2021)

Vértes, V.; Nochta, A.; Porpáczy, A.; **Nógrádi, Á.;** Czirják, L.; Komócsi, A.; Faludi, R. A szívizom érintettséget tükröző echokardiográfiás paraméterek korrelációt mutatnak az SF-36 életminőség kérdőív „fizikai funkció" pontszámával szklerodermás betegekben = Echocardiographic markers of the myocardial involvement are related to the physical functioning dimension of SF-36 health survey in systemic sclerosis. CARDIOLOGIA HUNGARICA 51: Suppl. B pp. B224-B225. (2021)

Kengyelné, Fődi E.; **Nógrádi, Á.;** Tóth, L.; Simor, T.; Faludi, R. Progresszív szívbetegség a benignusnak látszó palpitációs panaszok mögött: esetismertetés. CARDIOLOGIA HUNGARICA 50: Suppl. D pp. 203-204. (2020)

Vértes, V.; Tőkés-Füzesi, M.; Porpáczy, A.; **Nógrádi, Á.;** Czirják, L.; Komócsi, A.; Faludi, R. A szívizom fibrózis keringő biomarkerei mutatnak-e összefüggést a miokardiális funkciót jellemző echokardiográfiás paraméterekkel szisztémás szklerózisban? CARDIOLOGIA HUNGARICA 50: Suppl. D p. 159. (2020)

Porpáczy, A.; **Nógrádi, Á.;** Vértes, V.; Tőkés-Füzesi, M.; Czirják, L.; Komócsi, A.; Faludi, R. A bal pitvari stiffness hatékonyabb az emelkedett NT-proBNP szint azonosításában szisztémás szklerózisban szenvedő betegekben, mint a volumen és strain paraméterek. CARDIOLOGIA HUNGARICA 49: Suppl. B pp. B116-B117. (2019)

Hepp, T.; Zsigmond, Á.; Kis, E.; Maláti, É.; Pere, T.; Szukits, S; Tóth, L.; Faludi, R.; **Nógrádi, Á.;** Cziráki, A. et al. Mitrális műbillentyű endocarditis diagnózisa 3D renderelt szív CT képekkel alátámasztva CARDIOLOGIA HUNGARICA 48: Suppl. C p. C47 (2018)

Vértes, V.; Porcsa, L.; Strenner, M.; **Nógrádi, Á.;** Porpáczy, A.; Minier, T.; Czirják, L.; Komócsi, A.; Faludi, R. A galectin-3 szérum szintje korrelál a bal kamrai globális longitudinális strain értékekkel systemás sclerosisban. CARDIOLOGIA HUNGARICA 48: Suppl. C p. C24 (2018)

Porpáczy, A.; **Nógrádi, Á.;** Varga N.; Minier, T.; Czirják, L. ; Komócsi, A.; Faludi, R. Left atrial stiffness is a robust predictor of the elevated NT-proBNP levels in systemic sclerosis patients with preserved left ventricular ejection fraction. EUROPEAN HEART JOURNAL 38: Suppl. 1 p. 422 Paper: P2076 (2017)

Porpáczy, A.; **Nógrádi, Á.;** Strenner, M.; Minier, T.; Czirják, L.; Komócsi, A. ; Faludi, R. A bal pitvari stiffness meghatározói systemás sclerosisos betegekben CARDIOLOGIA HUNGARICA 47: Suppl. C p. C66. (2017)

Vértes, V.; Porcsa, L. ; Strenner M.; **Nógrádi, Á.;** Porpáczy, A.; Minier, T. ; Czirják, L.; Komócsi, A.; Faludi, R. Galectin-3 levels correlate with left ventricular global longitudinal strain in systemic sclerosis patients. EUROPEAN HEART JOURNAL-CARDIOVASCULAR IMAGING 18: Suppl. 3 p. iii112-iii113. (2017)

Vértes, V.; Porcsa, L. ; Strenner, M.; **Nógrádi, Á. ;** Porpáczy, A.; Minier, T.; Czirják, L.; Komócsi, A.; Faludi, R. A galectin-3 szérumszintje korrelál a bal kamrai globális longitudinális strain értékekkel systemás sclerosisban. In: Bódog, Ferenc; Csiszár, Beáta; Hegyi, Dávid; Pónusz, Róbert (szerk.) DKK17-Doktoranduszok a Klinikai Kutatásokban absztraktkötet. Pécs, Magyarország: Pécsi Tudományegyetem Doktorandusz Önkormányzat (2017): p. 12.

Vértes, V.; **Nógrádi, Á.;** Porpáczy, A.; Minier, T.; Czirják, L.; Komócsi, A.; Faludi, R. A globális longitudinális strain alkalmas a subklinikus bal kamrai funkciózavar kimutatására systemás sclerosisban. CARDIOLOGIA HUNGARICA 47: Suppl. C p. C4. (2017)

Porpáczy, A.; **Nógrádi, Á**.; Strenner, M.; Minier, T.; Czirják; A.; Komócsi, A.; Faludi, R. Determinants of the left atrial stiffness in systemic sclerosis. EUROPEAN HEART JOURNAL-CARDIOVASCULAR IMAGING 17: Suppl. 2 p. ii243. (2016)

Porpáczy, A; **Nógrádi, Á.;** Strenner, M. ; Minier, T.; Czirják, L.; Komócsi, A.; Faludi, R. Left ventricular diastolic function is a determinant of the left atrial mechanics in systemic sclerosis. EUROPEAN HEART JOURNAL 37: S1 p. 261. Paper: P1446 . (2016)

Porpáczy, A.; **Nógrádi, Á.;** Strenner, M.; Minier, T.; Czirják, L.; Komócsi, A.; Faludi, R. A bal pitvari funkció összefüggést mutat a bal kamrai diasztolés funkcióval szisztémás szklerózisos betegekben. CARDIOLOGIA HUNGARICA 46: Suppl. F pp. 4-5. (2016)

Vértes, V.; **Nógrádi, Á.;** Porpáczy, A.; Minier, T.; Czirják, L.; Komócsi, A.; Faludi, R. Global longitudinal strain is a suitable tool to unmask the subclinical left ventricular dysfunction in patients with systemic sclerosis. EUROPEAN HEART JOURNAL-CARDIOVASCULAR IMAGING 17: Suppl. 2 p. ii177. (2016)

Nógrádi, Á.; Kónyi, A.; Cziráki, A.; Szabados, S.; Faludi, R. Iszkémiás DCM-es beteg eredményes kezelése külső ellenpulzációs pumpával. CARDIOLOGIA HUNGARICA 45: Suppl. D p. D62 (2015)

Nógrádi, Á.; Faludi, R.; Cziráki, A.; Szabados, S. Mellkasi irradiatio késői cardialis szövődményei. CARDIOLOGIA HUNGARICA 44: Suppl. E p. E5. (2014)

Nógrádi , Á.; Faludi, R.; Fődi, E.; Szűcs, A.; Tóth, A.; Szabados, S.; Simor, T. Trouble never comes alone-case of left ventricular noncompaction complicated by bicuspid aortic valve. EUROPEAN JOURNAL OF HEART FAILURE 11: S1 p. S78 (2012)

Nógrádi, Á.; Faludi, R.; Fődi, E.; Szűcs, A.; Tóth, A.; Szabados, S.; Simor, T. A baj nem jár egyedül... - Noncompact cardiomyopathia bicuspidalis aorta billentyűvel szövődött esete. CARDIOLOGIA HUNGARICA 42: Suppl. A p. A109 (2012)

8. Acknowledgments

I would like to express my gratitude to all who supported me throughout my research and work on this doctoral thesis.

First of all, my heartfelt thanks to my supervisor, Dr. Réka Faludi, for her guidance, teaching and her unfailing support. Her dedication and high standards have been a formative example to me throughout my clinical and scientific career. Without her, this work could not have been realized.

I would like to express my thanks to Prof. Dr. Attila Cziráki, the present Chair of the Heart Institute as well as Prof. Dr. Lajos Papp and Prof. Dr. Sándor Szabados, previous Chairs of the Heart Institute for providing the opportunity for my clinical work and to do my research and write my thesis.

The longstanding collaboration with Prof. Dr. László Czirják and Dr. Tünde Minier from the Rheumatology and Immunology Department provided the opportunity to recruit the systemic sclerosis patients and to collect the clinical data on their disease. I would like to express my gratitude to them.

I am deeply grateful to the community of colleagues, doctors, nurses and assistants in the Heart Institute who accompanied, assisted and supported me throughout my working and research career.

Last but not least, the love and encouragement of my husband and my family was an invaluable help. Without their support this work would not have been possible.