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# The Year in Hungarian Cardiology 2022: Cardiac Imaging

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A szerző video-összefoglalója

In 2022, the Hungarian Cardiovascular Imaging community contributed to several scientific papers that were published in international journals. Clinical research activities employed novel echocardiographic methods including two- and three-dimensional, strain and tissue Doppler imaging of all cardiac chambers. These echocardiographic modalities were applied in different patient populations such as patients with severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) or post-SARS-CoV-2 affected individuals, athletes, patients with systemic autoimmune diseases, cardiomyopathies, hematologic diseases, metabolic diseases, congenital heart disease or valvular interventions. Beyond resting echocardiography, original research results revealed important information in the field of exercise stress echocardiography as well. Hungarian studies using cardiac magnetic resonance imaging evaluated patients with different pathologies such as cardiac amyloidosis, cardiomyopathies, myocarditis due to SARS-CoV-2 vaccinations, and athletes in post-SARS-CoV-2 states. Hungarian research activities in the field of cardiac computed tomographic imaging covered the evaluation of moderate coronary lesions, correlates of myocardial ischemia, coronary plaques, coronary calcium, recurrence of atrial fibrillation after radiofrequency ablation and morphological changes after valvular interventions. Novel technologies have been applied in cardiac computed tomographic imaging by Hungarian researchers, with higher spatial resolution and enhanced spectral capabilities in coronary artery assessment.

**Keywords:** echocardiography, cardiac magnetic resonance imaging, cardiac computed tomography

**A magyar kardiológia eredményei 2022-ben: kardiális képalkotás**

2022-ben a magyar kardiovaszkuláris képalkotó közösség számos, külföldi folyóiratban megjelent közleménnyel járult hozzá a nemzetközi kardiológiai kutatáshoz. A publikációk alapját képező egyes vizsgálatokban a pitvarok és kamrák morfológiai és funkcionális jellemzőit két- és háromdimenziós echokardiográfiás strainnel és szöveti Dopplerrel tanulmányozták. E módszerekkel olyan betegcsoportokat vizsgáltak, mint súlyos akut légzőszervi szindróma koronavírus-2 (COVID), poszt-COVID-betegcsoport, szisztémás autoimmun betegek, cardiomyopathiák, hematológiai betegek, metabolikus betegségek, veleszületett szívbetegségek, billentyűbetegség miatt beavatkozáson áteső betegek, illetve sportolók. A nyugalmi echokardiográfiás vizsgálatokon túl a klinikai kutatások fontos eredményeket tártak fel a terheléses stresszechokardiográfia területén is. A magyar képalkotó munkacsoport kardiális mágneses rezonanciás képalkotással végzett vizsgálataiban szívamiloidózisos, kardiomiopátiás, COVID-oltás utáni myocarditis miatt kezelt betegek, valamint COVID-fertőzés utáni állapotban lévő sportolók körében végeztek jelentős eredményű klinikai kutatásokat. A kardiális CT és koronária CT-angiográfia területén közelmúltban észlelhető új technológiai fejlesztéseknek köszönhetően a szív és koronáriák eltéréseinek eddiginél részletgazdagabb megjelenítése vált elérhetővé. A magyar kutatók ezen új, modern CT-képalkotási módszereket használva kiemelkedő eredményeket értek el a mérsékelt koszorúér-elváltozások értékelésében, a szívizom-iszkémia összefüggéseinek megállapításában, a koszorúérplakk-szerkezet és kalciumtartalom megítélésében, valamint a billentyűbeavatkozásokat követő morfológiai változások összefüggéseinek vizsgálatában.

**Kulcsszavak:** echokardiográfia, kardiális mágnesesrezonancia-képalkotás, kardiális számítógépes tomográfia

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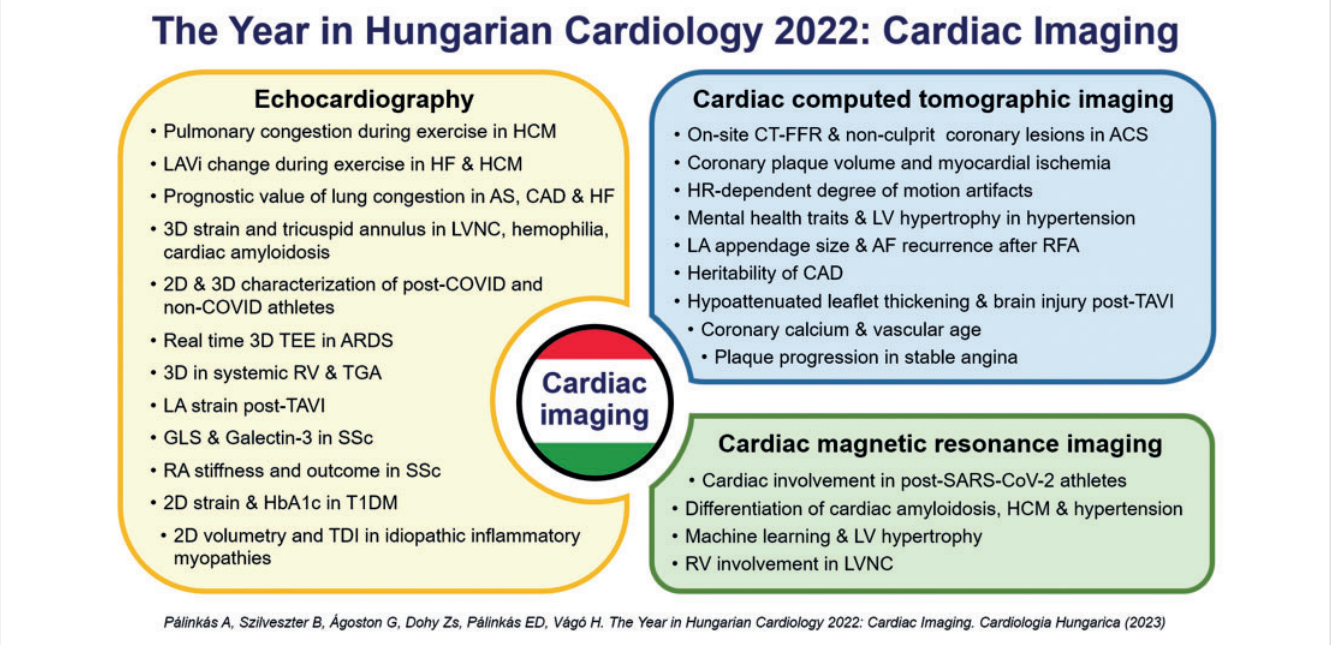


GRAPHICAL ABSTRACT. Topics covered in published clinical investigations involving Hungarian researchers in 2022. The papers were published in peer-reviewed journals with impact factors and were at least partially written by Hungarian authors and the research was at least in part carried out at Hungarian research sites.
Abbreviations: 2D: two-dimensional, 3D: three-dimensional, ACS: acute coronary syndrome, AF: atrial fibrillation, ARDS: acute respiratory distress syndrome, AS: aortic stenosis, CAD: coronary artery disease, COVID: coronavirus disease, CT-FFR: computed tomography fractional flow reserve, GLS: global longitudinal strain, $HbA_{1C}$: hemoglobin A1C, HCM: hypertrophic cardiomyopathy, HF: heart failure, HR: heart rate, LA: left atrium, LV: left ventricular, LVNC: left ventricular noncompaction, RA: right atrium, RV: right ventricle, SARS-CoV-2: severe acute respiratory syndrome coronavirus 2, SSc: systemic sclerosis, T1DM: type 1 diabetes mellitus, TAVI: transcatheter aortic valve implantation, TDI: tissue Doppler imaging, TEE: transesophageal echocardiography, TGA: transposition of great arteries

## Introduction

The year 2022 provided numerous scientific publications from Hungary in different sections of cardiac imaging. The current paper summarizes those original clinical research studies that were published in peer-reviewed journals with impact factors and were at least partially written by Hungarian authors and the research was at least in part carried out at Hungarian research sites. Specific care was taken by the authors to avoid duplication of publications discussed in previous thematic sections of the journal. This review summarizes the results from cardiac imaging studies incorporating echocardiography, cardiac magnetic resonance imaging (CMR) and cardiac computed tomography (CT).

## Echocardiography

In a multicenter collaborative work, *Pálinkás ED and colleagues* from the University of Szeged assessed clinical, anatomical and functional correlates of pulmonary congestion (defined as B-lines on lung ultrasound [LUS]) during dynamic exercise stress echocardiography (ESE) in 128 patients with hypertrophic cardiomyopathy (HCM) (1). The authors found that pulmonary congestion occurs in about 10% at rest and in 30% during exercise in patients with HCM, and two-thirds of the patients with exercise pulmonary congestion have no evidence of B-lines at rest. Exercise B-lines were associated with worse resting and stress diastolic function, more abnormal blood pressure response, more

*Abbreviations:*
2D: two-dimensional, 3D: three-dimensional, AF: atrial fibrillation, CA: cardiac amyloidosis, CAD: coronary artery disease, CCTA: coronary computed tomography angiography, CMR: cardiac magnetic resonance imaging, SARS-CoV-2: severe acute respiratory syndrome coronavirus 2, CT: computed tomography, EF: ejection fraction, ESE dynamic exercise stress echocardiography, GCS: global circumferential strain, GLS: global longitudinal strain, HALT: hypoattenuated leaflet thickening, HCM: hypertrophic cardiomyopathy, HF: heart failure, LASr: left atrial peak reservoir strain, LAVi: left atrial volume index, LUS: lung ultrasound, LV: left ventricular, LVH: left ventricular hypertrophy, LVNC: left ventricular noncompaction, RV: right ventricular, TA: tricuspid annulus

mitral regurgitation increment and lesser cardiac output reserve with similar heart rate response, indicating greater clinical and functional severity and hemodynamic vulnerability. These findings underscore the importance of noninvasive hemodynamic and LUS assessment during ESE in HCM, particularly in the presence of unexplained symptoms and functional limitation. The same multicenter study group investigated the alteration of left atrial volume index (LAVi) change during ESE including 363 heart failure (HF) and HCM patients (2). The authors found that LAVi dilation during ESE occurred in 30% of all patients. The LAVi dilator pattern was three-fold more frequent in HCM and HF with reduced ejection fraction (EF) patients compared to HF with preserved EF patients and could be predicted by increased resting E/e' and impaired resting EF as well as smaller baseline LAVi. The authors concluded that only a minimal increase in analysis time, rest and stress LAVi evaluation can be a further useful adjunct to comprehensive stress echo beyond coronary artery disease.

*Szabó IA and colleagues* from the University of Szeged studied the prognostic value of LUS in 75 patients with moderate or severe aortic stenosis (3). A severe degree of lung congestion (B-lines ≥30) was found in 29% of the patients, which proved to be an independent predictor of the composite endpoint (death, hospitalization for HF, and worsening HF with the intensification of loop diuretic therapy) along with the mean aortic transvalvular gradient. Researchers from the same group participated in a multicenter study evaluating the prognostic role of pulmonary congestion by LUS during stress echocardiography in 4392 patients with ischemic heart disease and HF (4). The study population consisted of a control group, four groups of patients with chronic coronary syndrome, HF with preserved EF, HF with reduced EF, or at least moderate ischemic mitral regurgitation. The results showed that stress B-lines EF <50% were independent predictors of all-cause death after a median follow-up of 29 months.

*Nemes A and colleagues* from the Department of Medicine, University of Szeged evaluated morphological and functional abnormalities of the tricuspid annulus (TA) by three-dimensional (3D) strain echocardiography in 21 patients with left ventricular noncompaction (LVNC) without right ventricular (RV) involvement (5). The study demonstrated that TA is dilated with preserved sphincter-like function in patients with isolated LVNC. The authors also found that longitudinal and sphincter-like TA movements were correlated and TA dilation was associated with increased right atrial volume in patients with LVNC. In another study of the same group, it was tested using 3D strain echocardiography whether cardiac amyloidosis (CA) is associated with morphological or functional abnormalities of the TA (6). Moreover, differences in TA parameters between light-chain and transthyretin CA were also evaluated. The study comprised 27 CA patients, their results were compared to those of 20 age- and gender-matched healthy volunteers. Dilated end-diastolic and end-systolic TA diameter, area and perimeter could be detected in all CA patients. Morphologic TA parameters in transthyretin CA patients proved to be tendentiously higher as compared to light-chain CA patients. Functional parameters of TA were found to be reduced in CA patients, which were more deteriorated in light-chain CA patients. *Nemes A and colleagues* also studied LA volumetric and functional properties in 14 patients with hemophilia using 3D strain echocardiography. LA volumes and LA stroke volumes did not differ between controls and hemophilia patients (7). While the total atrial emptying fraction featuring LA reservoir function was reduced in patients with hemophilia compared to that of controls, passive and active atrial emptying fraction, characterizing LA conduit and booster pump functions, were similar between the groups. From LA strains, peak mean segmental circumferential and longitudinal LA strains were impaired in patients with hemophilia, The authors concluded that hemophilia is not associated with LA volumetric changes, but mild LA functional abnormalities are present.

*Lakatos BK and colleagues* from the Heart and Vascular Center of Semmelweis University evaluated global and axial RV EF by real-time 3D transesophageal echocardiography in 64 ventilated patients for acute respiratory distress syndrome secondary to severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) pneumonia or to other causes (8). The authors showed that global RV EF was significantly lower in patients with acute respiratory distress syndrome related to non-SARS-CoV-2 compared to SARS-CoV-2 pneumonia. Longitudinal and anteroposterior axis shortening of RV had a similar relative contribution to global RV EF in all groups. Radial shortening of the right ventricle was lower in non-SARS-CoV-2 when compared to SARS-CoV-2 pneumonia and control patients. In another study, the same research team performed comprehensive two-dimensional (2D) and 3D echocardiographic characterization of elite post-SARS-CoV-2 athletes (N=107) (9). Post-SARS-CoV-2 and non-SARS-CoV-2 athletes had comparable left ventricular (LV) and RV end-diastolic volumes and LV global longitudinal strain (GLS) values, while post-SARS-CoV-2 athletes had significantly higher LV EF and eccentricity index. In the subgroup of SARS-CoV-2 athletes demonstrating septal flattening during diastole, the eccentricity index was markedly higher compared to the rest of the post-SARS-CoV-2 athletes. Moreover, the free wall to septal longitudinal strain ratio was significantly lower in the septal flattening subgroup. The authors concluded that the pathophysiological background and clinical relevance of these specific echocardiographic findings are unclear and require further research. In the frame of

an international collaboration, researchers of the same working group investigated the contraction patterns of the systemic RV by 3D echocardiography in 38 patients with transposition of great arteries post-atrial switch operation and with congenitally corrected transposition of great arteries (10). Systemic RV of patients was significantly larger with lower RV systolic function compared with healthy controls. In patients with transposition of great arteries, the anteroposterior RV component was significantly higher than longitudinal and radial components reflecting the adaptive process to systemic circulation and previous surgical repair. In patients with congenitally corrected transposition of great arteries, there was no significant difference between the three systemic RV components. The authors concluded that 3D evaluation should be a part of routine echocardiographic assessment of the systemic RV, especially in patients with transposition of great arteries since no conventional echo parameters of RV systolic function consider anteroposterior contraction.

*Fábián A and colleagues* from the Heart and Vascular Center of Semmelweis University evaluated biventricular volumetric and strain data of elite competitive athletes (n = 422) by 3D echocardiography (11). Athletes had significantly higher LV and RV end-diastolic volume index and lower resting LV and RV EF compared with controls. The exercise-induced relative decrease in LV GLS and global circumferential strain (GCS) was similar; however, the decrement in RV (GCS) was disproportionately larger compared with RV GLS. RV end-diastolic volume index was found to be the strongest independent predictor of peak oxygen uptake by exercise testing. The authors emphasize the importance of 3D imaging in the evaluation of the athlete's heart to understand normal exercise physiology.

*Vattay B and colleagues* from the same institute, aimed to evaluate the association of left atrial strain measured shortly post-transcatheter aortic valve implantation with functional and anatomical reverse remodelling of the LA and LV, and its association with mortality in 90 patients using echocardiography and cardiac computed tomography (CT) (12). They demonstrated that severely reduced left atrial peak reservoir strain (LASr) at baseline was associated with more pronounced LASr and LV mass index reduction on follow-up, however was not linked to anatomical reverse remodelling of the left atrium based on LAVi. Notably, the majority of the patients with severely reduced LASr at baseline had impaired LA function even after 6 months of the procedure. No significant difference in survival was found between patients with baseline severely reduced LASr and higher LASr.

*Vértes V and colleagues* from the Heart Institute of the University of Pécs investigated the potential correlations between biomarkers of cardiac fibrosis and echocardiographic markers of the myocardial mechanics in 40 patients with systemic sclerosis (13). In age-adjusted analysis galectin-3 level showed a significant correlation with LV GLS, the grade of left ventricular diastolic dysfunction and the grade of mitral regurgitation. No significant correlation was found between soluble suppression of tumorigenicity-2 levels and the echocardiographic variables. The authors concluded that Galectin-3 may be a useful biomarker for the screening and early diagnosis of systemic sclerosis patients with cardiac involvement.

*Nógrádi Á and colleagues* evaluated the prognostic value of detailed volumetric and strain data of the right heart by 2D echocardiography in 70 systemic sclerosis patients (14). Their results showed that right atrial stiffness is associated with all-cause mortality in systemic sclerosis patients without manifest pulmonary arterial hypertension and its prognostic value is independent of and incremental to the RV longitudinal systolic function. The best cutoff value of right stiffness to predict all-cause mortality was ≥0.156.

*Hajdu M. and colleagues* also from the University of Pécs, investigated the potential associations between disease duration, glycemic control, and the echocardiographic markers of the myocardial mechanics in 70 asymptomatic type 1 diabetes patients. This study showed that current hemoglobin A1C level remained an independent predictor of LV GLS, GCS, mitral e', tricuspid e' and left and right atrial conduit strain in multiple linear regression models. Their study concluded that the quality of glycemic control has a significant impact on myocardial mechanics in type 1 diabetes (15).

*Péter A and colleagues* studied cardiac involvement and its alteration in 28 patients with idiopathic inflammatory myopathies by echocardiography (16). They demonstrated subclinical LV systolic dysfunction by 2D LV volumetric and tissue Doppler imaging that was accompanied by left atrial enlargement in polyphasic idiopathic inflammatory myopathies patients at 2 years follow-up compared to controls. tissue Doppler imaging measurements confirmed subclinical RV systolic dysfunction at follow-up studies. Similar, but not significant tendencies could be detected in patients with monophasic disease patterns. The authors concluded that subclinical cardiac dysfunction could be detected by detailed echocardiographic examination in idiopathic inflammatory myopathies patients with polyphasic disease course, and helps to identify patients at high cardiac risk.

## Cardiac computed tomographic imaging

In a multimodality study involving 68 patients with acute coronary syndrome and non-culprit lesions, on-site CT-fractional flow reserve showed improved diagnostic accuracy compared to traditional coronary computed tomography angiography (CCTA) based analysis for

describing the functional relevance of moderate coronary lesions (30−70% diameter stenosis) (17). CT-fractional flow reserve did not offer insights into microvascular dysfunction within the non-culprit lesion territory, as evidenced by its comparison with dobutamine stress echocardiography.

*Vattay B and colleagues* from the Heart and Vascular Center of Semmelweis University aimed to investigate the relationship between volumetric measurements of coronary plaque obtained from CCTA and the presence of corresponding myocardial ischemia detected by dynamic perfusion CT (18). In multivariate analysis, total plaque volume was independently associated with myocardial ischemia based on myocardial blood flow, whereas area stenosis and high-risk plaque were not. These findings suggest that quantitative plaque assessment could be a valuable tool for identifying myocardial ischemia.

Wide detector scanner technology dedicated for coronary imaging offers significant benefits. *Vecsey-Nagy M and colleagues* compared 2328 coronary segments from a dedicated cardiac CT scanner to those from a conventional multidetector CT scanner focusing on motion artifacts at different heart rates (19). Results showed that the dedicated cardiac CT scanner consistently provided superior image quality with fewer motion artifacts, even in patients with a heart rate above 70/min.

A cross-sectional study including 296 patients referred to CCTA due to suspected coronary artery disease (CAD) explored the connection between affective temperaments and left ventricular hypertrophy (LVH) in chronic hypertensive patients. Higher body mass index and the presence of a cyclothymic affective temperament were associated with an increased likelihood of LVH. The collaborative aspect of this study lies in the integration of psychological assessments (affective temperaments) with cardiac CT findings (LVH), providing a more comprehensive understanding of the relationship between mental health traits and cardiovascular health in hypertensive patients (20).

*Simon J and colleagues* evaluated the role of left atrial appendage enlargement in the recurrence of atrial fibrillation (AF) after radiofrequency ablation. In this multimodality study, they included 561 AF patients. Notably, left atrial appendage volume and LV EF<50% were independently associated with the risk of AF recurrence in patients with persistent AF. No independent predictors were identified in those with paroxysmal AF. Furthermore, pulmonary vein anatomy was proposed as a possible risk marker for AF recurrence (21).

The BUDAPEST-GLOBAL study conducted also by the Heart and Vascular Center of Semmelweis University aimed to investigate the impact of both genetic and environmental factors on the burden of CAD (22). The study involved adult twin pairs who did not have a documented history of CAD. *Drobni Zs. and colleagues* investigated the heritability of different types of coronary artery plaques in twins who underwent 256-slice CCTA. The authors discovered that non-calcified plaque volume was mainly influenced by shared environmental factors, while calcium score and calcified plaque volumes had a stronger genetic determination. These findings emphasize the importance of early lifestyle interventions in preventing high-risk plaque formation.

Vascular age is a concept to provide individuals with an estimate of their cardiovascular risk based on the health status of their blood vessels. It is typically expressed as an age that represents the condition of a person's coronaries in relation to their chronological age. In their study, *Vecsey-Nagy M and co-workers* compared different methods for assessing vascular age in 241 consecutive patients undergoing coronary CT (23). They found that vascular ages based on the Framingham Risk Score and the Systematic Coronary Risk Evaluation were significantly higher than those based on coronary calcium score derived from coronary CT. This study further supports the role of calcium scoring in the process of refining risk assessment.

Serial CCTA is increasingly used to monitor changes in coronary plaque burden in clinical trials. *Szilveszter B and colleagues* from the same institute evaluated how different clinical definitions of, specifically Segment Stenosis Score, Segment Involvement Score, and Coronary Artery Disease-Reporting and Data System, affect the identification of patients with CAD progression and the influence of risk factors on this progression (24). Based on the findings of this study the choice of CAD definition had a significant impact on which patients were considered to have progressed and which risk factors were associated with CAD progression, emphasizing the importance of standardizing CAD assessment methods for accurate monitoring and management.

Cardiac CT has an evolving role in the assessment of valvular diseases and interventions. *Apor A. and colleagues* from the Heart and Vascular Center of Semmelweis University studied the association between hypoattenuated leaflet thickening (HALT) and subclinical brain injury in 153 patients who underwent transcatheter aortic valve implantation (25). At 6 months, 9% of the patients had HALT on cardiac CT. New silent cerebral ischaemic lesions and white matter hyperintensities on brain magnetic resonance imaging were evident in 16% and 66% of the patients. New white matter hyperintensities were more frequent with higher volume among HALT-patients. In uni- and multivariate analysis, HALT was associated with new white matter hyperintensity volume. However, the presence of HALT did not carry an increased risk of cognitive decline or mortality over a 3.1-year follow-up.

## Cardiac magnetic resonance imaging

*Szabó L and colleagues* studied the cardiovascular consequences of SARS-CoV-2 infection in highly trained, otherwise healthy athletes using CMR imaging (N=147) (26). Overall, only seven patients (4.7%) of the athletes had alterations in their CMR as follows: late gadolinium enhancement showing a non-ischaemic pattern with or without T2 elevation (n=3), slightly elevated native T1 values with or without elevated T2 values without pathological late gadolinium enhancement (n=3) and pericardial involvement (n=1). Only two (1.4%) athletes presented with definite signs of myocarditis. Comparing athletes after SARS-CoV-2 infection and healthy sex and age-matched athletes showed no difference between CMR parameters. The authors concluded that in highly trained athletes after SARS-CoV-2 infection, cardiac involvement on CMR showed a modest frequency, with definite signs of myocarditis present in only 1.4%.

*Dohy Zs and colleagues* investigated the diagnostic role of CMR in the differentiation of cardiac amyloidosis from HCM and hypertension-associated LVH (27). In the study, 35 CA, 330 HCM patients and 70 patients with hypertension were involved. CA was characterized by diffuse subendocardial contrast enhancement and abnormal contrast kinetics. By strain analysis, lower global and basal LV longitudinal strain values were measured in patients with CA compared with patients with HCM and hypertension, and apical sparing in patients with CA was also detectable.

*Budai A and colleagues* conducted a study in the frame of a collaboration between Budapest University of Technology and Economics and Semmelweis University (28). They aimed to detect left LVH automatically on CMR examinations using a machine learning model. They included 428 patients with LVH (346 HCM, 45 CA, 11 *Anderson–Fabry disease,* 16 endomyocardial fibrosis, 10 aortic stenosis), and a control group consisted of 234 healthy subjects. The developed machine-learning-based model achieved a 92% F1 score and 97% recall on the hold-out dataset, which was comparable to the medical experts. Experiments showed that the standardization method was able to significantly boost the performance of the algorithm.

*Kiss AR and colleagues* evaluated the RV involvement in LVNC, enrolling 100 LVNC patients with preserved EF and 100 healthy controls (29). Patients had higher RV volumes, lower RV EF, and worse RV strain values than controls. A total of 22% of patients had RV hypertrabeculation, who had higher RV and LV volumes, lower RV- and LV EF, and worse RV strain values than patients with normal RV trabeculation. These results suggest that some patients with LVNC phenotype might have RV non-compaction with subclinical RV dysfunction and without more severe clinical features.

## Conclusion

Hungarian researchers participated in several valuable scientific papers in the field of cardiac imaging in 2022. The current review summarizes a total of 29 international publications with impact factors. The vast majority of the presented scientific works are based on cutting-edge imaging modalities of echocardiography, cardiac CT, and magnetic resonance imaging and evaluate clinically important problems in various cardiovascular patient populations. The important results of these studies help us to understand better the mechanisms and consequences of cardiac diseases allowing more accurate differentiation between cardiac pathologies and hence selecting more appropriate treatment modalities for the patients. Furthermore, the reported publications demonstrate the high activity and outstanding quality of the Hungarian imaging community which has already been recognised at international level.

### Declaration of interest

All authors declare no conflict of interest for this contribution.

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