ESC European Society of Cardiology

European Heart Journal - Cardiovascular Imaging (2023) **24**, 276–284
https://doi.org/10.1093/ehjci/jeac273

EACVI DOCUMENT

The year 2021 in the European Heart Journal: Cardiovascular Imaging Part II

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Received 16 December 2022; accepted 20 December 2022; online publish-ahead-of-print 31 January 2023

The European Heart Journal—Cardiovascular Imaging was launched in 2012 and has during these years become one of the leading multimodality cardiovascular imaging journals. The journal is currently ranked as Number 19 among all cardiovascular journals. It has an impressive impact factor of 9.130. The most important studies published in our Journal from 2021 will be highlighted in two reports. Part II will focus on valvular heart disease, heart failure, cardiomyopathies, and congenital heart disease, while Part I of the review has focused on studies about myocardial function and risk prediction, myocardial ischaemia, and emerging techniques in cardiovascular imaging.

European Heart Journal—Cardiovascular Imaging has successfully consolidated as a multimodality journal during its first 10 years. It has now an important role as a significant resource for cardiologists, specialists in all imaging modalities, and other physicians working in the field of cardiovascular imaging. It is currently ranked as Number 19 among all cardiovascular journals. It has an impressive impact factor of 9.130, and our journal is well established as one of the top cardiovascular journals. The tradition of highlighting the most important studies that were published in the last year is continued.[1,2] In two articles, we will summarize the most important papers from the Journal in 2021. Part I has just been published. Part II will focus on cardiomyopathies, congenital heart diseases, valvular heart diseases, and heart failure (HF).

Position papers and expert consensus documents from the European Association of Cardiovascular Imaging

One important assignment of European Heart Journal—Cardiovascular Imaging is to publish position papers and expert consensus papers from the European Association of Cardiovascular Imaging (EACVI). The journal published recommendations and expert consensus papers in the field of cardiac imaging and also the best research presented at our conferences in 2021. These papers are commented on in more detail elsewhere in the two documents.[3–9]

The EACVI-Scientific Initiatives Committee published four surveys in 2021 regarding the role of imaging in chronic coronary syndromes, for the detection of patent foramen ovale and cryptogenic stroke, to assess left ventricular (LV) diastolic dysfunction, and finally in cardio-oncology.[10–13] These surveys are indicative for the use of imaging in the community and illustrate some gaps in evidence between consensus papers or guidelines and the real life. They allow a critical appraisal of the EACVI educational programme and identify the unmet needs at the medical population level.

Cardiomyopathies

Tjahjadi C[14] estimated the left atrial (LA) electro-mechanical delay by tissue Doppler imaging (TDI) in 208 patients with hypertrophic cardiomyopathy (HCM) without atrial fibrillation (AF). PA-TDI duration—measured from the onset *P* wave on electrocardiogram to the peak A' wave of the lateral LA wall using TDI—was independently associated with new-onset AF (hazard ratio: 1.03, 95% confidence interval: 1.01–1.05, $P < 0.001$). This novel echocardiographic parameter could be useful to risk-stratify patients with HCM who are at risk of having AF.

Clemmensen TS *et al.*[15] reported that global LV myocardial work index and apical-to-basal segmental work ratio predicted all-cause mortality and major adverse cardiac events (MACE) in 100 patients with cardiac amyloidosis (CA). Conversely, LV global longitudinal strain (GLS) predicted only MACE but not all-cause mortality in this CA cohort. Brand *et al.*[16] demonstrated that LA phasic function by speckle-tracking echocardiography (STE) could be more useful than relative

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apical sparing pattern to discriminate CA from other causes of LV wall thickening. LA strain parameters were significantly altered in CA patients, and LA reservoir strain had a larger area under the curve (AUC 91, 95% confidence interval CI: 0.82–0.99) to discriminate CA than LV relative apical sparing (AUC 0.74, 95% CI: 0.59–0.88). This study supports the integration of LA strain analysis by STE into the routine echocardiographic assessment of patients with unclear LV hypertrophy, alongside with GLS assessment.

Hwang *et al.*[17] evaluated the time-serial change of cardiac function in 72 patients with AL CA undergoing active chemotherapy. They noted a significant decline in LV GLS and E/e' increase starting at 3–6 months after the first chemotherapy in the patients who experienced adverse events on follow-up. At multivariable analysis, BNP > 500 pg/mL, troponin I > 0.15 ng/dL, hospitalization for heart failure (HF), E/e' > 15, and GLS <10% during follow-up were independent predictors of outcome. This study highlights the importance of serial echocardiographic evaluation in AL CA patients on active chemotherapy to predict their prognosis.

Yakupoglu *et al.*[18] evaluated 30 patients with ongoing symptoms after a median of 15 months following an episode of Takotsubo syndrome (TTS). This is the first study aiming to evaluate exercise-induced changes in regional and global LV contractile function using exercise echocardiography in TTS patients and compare them with the imaging findings from controls with normal stress results. In TTS patients, there was an abnormal LV contractile response to exercise, with particularly marked reversible LV dysfunction in two-thirds of TTS patients who developed clear exercise-induced wall motion abnormalities (mainly involving the apex or more globally) with mean ΔLVEF of 1% compared with 12% in controls. This blunted contractile to exercise may be an expression of a continued abnormal response to increased sympathetic activity and contribute to the persistence of symptoms after the index TTS episode.

Pena *et al.*[19] reported the findings from standard and advanced echocardiography techniques applied in 30 patients with genetically proven PRKAG2 cardiomyopathy, being the largest study published to date on this rare form of genetic disease. The Authors reported a high prevalence of right ventricle (RV) hypertrophy (90%) and LV hypertrophy (86%, mostly concentric pattern) without LV outflow obstruction, associated with LV diastolic dysfunction (63%) and elevated filling pressures (30% of patients). A quarter of patients had an impaired LV ejection fraction (EF) by 3D echocardiography, and GLS was −16.4% ± −5.3% with a stripe-like strain pattern on bull's eye map in 60% of patients.

In ischaemic cardiomyopathy, invasive high-density electroanatomic mapping (EAM) can be used to identify LV scar, which is the electrophysiologic substrate for re-entrant ventricular tachycardia (VT). Trivedi SJ *et al.*[20] found a good correlation between low-voltage scar by EAM and multilayer strain, suggesting that scar burden may be potentially quantifiable using non-invasive STE analysis. Endocardial GLS −9.3% or worse had 93% sensitivity and 82% specificity for predicting endocardial bipolar scar >46% of LV surface area. This study provides data also on the potential utility of STE for quantifying scar location to facilitate VT mapping and ablation.

LV twisting and untwisting mechanics play a pivotal role for an efficient LV function. As several cardiomyopathies and HF with reduced EF were demonstrated to be associated with variable extents of LV twist and untwisting abnormalities, Sabatino *et al.* provided a useful practical guide with tips and pitfalls for the measurement of LV twist by STE.[21] Mizia-Steg *et al.*[22] evaluated the current real-life use of cardiovascular magnetic resonance (cMR) in 3208 consecutive patients with cardiomyopathies in the in the ESC EORP registry. They found that the use of cMR significantly differed in tertiary referral centres located among different European countries, and varied greatly between cardiomyopathy subtypes, and clinical profiles of patients, as it as was used less elderly and symptomatic patients and in patients with devices. This study highlighted an important gap between society recommendations and clinical practice which needs to be better understood to overcome limitations to access to imaging. Also it should be considered more deliberately in the drafting of practice guidelines.

A very important paper on HCM was published by Greulich *et al.*[23] who evaluated the prognostic value of late gadolinium cMR to predict 10 year sudden cardiac death risk relative to the ESC SCD risk score. They evaluated 220 consecutive patients with HCM undergoing cMR over a median FU of 10.4 years and found SCD rates of 2.3% at 5 years, 4.8% at 10 years, and 15.7% at 15 years, which could not be predicted by established risk factors and scores. By contrast An LGE amount of >5% LV mass portends the highest risk for SCD up to 15 years later. Conversely, patients with no or < _5% LGE of LV mass have favourable prognosis. This study underscores that cMR could meet the unmet need of further predictors to identify patients at high SCD risk who subsequently should be offered an ICD during the clinical course.

In dilated cardiomyopathy, late gadolinium enhancement by cMR is well-known prognostic parameter, which is postulated to be a substrate for arrhythmia. Chen *et al.*[24] evaluated the prognostic value of different patterns of LGE (no LGE, focal, multi-focal, and ring-like LGE) in 157 patients to predict compound VTAs, which was defined as a composite of sustained VT, VF, aborted SCD, SCD, and appropriate ICD and observed that no LGE and focal LGE pattern in patients with DCM were associated with a better prognosis with low risk of ventricular arrhythmias, whereas both ring-like and multi-focal LGE pattern are closely related with VTAs in DCM. This suggests that the identification of such high-risk LGE patterns may have a clinical significance and could potentially be used to guide ICD implantation.

In another elegant study, Antonopoulos[25] evaluated the diagnostic and prognostic value of cMR in 250 patients with eosinophilia. They reported prevalence of cMR findings suggestive of eosinophilic heart disease in 39% of patients. Such positivity of cMR for EHD as well as the presence of subendocardial LGE pattern were independently associated with the composite clinical endpoint of death, acute coronary syndrome, hospitalization for acute heart failure, malignant ventricular arrhythmias, or the need for implantable cardiac defibrillator/pacemaker.

Finally, Baritusso *et al.*[26] evaluated the ability of cMR LGE to explore the long-term outcome of myocardial scarring and deformation in 121 consecutive survivors of out of hospital ventricular fibrillation. They found that LGE was present in 71% of patients, mainly with an ischaemic pattern. Presence and mass of LGE was significantly with all-cause mortality and recurrent arrhythmic events, while LV EF and myocardial deformation did not identify patients with an unfavourable outcome and thus adding relevant information for prognostic screening.

Myocardial function

Large population registries are needed to evaluate changes of cardiac structure and function relative to genetic markers and exposure of various risk factors. Rasi-Estabagh[27] describes how the large UK biobank data which performed characterization of >500 000 subjects can be used for those purposes. Subsequently, Simon *et al.*[28] using the UK biobank showed that higher alcohol consumption was independently associated with a marginal increase in left and right ventricular volumes in men, but not in women, and with increased left atrium volume in women. In another population-based study, the generation R study, Toemen *et al.*[29] evaluated the association of pericardial adipose tissue by cMR with cardiac structures and cardiovascular risk factors. They observed that both in normal weight and obese children increased pericardial fat was associated with higher LV mass-to-volume ratio structures, high android adipose tissue, insulin concentrations, and an atherogenic lipid profile. Finally, Raisi-Estabagh[30] evaluated in a meta-analysis the variation in LV cMR normal reference ranges. They

found that LV volumes and mass were influenced by gender, age, and ethnicity. However, despite stratification by population-related factors, significant heterogeneity exists in reported values, resulting from variations in contouring methodology, magnet strength, and post-processing software. This calls for further standardization of image analysis and wider representation of different populations to better establish normal reference values.

Cardio-oncology is a very important growing field in cardiac imaging, as highlighted by the recent 2022 guidelines. Stankovitch *et al.*[10] reported on the EACVI survey of use of imaging in cardio-oncology in 104 centres and 35 different countries, however, revealing between guidelines recommendations and everyday clinical practice. Saunderson[31] provided a very comprehensive review of how multi-parametric cMR is able to assess cardiac structure, function, and provide myocardial tissue characterization, and hence can be used to address a variety of important clinical questions in the emerging field of cardio-oncology. Kondapalli *et al.*[32] describe a practical approach for diagnosis of myocarditis by such multiparametric cMR in patients under immune checkpoint inhibitor treatment. Uncertainty remains about the presence of fibrosis in anthracycline cardiotoxicity. Therefore, Modi *et al.*[33] used cMR to evaluate the frequency of LGE in 298 patients with exposed to anthracyclines or trastezumab relative to 100 age-matched cancer patients who did not receive those drugs. They found that only a majority of patients had LGE but in patterns and locations that did not fit into a single unique profile and with alternative explanations in virtually all cases. Finally, LGE was also present in cancer patients who received neither anthracyclines nor trastuzumab. This study showed thus that the absence of LGE indicating focal fibrosis can help distinguish anthracycline- and/or trastuzumab-related cardiomyopathy from unrelated cardiomyopathies. By contrast, Mawad *et al.*[34] using more advanced techniques mapping techniques in a cohort of 52 childhood cancer survivors exposed to anthracycline chemotherapy observed increased extracellular fraction indicating diffuse interstitial fibrosis and decreased LV mass, suggesting that myocyte loss could be part of anthracycline cardiotoxicity which was found to be accompanied by subtle changes in systolic and diastolic function. Also in cardio-oncology patients, serial follow-up of cardiac function is key. Therefore, Houard *et al.*[35] evaluated the test–retest reproducibility of left and right ventricular functional parameters by strain echocardiography vs. that of cMR. The study found that although cMR LVEF had the highest reproducibility, among echocardiographic parameters LVGLS and RVGLS were also very highly reproducible, with better test–retest reliability than other echocardiographic measurements of LV and RV function. They evaluated the ability of these parameters to detect differences in prospective trials and showed that LV and RVGLS allowed smaller calculated sample sizes, than traditional echocardiographic parameters supporting the use of STE-LV and RV-GLS for longitudinal follow-up of LV and RV function, particularly in cardio-oncology.

Several papers evaluated the myocardial changes due to inflammation in patients with COVID-19. Chen *et al.*[36] evaluated early inflammatory changes of patients with acute COVID infection and found significant differences in native T2, T1, and ECV, which are marker of myocardial oedema, as well as lower GLS than in controls, however, no late gadolinium enhancement suggesting irreversible myocardial injury. Similarly Theocharis[37] evaluated 20 children or young adults with multimodality imaging. By echocardiography, they demonstrated abnormal strain and Doppler indices and reduced EF, valvular regurgitation and pericardial effusion, by CT coronary dilatation, and by cMR myocardial oedema in half of patients while one had a subendocardial infarct.

Wu *et al.*[38] compared cmR parameters in 430 subjects according to HIV serostatus and found no difference in LV and RVEF, presence of LGE, however, observed larger extracellular volume indicating greater diffuse interstitial fibrosis. They also found that HIV-positive patients had larger left atrial volumes, resulting potentially from higher LV stiffness.

Heart failure

Results from the EACVI survey on the assessment of diastolic function included data from 93 worldwide centres in 27 countries (mainly from tertiary care European institutions.[11]

The survey showed that there is a widespread adoption of 2016 ASE/EACVI recommendations on the evaluation of LV diastolic function, including the performance of LV and LA strain analysis, and that this information is considered useful to guide patient management by three-quarters of the responders.

In a retrospective study including 311 patients with heart failure with preserved ejection fraction (HFpEF), Harada *et al.*[39] evaluated the prognostic value of tricuspid regurgitation (TR) severity over pulmonary hypertension and right heart remodelling. All-cause mortality or heart failure hospitalization occurred in 101 patients over a 2.1-year median follow-up.

The Authors observed that there was a continuous association between the semiquantitative measures of TR and the relative risk for the outcome, with a steeper increase in the outcome with a larger vena contracta width (VCW) and jet area. Notably, VCW remained independently and incrementally associated with the outcome after adjusting for established prognostic factors (age, gender, left atrial volume index, AF, mitral regurgitation severity, BNP, and the presence of cardiac implantable electronic device), as well as right ventricular diameter and pulmonary hypertension. Conversely, TR severity (absent, mild, moderate, and severe) as defined by the guideline-based qualitative approach did not remain significantly associated with outcome after adjusting for pulmonary pressures. This study highlighted the importance of TR quantification by VCW compared with multiparametric TR grading for the risk stratification in patients with HFpEF.

Another study by D'Andrea A *et al.*[40] evaluated prospectively 230 patients with HFpEF and compared them with 150 age- and sex-comparable healthy controls. HFpEF patients showed evidence of early subclinical LV myocardial damage in terms of lower resting values of LV GLS and myocardial work (MW) efficiency. During exercise, the HFpEF group showed an impaired LV systolic and diastolic reserve, along with a reduced exercise tolerance. MW efficiency at rest was correlated with functional measurements and pulmonary congestion during physical effort in HFpEF patients, suggesting a potential incremental value of performing a complete LV GLS and MW study at rest and during exercise echocardiography for guiding the management of these patients.

Schmeisser A *et al.*[41] compared the RV-PA coupling estimation by TAPSE/PASP ratio against invasive pressure-volume loop RV elastance/PA elastance (Ees/Ea) in 110 patients with HFrEF with and without pulmonary hypertension. They found that both TAPSE (cut-off <17 mm) and TAPSE/PASP (<0.38 mm/mmHg) were independent prognostic indices, and that the TAPSE/PASP ratio did not improve the coupling and prognostic information provided by TAPSE alone in PH due to HFrEF.

Wang C *et al*[42] conducted a retrospective study in 508 patients with HFrEF and reported that global myocardial work (GMW) may provide incremental prognostic information over LVEF and GLS analysis regarding the patient risk of all-cause death and hospitalization. Specifically, patients with GMW <750 mmHg% had a higher risk of adverse outcome than patients with GMW ≥750 mmHg%.

In the largest study to date on the prognostic value of peak left atrial strain (PALS) in acute HF by Park *et al.*[43], PALS showed significant prognostic value in hospitalized patients with acute HF, irrespective of HF phenotypes. Notably, this effect was independent of age, LA volume index, E/e', and LVEF. However, PALS failed to demonstrate prognostic value in the subgroup of patients with acute HF and AF.

In 1407 participants randomly recruited from the general population, Sabovčik F *et al.*[44] showed that the application of machine-learning classifiers combining routinely measured clinical, biochemical. and ECG

features showed a high accuracy to identify individuals with subclinical echocardiographic abnormalities holding prognostic implications, such as LV diastolic dysfunction and LV hypertrophy. Thus, machine learning may be used for selecting patients at risk of subclinical LV impairment who might benefit from a subsequent echocardiographic examination. Moreover, using supervised machine-learning model in 237 women with breast cancer receiving doxorubicine with or without trastuzumab, Demissei BG *et al*. reported that LV segmental strain analysis by STE had incremental value to predict cancer therapy-related cardiac dysfunction (CRTCD).[45] The addition of predictive LV segmental strain measures to a model including age, cancer therapy regimen, hypertension, and LVEF increased the area under the curve (AUC) from 0.70 to 0.87 for the prediction of CTRCD.

The use of nuclear cardiology has a great impact in the evaluation of patients with CA. Technetium-99m-labelled 3,3-diphosphono-1, 2-propanodicarboxylic acid (99mTc-DPD scintigraphy) is recognized as highly accurate for the non-invasive diagnosis of transthyretin (ATTR) CA. A proportion of patients with immunoglobulin light chain (AL) CA have also been reported to show cardiac 99mTc-DPD uptake. Quarta and coll.[46] assessed the frequency and degree of cardiac 99mTc-DPD uptake and its clinical significance among patients with AL CA. In this cohort of 292 patients with AL CA, 99mTc-DPD scintigraphy ~40% of cases showed cardiac uptake, including grade 2–3 in 10% of all patients (25% of those with cardiac 99mTc-DPD uptake). Cardiac 99mTc-DPD uptake was associated with poorer cardiac function and outcomes. These data highlight the critical importance of ruling out AL amyloidosis in all patients with cardiac 99mTc-DPD uptake to ensure such patients are not assumed to have ATTR CA.

Congenital heart disease

A position paper focusing on atrial septal defect (ASD), ventricular septal defect (VSD), and persistent arterial duct has been published on pre-, intra-, and post-procedural imaging techniques. This position paper offers algorithms for imagers to select the most appropriate imaging modality for detecting the requested information for each specific lesion.[3] A survey has been published that reveals interesting results about the adherence to guidelines in the diagnostic algorithm of patent foramen ovale and cryptogenic stroke regarding the use of transcranial colour Doppler, contrast-enhanced TTE and TOE from real-life experiences.[7]

Morphological and quantitative changes in pulmonary artery vasa vasorum (VV) in Fontan candidates after bidirectional Glenn and Fontan operations were examined by Hayabuchi *et al*.[47] The authors were able to demonstrate by multiplanar reconstruction of 3D rendered optical coherence tomography (OCT) images that the adventitial VV are present in patients with a Glenn bidirectional shunt but decreases following Fontan palliation.

Egbe *et al*.[48] showed that after coarctation of aorta (COA) intervention aortic isthmus ratio had the strongest correlation with LV remodelling, and residual COA as measured by aortic isthmus ratio also had a correlation with LV reverse remodelling. Aortic isthmus ratio is independent of loading conditions and can be obtained easily from non-invasive cross-sectional imaging. It remains to determine if timing of COA intervention and the assessment of adequacy of COA intervention based on aortic isthmus ratio will result in improved long-term survival.

Kroon *et al*.[49] defined a new method, echo density quantification method, to show pulmonary arteriovenous malformations with the use of contrast echocardiogram as a quick and easy tool. Quantification of pulmonary shunt by the change in echo density showed a reduction in number of needed chest CT scans without missing any treatable pulmonary arteriovenous malformations.

Finally, cardiac CT adds important variables in patients with congenital heart disease. Manuel and coll[50] evaluated retrospectively imaging exams database of one tertiary centre to search patients with Quadricuspid aortic valve (QAV). Aim of this study was to describe QAV prevalence, characterize the disease by multimodality imaging, evaluate predictors of severe AR, and assess mid-term prognosis. Multimodality imaging may play a pivotal role in assessing patients with QAV with significant valve dysfunction or associated congenital heart disease and improves their treatment strategy.

Valvular heart disease

Mitral valve

In a short review, a stepwise echocardiographic approach to mitral regurgitation has been published describing an integrative evaluation of mitral valve morphology and LV remodelling. This approach is practical for discriminating the underlying mechanism of mitral regurgitation as well as its severity.[51]

The study of Izumo *et al*.[52] stressed the expansion of indications for transcutaneous mitral valve repair (TMVR) by showing favourable results of TMVR in patients with exercise-induced secondary MR (increase in effective regurgitant orifice area (EROA) of ≥ 0.13 cm^2) as compared to those followed by medical therapy in a small sample having COAPT-like relationship between LV end-diastolic volume and EROA, during exercise.

Chivulescu *et al*.[53] assessed the association of mitral annular dysjunction (MAD) with aortic events and mitral valve surgery in patients with Marfan syndrome (MFS) and Loeys–Dietz syndrome (LDS). MAD was prevalent in 41% of the patients. MAD was a marker of severe disease including aortic events at younger age and need of mitral valve surgery. Screening patients with MFS an LDS for MAD may provide prognostic information and infer closer clinical follow-up from younger age (*Figure 1*).

On the other hand, Toh *et al*.[54] showed that MAD is frequent in structurally normal hearts occupying on average $39.0 \pm 18.2\%$ of the entire posterior mitral valvar attachment, by computerized tomography (CT). Median value of the maximal height of disjunction was 3.0 (1.5–7.0) mm. Disjunction location revealed characteristic double peaks, with frequent sites of the disjunction located at the anterior to antero-lateral and inferior to infero-septal regions. (*Figure 2*)

New data about the phenotypic spectrum of MVP syndrome came from the study of Moura-Ferreira *et al*.[55] The authors showed that apical papillary muscle (PM) insertion as part of the phenotypic spectrum of MVP (in 58% of their population) impacts significantly LV remodelling with significant focal thinning of the mid-lateral wall, higher prevalence of mid-LV eccentricity, reduced mid-LV GCS, and increased lateral wall angulation in end-diastole. Prevalence of PM fibrosis and ventricular tachyarrhythmias were markedly higher in patients with apical PM insertion. In addition, apical PM insertion was associated with a trend towards higher prevalence of MAD.

Uno *et al*.[56] investigated geometric differences in mitral valve apparatus between atrial (AFMR) and ventricular functional mitral regurgitation (VFMR) in patients with AF using 3D TOE. The size of the annulus was similar between the two forms of FMR. They showed that the degree of leaflet coaptation (= total leaflet area in end-diastole—closed leaflet area in mid systole) and MR severity were similar in both groups despite different mechanisms: Leaflet remodelling (total leaflet area/annulus area) and tethering were more extensive in VFMR as compared to AFMR that showed lesser degree of leaflet adaptation (remodelling).

Landi at *et al*.[57] published an important review where they discussed in depth secondary and 'tertiary MR' notions. The term 'tertiary' MR identifies a subtype of functional MR which is too severe to be considered a strict consequence of LV remodelling, but instead, a subtype that actively contributes to ultimate LV dysfunction. Hence MITRA-FR as representing 'secondary' MR, and COAPT as representing 'tertiary' (disproportionate) MR. Echocardiography (2D, 3D) and CMR are also discussed for an integrated appraisal of LV volumes, regurgitation

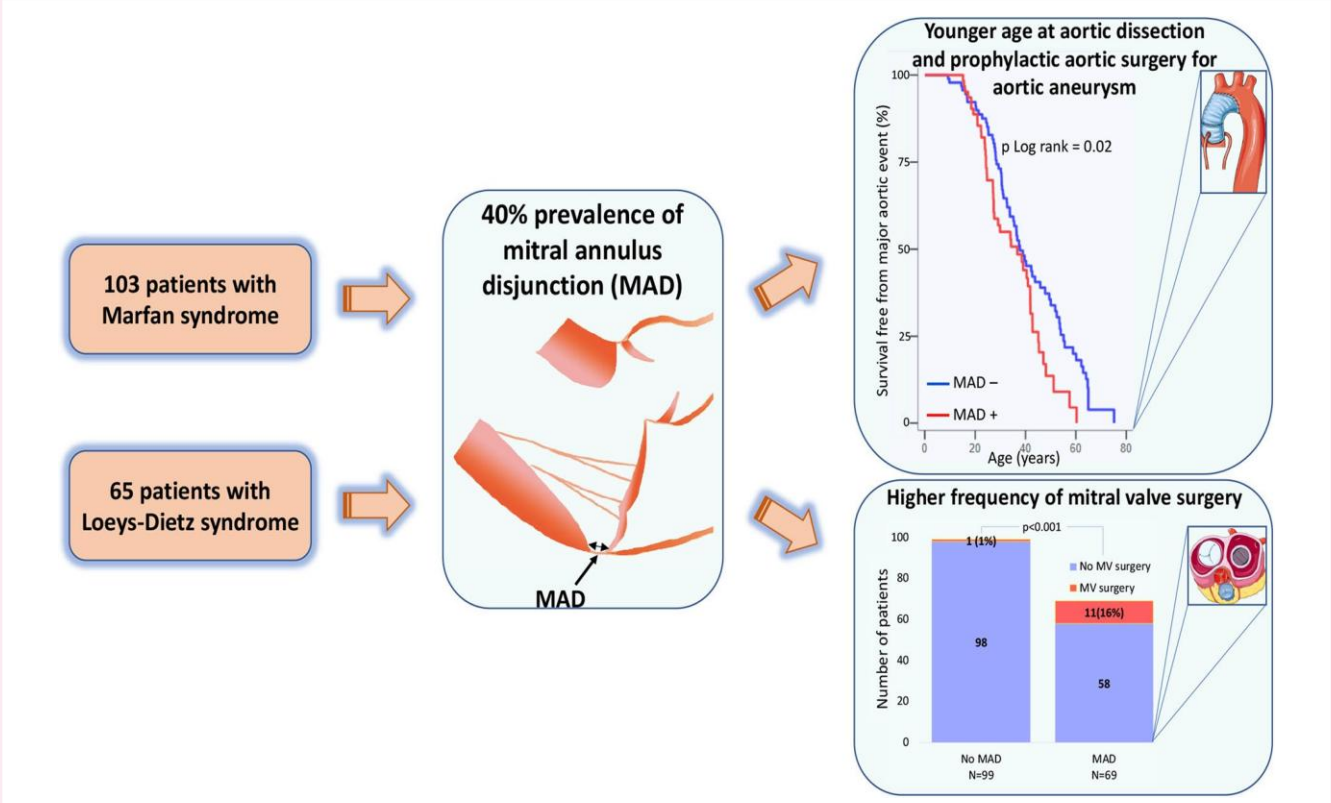

Figure 1 Mitral annulus disjunction (MAD) in Marfan and Loeys–Dietz syndromes. Note that patients with MAD had more frequent aortic dissection or prophylactic aortic surgery, and more frequent mitral valve surgery. Patients with MAD were younger at aortic event than those without MAD.

severity, and MV leaflet morphology findings in the context of this novel concept.

Tricuspid valve

Vieitez *et al.*[58] showed that the prevalence of significant TR was 6% in a prospective multicentre registry including 35 099 echocardiograms from consecutive patients. From these, 92.6% were secondary, mostly in the setting of mitral and aortic valve diseases. More importantly, >50% of patients with severe, massive, and torrential TR were at high surgical risk with NYHA class III–IV symptoms, LVEF <35%, age > 85 years, and sPAP > 50 mmHg with more severe consequences on the RV and atrium. These findings implicate careful monitoring of patients with TR to optimize treatment.

Muraru *et al.*[59] studied threshold values of the quantitative parameters for functional TR severity in relation to outcome. Lower than previously thought thresholds (VC > 6 mm, EROA > 0.30 cm^2, RegVol > 30 mL, and RegF > 45%) were found associated with dismal prognosis.

Harada *et al.*[60] showed another important finding about the quantification of TR severity. They found a continuous association between VC width and adverse outcomes independently and incrementally over the established prognostic markers such as age, sex, left atrial volume index, AF, mitral regurgitation severity, BNP, and the presence of implantable devices, right ventricular (RV) remodelling and pulmonary hypertension emphasizing the value of VC width as a potential therapeutic target.

Regarding the pathophysiology of secondary TR, Muraru *et al.*[61] showed that right atrial enlargement is an important mechanism of tricuspid annular dilation irrespective of cardiac rhythm and RV loading conditions in patients with left heart disease, pulmonary hypertension, corrected tetralogy of Fallot, and chronic AF raising awareness about the crucial role of RA volume as a determinant of FTR

A step-by-step guide for periprocedural imaging by TOE for transcatheter edge-to-edge repair of tricuspid valve has been published.[62] This paper was complemented by another 'how to' paper on improving navigation during cardioband transcatheter tricuspid annuloplasty underlining the use of fusion imaging of live fluoroscopy and preprocedural computerized tomography for optimizing the navigation.[63]

A position paper by EACVI on the structural heart disease interventional imager rationale, skills, and training has also been published to provide the standard requirements for the training in SHD imaging, as well as a starting point for an official certification process for SHD interventional imager.[8]

Ancona F *et al.*[64] showed prognostic relevance of RV-free wall strain in severe TR. Approximately 50% of patients deemed to have normal RV systolic function by conventional parameters were reclassified into RV failure group with an RV-free wall strain cut-off of −17%. RV-free wall strain predicted also mortality (cut-off −14%) independently of conventional markers including TAPSE, S' fractional area change. This study underpined the limitation of conventional parameters that pseudo-normalize in patients with severe TR.

Chen *et al.*[65] evaluated the outcome from natural progression of functional TR in function of cardiac output (CO) in patients with LV EF ≥40% over 1-year follow-up. Mortality rate was higher in low- and high-CO groups compared to patients with normal CO, emphasizing the importance of integrating the CO when monitoring patients with severe functional TR. The authors speculated on lower arterial afterload and higher metabolic demand to explain the detrimental effect of high CO. These findings question the integration of CO in the phenotyping of TR.

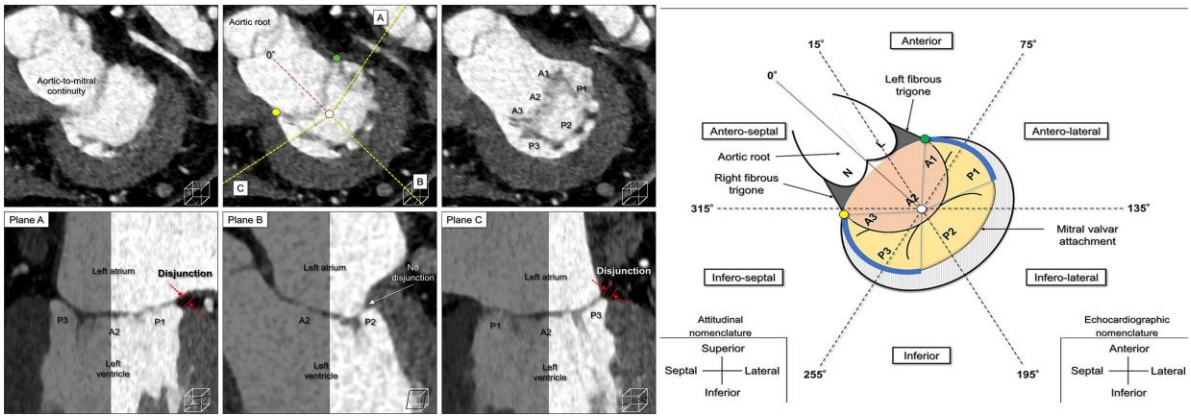

Figure 2 Left panel: the quantification of dysjunction hight by CT. Right panel: Blue curves suggest representative locations of the bilateral disjunction. Green and yellow circles denote supero-lateral and infero-medial commissures, respectively. Ninety-four of 98 cases (96%) have disjunction.

Aortic valve

The design of the multicentre ROTAS (randomized study for the optimal treatment of symptomatic patients with low-gradient severe aortic stenosis (AS) and preserved LVEF)) study has been published. The study will test the superiority of aortic valve replacement over 'watchful waiting strategy' in terms of all-cause mortality or cardiovascular hospitalization during 2-year follow-up.[66]

Two studies looked into details of AS pathophysiology and questioned the aortic valve calcium (AVC) score as a standalone parameter of AS. Linde *et al.*[67] examined explanted valves from patients with severe AS undergoing aortic valve replacement and demonstrated that AVC score derived from cardiac CT correlates modestly with valve calcium concentration and females present lower valvular calcium concentrations than males irrespective of AS severity. Grodecki *et al.*[68] evaluated aortic valve tissue volume and composition by quantitative CTA which is currently used for plaque characterization without the need for an additional non-contrast study. Interestingly, total tissue volume was the best predictor of severe AS followed by non-calcified tissue volume. Predictive value of AVC score for severe AS improved after the addition of non-calcific tissue volume. Higher non-calcific tissue indices were found in patients with LFLGAS compared to HG-AS. The addition of non-calcific tissue to AVC score improved the differentiation between HG and LFLG AS and the prediction of 30-day MACEs post-TAVI.

Einersen *et al.*[69] showed the graded relationship between increasing AS severity and decreasing first-phase EF (LVEF1). LVEF1 was modestly reduced in moderate AS but significantly in severe AS. Lower LVEF1 was associated with lower GLS rate and higher pulse pressure/SVi (a measure of arterial stiffness), independently of AS severity. This suggests that LVEF1 may be used as a global parameter reflecting the haemodynamic burden (i.e. both valvular and arterial) on LV myocardial function. This may be helpful for the management of patients with AS since evidence in favour of early intervention in the absence of symptoms or impaired LVEF is growing.

Saeed *et al.*[70] explored sex differences in the determinants of flow rate in patients with symptomatic severe AS. Transaortic flow rate (FR = stroke volume/LV ejection time) is considered a better index of AS severity in discordant AS, independent of EF and safe from overcorrection with BSA in contrast to SV and AVA. They found that lower FR was associated with increased risk of all-cause mortality, after adjustment for important prognostic markers in men and women with different cut-offs (179 mL/s in women and 209 mL/s in men).

An interesting and practical study)[71] was published by a Vulesevic et al showing that AVA indexed to height better correlates with absolute AVA than AVA indexed to BSA. An AVA/H cut-off value of 0.6 cm^2/m provided a better agreement than an AVA/BSA cut-off value of 0.6 cm^2/m^2 for the diagnosis of severe AS (AVA < 1 cm^2) and a better predictive accuracy for the occurrence of AS-related events.

Cardiac CT can be used to implement the risk stratification of patients with a different kind of disease, also. In fact, the presence of aortic valve calcification (AVC) was investigated by Han and coll[72] to evaluate its impact on cardiovascular disease risk. Although the overall prognostic significance of AVC was attenuated after accounting for coronary artery calcification, high AVC was independently associated with all-cause and CVD deaths in patients with low coronary atherosclerosis burden.

Moreover, Williams and Coll[73] assessed aortic and mitral valve calcification in patients presenting with stable chest pain and their association with cardiovascular risk factors, coronary artery disease, and cardiovascular outcomes. In these 1796 enrolled patients, aortic and mitral valve calcification occurs in one in six patients with stable chest pain undergoing CCTA and is associated with concomitant coronary atherosclerosis. While valvular calcification is associated with a higher risk of cardiovascular events, this was not independent of the burden of coronary artery disease.

Valve prostheses

Koschutnik *et al.*[74] studied right ventricular (RV) dysfunction by echocardiography and CMR to predict outcomes after TAVR. RV fractional area change (FAC), tricuspid annular plane systolic excursion, RV-free lateral wall tissue Doppler (S'), and strain were assessed on echocardiography, and RVEF on CMR. After adjustment for the EuroSCORE-II and NT-proBNP levels, only RV EF on CMR but not RV dysfunction by echocardiographic parameters emerged as strong and independent predictor of outcome.

Ternacle *et al.*[75] compared predicted and measured effective orifice area index (EOAi) in a large population ($n = 1088$) following transcutaneous aortic valve replacement (TAVR). The study draws attention to a large proportion of TAVR patients who are in low-flow state and presenting a pseudo-patient prosthesis mismatch (PPM) by measured EOAi. True severe PPM defined by the predicted EOAi was very rare following TAVR. The utilization of the predicted EOAi reclassified the majority of patients with PPM to no PPM following TAVR. Compared with measured PPM, predicted PPM had stronger

association with haemodynamic outcomes, while both methods were not associated with clinical outcomes.

Jain *et al.*[76] evaluated 35 patients with severe AS who underwent TAVR and showed that non-invasive assessment of MW can be reliably performed in AS by the addition of mean aortic gradient to non-invasive systolic blood pressure. They showed that GLS improves while myocardial work reduces post-TAVR.

Kim *et al.*[77] sought to determine mechanisms of paravalvular leak in bicuspid (BAV) and tricuspid aortic valve (TAV) in 2394 consecutive patients (242 cases with BAV). They analysed the aortic root anatomy, calcification, circumferential distribution of calcium, and predilection sites of PVL using pre-procedural multidetector CT and post-TAVR echocardiography. They found that BAV anatomy was associated with more eccentric calcium distribution and more procedural challenges including longer procedure and fluoroscopy times, higher amounts of contrast agent, and more frequent device malpositioning when compared with TAV patients. However, the incidence, spatial distribution, predilection sites, and predictors of PVL were similar between BAV and TAV patients, matched for baseline characteristics and AVC density.

Winter *et al.*[78] studied the evolution of concomitant secondary atrioventricular regurgitations and their impact on long-term prognosis after TAVR in a prospective large cohort. They demonstrated that in up to 50% of patients, atrioventricular regurgitation regress after TAVR translating into favourable outcome. By contrast, persistence of atrioventricular regurgitation inferred an excess mortality risk and therefore proposes a window of early staged reintervention of the concomitant valvular lesions.

Issa *et al.*[79] investigated the effect of structural degeneration of surgical bioprosthetic aortic valves on ventricular remodelling. Eighty-two out of 451 patients developed moderate to severe degeneration over a median period of 5.1 years. Structural degeneration was associated with adverse LV remodelling, reduction in LV function during follow-up, increased risk of death or reoperation, and hospitalization for heart failure.

In terms of short-term follow-up, CCT was used to evaluate the predictive value of extracellular volume fraction (ECV) for LVEF recovery in patients with AS after transcatheter aortic valve replacement (TAVR).[59] According to the showed results, increased myocardial ECV on CCT is associated with impaired LVEF recovery post-TAVR in severe AS patients with impaired LV systolic function. These results indicated the use of different imaging variables obtained bt CCT for risk stratification and outcome evaluation in patients with valvular heart disease.

In fact, CCT can be used to evaluate paravalvular leakage (PVL) after TAVR, that is a common complication in patients with bicuspid aortic valve (BAV). Kim *et al.* selected from a series of 2394 patients undergoing transfemoral TAVR, 242 cases with BAV.[80] According to the CCT results, the incidence, circumferential distribution, predilection sites, and predictors of PVL were similar in matched population of BAV and tricuspid aortic valve patients undergoing transfemoral TAVR using new-generation devices. These novel findings suggest a common underlying mechanism of PVL in both entities.

Funding

None declared

Conflict of interest: None of the authors have conflict of interest to declare

Data availability

No new data were generated or analysed in support of this research.

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