Imaging of the right ventricle (RV) has gained popularity. Terms such as “the forgotten ventricle” or “difficulties in assessing RV function attributed to its shape” are frequently used as opening statements in new research. Two things make the RV challenging to assess by any imaging modality: the thin wall and the overall asymmetric shape in the form of a crescent shell covering part of the left ventricle. The RV has also an anatomically distinct inflow and outflow that are placed in different planes.

What is important in diagnostic imaging is the ability to link patterns or numbers to clinical outcomes. While “a pretty picture is worth a thousand words” holds true, the 5 general rules for a diagnostic test to be clinically useful are: to be feasible for most patients, to be noninvasive (including absence of ionizing radiation), to be consistent between and within observers, to be cost-effective, and to be linked to clinical outcomes. Cardiac magnetic resonance (CMR) generally fulfills most of those criteria and is probably cost-effective in the assessment of RV function, for this it is widely perceived as the reference method.

RV ejection fraction provides substantial functional and prognostic information (1,2). This, until recently, could only be determined by CMR or radionuclide angiography with some accuracy. Two-dimensional echocardiography cannot assess RV ejection fraction and instead, several other surrogate parameters have been advocated (3). Recently, a joint effort between the American Society of Echocardiography (ASE) and the European Association of Echocardiography (EAE) published guidelines for the echocardiographic assessment of the right heart in adults (4). These do not include ejection fraction but rather a number of linear parameters, the most popular being the longitudinal motion by M-mode of the tricuspid annular excursion (TAPSE). TAPSE is easily obtainable and is a measure of RV longitudinal function. Although it only measures tricuspid annular excursion and therefore the RV inflow track alone, it has shown good correlation with radionuclide-derived RV ejection fraction (5) and is recommended by the joint ASE/EAE guidelines for routine use (4). The main disadvantage, however, is that TAPSE assumes that the displacement of a single segment (tricuspid annulus) represents the overall function of a complex structure, and there are no large-scale validation studies for this.

It is only with the recent development of 3-dimensional (3D) echocardiography that attempts to estimate RV ejection fraction by echocardiography have re-emerged. As expected, all comparisons have been made against CMR (6–9), and normal reference values have been published (10). The use of 3D echocardiography for valve disease and also for the assessment of left and right ventricular function is rapidly gaining acceptance, and guidelines have been reported (11). In expert hands, 3D has become a credible alternative to CMR for assessing RV volumes albeit with some negative bias as indeed for the left ventricular volumes calculations.

But is assessing RV volumes what we should be doing in functional RV assessment? Until now we had nothing else. There is no doubt that ejection fraction is the best we can do today, and it is linked to outcomes. Ventricular volume calculations are notoriously bad and are load dependent. Reproducibility varies among imaging techniques from 10% to 20% (and possibly more). Volume calculations have been used because they are easily derived and there has been little or no alternative. But there is more to phenotyping heart disease, as CMR has shown, that may be prognostically but also therapeutically more exciting, namely, the detection and quantification of myocardial fibrosis (12).

Myocardial fibrosis leads to impaired cardiac diastolic and systolic function and is related to adverse

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cardiovascular events (13,14). Most of the studies, however, are single-center and suffer from referral bias. In the recent European Guidelines for Patients With Hypertrophic Cardiomyopathy, CMR with late gadolinium enhancement is a class IIa level B category for the assessment of cardiac anatomy and ventricular function and for the detection of myocardial fibrosis (15).

Myocardial strain calculation is a relatively novel way to assess ventricular function. It provides angle-independent assessment of regional myocardial deformation and does not rely on geometric assumptions (16). Longitudinal strain can quantify systolic function, allows for the evaluation of regional and global deformation properties of the myocardium, and may be a more sensitive method to identify subclinical left ventricular dysfunction (17). An important study by Urbano-Moral et al. (18) showed an association between myocardial fibrosis detected by CMR and regional effect on myocardial function. Myocardial segments with hypertrophy and fibrosis had the most impaired regional function by all deformation parameters.

More recently, studies using myocardial strain of the RV have shown that RV systolic strain is a powerful predictor of clinical outcome of patients with known or suspected pulmonary hypertension (19,20). This is potentially a breakthrough method considering the thin-walled RV, which could be challenging to assess with any imaging modality. More recently, we used 3D strain in patients with pulmonary arterial hypertension and found that reduced area strain (AS), longitudinal strain, and circumferential strain were all associated with increased mortality risk (21). The new measurement of AS had strong associations with RV ejection fraction, whereas only AS was an independent predictor of death on multivariable analysis, suggesting the superiority of 3D-derived AS over other variables. Normal values for RV strain have also been published (22), thus moving a step closer to establishing strain as a valuable alternative to RV assessment.

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In this issue of iJACC, Lisi et al. (23) provide new information regarding the correlation between myocardial strain as assessed by echocardiography and myocardial fibrosis quantified histologically. This is a significant study because until now most correlations were made against surrogate techniques for myocardial fibrosis, such as late gadolinium enhancement using CMR. The authors examined 27 patients with end-stage heart failure undergoing cardiac transplantation and looked at histology for RV free wall fibrosis, comparing the findings with 2-dimensional fibrosis by speckle tracking echocardiography. The unique advantage of this study is that the authors could look at tissue samples of the RV free wall obtained from explanted hearts. Histology was performed from 3 full-thickness slices of the RV at basal, mid-, and apical levels. Fibrosis was calculated as an average of the 3 slices.

All patients were studied as part of their transplantation work-up including electrocardiography, cardiopulmonary exercise testing, and NT-pro-BNP assays. A comprehensive echocardiographic assessment included a number of standard parameters as recommended by the ASE/EAE guidelines, including TAPSE, RV sphericity, right atrial (RA) function, as well as RA longitudinal stain. Seventeen (63%) patients had severe RV myocardial fibrosis defined as >50% of myocardium. Not surprisingly, all echocardiographic parameters were also reduced. The major finding of this study, however, was that RV fibrosis clearly correlated with free wall longitudinal strain and oxygen consumption (VO₂) max, but poorly correlated with TAPSE and RA longitudinal strain. RV free wall longitudinal strain was the main determinant of myocardial fibrosis and predicted the limited exercise tolerance. Because of the nature of the study, they were unable to ascertain the relationship between alterations of RV free wall longitudinal strain and disease progression from subclinical disease to severe RV dysfunction.

The study has also a number of limitations. The etiology of RV dysfunction and fibrosis was secondary to left heart disease of variable etiologies (mostly ischemic [59%]), idiopathic cardiomyopathy (37%), and 1 hypertrophic cardiomyopathy so that most if not all would have had secondary (post-capillary) pulmonary hypertension. These left heart conditions are also responsible for myocardial fibrosis of the left ventricle and therefore relating with other patients’ clinical data may not be valid. The echo analysis was performed by excluding the ventricular septum, which is a good thing as its inclusion would have diluted their data because it would contain left heart abnormalities. The authors studied patients with end-stage heart failure with marked RV enlargement. In other words, they studied the worst of the worst scenarios, and it is not possible to extrapolate to patients with less severe heart failure or patients with precapillary pulmonary hypertension. Finally, they do not provide any information about cardiac arrhythmias. Studies, particularly in cardiomyopathy patients, have shown an association between fibrosis (assessed by CMR)
and arrhythmia. It would have been of interest for the authors to show us the extent of fibrosis by disease, but the number of patients would have been limited.

So, is assessing RV fibrosis the holy grail of RV imaging? These data do not provide sufficient support, but it is clearly a step forward to encourage further prospective studies looking at the predictive value of advancing fibrosis on RV strain in patients with pulmonary hypertension.

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