The Essential Role of Imaging in the Evaluation of Patients With Pulmonary Arterial Hypertension in Association With Congenital Heart Disease

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Pulmonary arterial hypertension (PAH) is a hemodynamic and pathophysiologic condition defined as an increase in mean pulmonary artery pressure (MPAP) of ≥25 mm Hg at rest measured at right heart catheterization (RHC).[1,2] Patients with PAH associated with congenital heart disease (PAH-CHD) are a growing population consisting of an anatomically and phenotypically heterogeneous group, where differences among specific cardiac defects, along with their varied clinical course and prognosis, influence treatment choices for the individual patient.

CLASSIFICATION OF PAH-CHD

The heterogeneity of cardiac morphology and its functional consequences require a customized classification, including a detailed description of cardiac morphology, previous surgical and/or catheter intervention/s, and current functional and hemodynamic status of the patient.

LEFT TO RIGHT SHUNTS

Left to right shunts are the most common substrate for PAH-CHD, accounting for approximately 38% of patients with CHD and pulmonary hypertension (PH) in a recent report from Canada.[3] This group includes patients with Eisenmenger syndrome, where the development of PAH occurs in the presence of a nonrestrictive left to right shunt—intracardiac (usually post-tricuspid) or extracardiac. In about 50%-70% of cases, patients develop irreversible and progressive pulmonary vascular disease in the first few years of life, resulting eventually in reversal of blood flow through the shunt and cyanosis.[4] Examples of these lesions are large ventricular septal defects (VSD), patent ductus arteriosus (PDA), complete atrioventricular septal defects (AVSD), truncus arteriosus, or functionally univentricular hearts without pulmonary stenosis. In cardiac lesions with a left to right shunt at the pre-tricuspid level, ie, patients with large atrial septal defects (ASD) with initial volume and not pressure overload, the development of pulmonary vascular disease is less frequent and later in life. Only one-tenth to one-fifth of patients with a hemodynamically important and large interatrial communication will eventually develop pulmonary vascular disease, mostly in late adulthood.

FONTAN CIRCULATION

Pulmonary arterial hypertension can also complicate other subgroups of CHD, both in their natural history and after surgical repair; such an example of the unique features of the pulmonary circulation in CHD is represented by the Fontan "circulation," where systemic venous return is directed to the lungs without an interposed ventricular pump (Figure 1). At first glance, it may appear to be out of line with the classical definition of PAH (increased pulmonary vascular resistance [PVR] of greater than 3 Wood units per meter squared or MPAP of more than 25 mm Hg). However, there is evidence of an abnormal pulmonary vascular bed in these patients, as suggested by an abnormal response to exogenous nitric oxide administration.[5] We submit, herewith, that patients with the Fontan circulation should be considered in the PAH-CHD group, as even a minimal increase in PVR can have a major adverse effect on the pulmonary circulation and thus cardiac output given the absence of a subpulmonary ventricle. Based on these considerations, a more refined classification of PAH that coexists with CHD has been proposed to better address this rather heterogeneous patient group that cannot be assumed to be similar in terms of pathophysiology and hemodynamics (Table 1).[6]

ROLE OF IMAGING

Multimodality imaging plays a key role in assessing and managing patients with PAH-CHD. It is important to recognize the strengths/weaknesses and the complementary nature of different imaging modalities as well as the complex nature of the diagnostic questions that need to be addressed.

In this review, we will focus on the imaging tools commonly employed to evaluate PAH in CHD patients and their relative contribution to diagnostic assessment, evaluation of the functional and hemodynamic impairment, and longer-term prognostication.

ECHOCARDIOGRAPHY

Transthoracic echocardiography (TTE) is the first-line cardiovascular imaging modality in the assessment of patients with various types of PAH because it is easy to apply, relatively inexpensive, and provides accurate information on cardiac anatomy and physiology.

In the setting of PAH-CHD, TTE is particularly suitable for the real-time interrogation of structural abnormalities as well as hemodynamic disturbances. In the majority of these patients, TTE allows the evaluation of cardiac anatomy (ie, orientation and veno-atrial, atrioventricular, and ventriculo-arterial connections), the morphology of cardiac structures, ventric-

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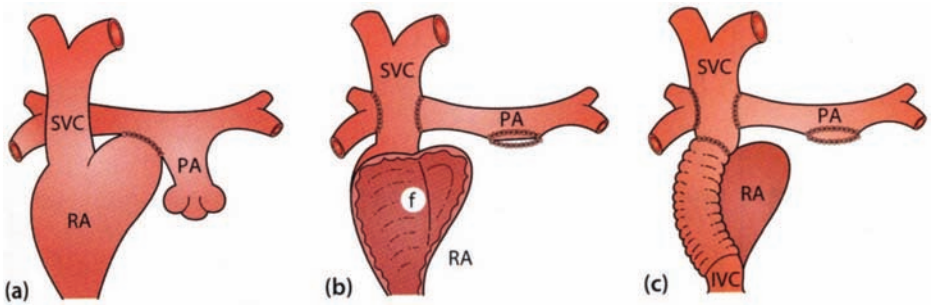


Figure 1: The Fontan operation and its various modifications. (a) Classic Fontan operation. (b) Lateral tunnel with fenestration, (c) extracardiac Fontan. f, fenestration; IVC, inferior vena cava; PA, pulmonary artery; RA, right atrium; SVC, superior vena cava. (Reprint from Gatzoulis MA, Webb GD, Daubeney PEF. *Diagnosis and Management of Adult Congenital Heart Disease*. Oxford, UK: Churchill-Livingstone. 2003; page 85.).

ular and valvular function, the presence of shunt lesions, and hemodynamic assessment (eg, severity of valvular regurgitation and evaluation of shunts and velocities across obstructive lesions).[7]

In addition, in the context of PAH-CHD, TTE is especially helpful in providing information on the following aspects:

- Pulmonary artery pressure
- Right ventricular (RV) involvement
- Prognostication/outcome

Pulmonary Artery Pressure

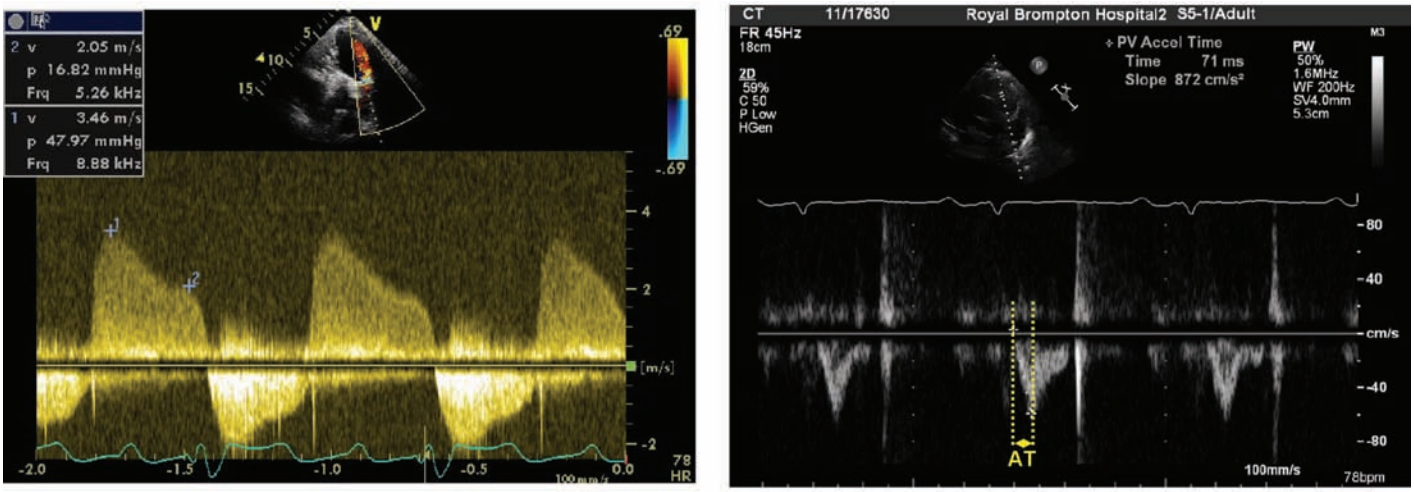
Pulmonary artery systolic pressure. Pulmonary artery systolic pressure (PASP) can be estimated using tricuspid regurgitation (TR) velocity (V) by applying the Bernoulli equation [PASP = $4V^2$ + estimated right atrial (RA) pressure, where V is the average peak TR velocity]. In patients with CHD, PASP can also be calculated using maximum flow velocity across a VSD or an aortopulmonary shunt (PDA, Blalock-Taussig shunt) (PASP = systolic blood pressure – $4V^2$).[8-9]

A few aspects must be kept in mind to ensure accurate estimates of PASP.

- Although PASP measured by echocardiography correlates relatively well with PASP measured invasively, Bland-Altman analysis in the clinical setting demonstrates that large (10-20 mm Hg) differences between invasive and non-invasive PASP are common. The most common causes of inaccurate estimation of PASP include an incomplete Doppler envelope, resulting in underestimation of pressure or an overestimate of RA pressure from inferior vena cava diameter and collapsibility.[10]

Table 1: Proposed classification of PAH in the setting of congenitally malformed hearts as based on circulatory pathophysiology (modified from [6]). Abbreviations: ASD, interatrial communication; AVSD, atrioventricular septal defect; (i)PAH, (idiopathic) pulmonary arterial hypertension; PVR, pulmonary vascular resistance; PDA, patent arterial duct; POF, patent oval foramen; PVH, pulmonary venous hypertension; VSD, ventricular septal defect

Significant shunting lesions	iPAH-like lesions	PAH due to past or present PVH	Eisenmenger physiology	Fontan-like physiology	Unilateral PAH	Hypoplastic PA system
a) For corrective surgery, PVR is low and presents no problem b) For corrective surgery, PVR elevated, risk increased but accepted c) For corrective surgery, PVR elevated, risk too high, not operable	a) Small unoperated lesion (eg, POF, ASD, VSD, PAD) not hemodynamically related to PAH b) Small residue after corrective surgery of a shunting lesion, not hemodynamically related to PAH	a) After corrective surgery of pulmonary venous stenosis or aortic/mitral valvar disease or coarctation, with normal wedge pressure and left ventricular function b) PAH due to left ventricular dysfunction with abnormal wedge pressure and increased PVR	a) Classical Eisenmenger physiology: no subpulmonary outflow obstruction; predominantly right to left shunting at atrial, ventricular, or arterial level, no intraventricular mixing b) Functionally univentricular physiology: no sub-pulmonary outflow obstruction; systemic desaturation is due to intraventricular mixing	a) After Fontan operation with the right atrium being incorporate b) Fontan with a lateral or extracardiac conduit, right atrium excluded, no fenestration c) Anatomy as above d) With fenestration	a) Due to a surgical shunt previously created to increase pulmonary blood flow, which has led to significant PAH on that side b) Due to congenital origin of one pulmonary artery or of major collateral vessels from the aorta, causing PAH	a) After corrective surgery of tetralogy of Fallot without major anatomical obstructions of the pulmonary vascular system, and PAH b) After corrective surgery of pulmonary atresia without major anatomical obstructions of the pulmonary vascular system, and PAH



a b

Figure 2: (a) Estimation of mean and diastolic pulmonary artery pressure by continuous-wave Doppler signal of pulmonary regurgitation (PR). Point 1 indicates maximal early diastolic PR velocity, which can be used to calculate MPAP. Point 2 marks end-diastole PR velocity used to calculate end-diastolic pulmonary artery pressure. (b) Measurement of pulmonary AT from the pulsed-wave Doppler signal of pulmonary arterial flow.

- The right ventricular systolic pressure (RVSP) calculated from TR velocity may only be taken as the PASP in the absence of RV outflow obstruction. In CHD, more care should be taken to exclude any obstruction along the pulmonary pathway, especially after pulmonic valve surgery or in patients with previous systemic to pulmonary shunts. In some cases, peripheral or segmental pulmonary stenosis may also be present; this will require complementary imaging such as cardiovascular MRI to delineate.
- Velocity measurements are angle dependent. Tricuspid regurgitant jets should be taken from multiple acoustic windows (apical 4-chamber views, RV inflow, and off axis if necessary) with accurate transducer angulation in order to obtain a parallel intercept angle between the ultrasound beam and jet to avoid underestimation. In some cases of trivial regurgitant jet and suboptimal continuous-wave Doppler spectrum, the injection of contrast agents (agitated saline, sonicated albumin, or air-blood-saline mixture) may be required to achieve clear delineation of the jet envelope.[11]
- Close relationship between PASP and RV cardiac output exists. In cases of "end-stage" PAH, where both advanced RV dysfunction and increased PVR cause a significant reduction in stroke volume, PASP may appear "pseudonormalized" as a consequence of the low driving pressure generated by the failing RV.[12] Underestimation of RV pressure may also occur with the development of diastolic RV dysfunction, characterized by high RA pressure and a stiff RV.
- Furthermore, in cases of severe TR the peak velocity may underestimate the trans-tricuspid pressure gradient because of early equalization of pressure between RA and RV, leading to truncation of the Doppler envelope.[12]

Pulmonary artery mean and end-diastolic pressure. Mean pulmonary artery pressure and pulmonary end-diastolic pressure (PADP) are especially useful when TR velocity cannot be obtained or when further information is required.

A jet of pulmonary regurgitation, present in the majority of patients with PAH-CHD, permits the measurement of the end-diastolic pulmonary pressure using the modified Bernoulli equation: [PADP = 4 × (end-diastolic pulmonary regurgitant velocity)^2 + RA pressure].

Similarly, MPAP can be determined from early peak pulmonic regurgitation velocity using the modified Bernoulli equation and adding the estimated RA pressure.[13] Mean pulmonary artery pressure can also be estimated by using pulmonary acceleration time (AT) measured from the onset of RV ejection to peak pulmonary flow velocity (Figure 2). Generally, the shorter the AT, the higher the PVR and hence the pulmonary artery pressure. A value <105 ms is suggestive of PH.[14] Mean pulmonary artery pressure can also be derived by regression formulas where: MPAP = 79 − (0.45 × AT). The same authors also found that in patients with ATs <120 ms, the formula [MPAP = 90 − (0.62 × AT)] performed better.[15]

In addition to AT, the shape of the flow wave is of interest, as PH is associated with a deceleration of flow in mid systole (notching). In the presence of increased PVR and low arterial compliance, pulse wave reflection has greater magnitude and propagates more rapidly, arriving at the right ventricular outflow tract (RVOT) during systole.[16]

In patients with a Fontan circulation, as previously discussed, even a minor increase in pulmonary artery pressure may have significant hemodynamic consequences on the Fontan circulation. Conventional diagnostic criteria for PAH cannot be applied in this type of circulation. Information about MPAP in this setting can be derived from mean flow velocity across a fenestration between the Fontan or total cavopulmonary connection pathway and the atria; when such a fenestration is

present and can be interrogated by echo Doppler [MPAP = 4 V^2 + left atrial (LA) mean pressure]. If this value is more than 17 mm Hg, it is highly suggestive of PAH.

Comprehensive diagnosis of PAH-CHD should combine Doppler pressure measurements with other accompanying echocardiographic features such as ventricular size and systolic function, as it is the RV that plays the key role in determining clinical presentation and prognosis in PAH-CHD.

Assessment of RV Morphology and Function

Right ventricular morphology. Normally the RV is a thin-walled chamber. In most forms of PAH, as a result of chronic progressive pressure loading, progressive RV remodelling occurs, initially in the form of hypertrophy and later as dilatation, along with progressive contractile impairment and, eventually, RV failure.

Compared to the patients with other forms of PAH, Eisenmenger syndrome hemodynamics and resulting RV remodelling are distinctly different. In adults with Eisenmenger syndrome with post-tricuspid defects and 2 ventricles, the RV often appears greatly hypertrophied with no significant dilatation. This unique physiopathologic adaptive model is explained by the preservation of a "fetal-like" phenotype without loss of RV hypertrophy and the presence of a ventricular communication, allowing both ventricles to function as a single entity.[17]

In contrast, adults with PH and a pretricuspid shunt (ie, ASD) show greater LA, RA, and RV dilatation. It can therefore be postulated that loss of RV hypertrophy during infancy, lack of a training effect on the RV during childhood, and the absence of a ventricular communication that pairs the 2 ventricles functionally likely explain the differing RV response.[18]

Eccentricity index. In patients with PAH, the high RV pressure may reduce the trans-septal pressure gradient between the 2 ventricles and leads to the frequently observed flattening of the intraventricular septum (IVS). M-mode analysis, with its high temporal resolution, can accurately estimate differences in the timing of leftward IVS shift during the cardiac cycle. Two-dimensional echo permits the quantification of the septal deformation using the eccentricity index, measured from a parasternal short axis view at the level of the chordae tendineae as the ratio of the left ventricle (LV) dimension parallel and perpendicular to the IVS respectively. It is usually measured both at end diastole and end systole with a normal value of 1.0, which occurs when the LV cavity maintains a round and symmetrical configuration on short-axis imaging. Mild, moderate, and severe septal bowing is represented by values of 1.1–1.4, 1.5–1.8, and >1.8.[19]

LV filling abnormalities. Intraventricular septum deformation also alters LV shape, size, and diastolic filling. Thus, a common echocardiographic finding in these patients is blunted early diastolic filling of the LV, which in this scenario is not indicative of LA hypertension, but instead represents a marker of abnormal ventriculo-ventricular interaction. In fact, increased RV pressure and prolonged RV systole cause early diastolic reversal of the IVS. As a result, early diastolic transmitral filling is reduced and redistributed to late diastole.[20]

Right ventricular function. Assessment of RV function is the single most important aspect of the echocardiographic examination in patients with PAH, because symptoms and outcome both depend on the ability of the RV to adapt to an increased pulmonary vascular load.

Right ventricular dysfunction is challenging to quantify on echocardiography. All available acoustic windows and views should be used to provide complementary information and allow for a comprehensive assessment. Qualitative assessment of function based on visual inspection is commonly used in practice, but is limited by a significant interobserver variability, which is especially problematic when assessing relative changes in RV function in the same patient.

Tricuspid annular plane systolic excursion. Differences in muscle fiber orientation of the RV suggest that longitudinal shortening plays a greater role in RV emptying than in the LV. This predominantly longitudinal contractile pattern of the RV can be easily obtained.

Tricuspid annular plane systolic excursion (TAPSE) is the longitudinal systolic displacement of the RV base toward the RV apex and has been shown to correlate strongly with RV ejection fraction (EF).[21] Tricuspid annular plane systolic excursion can be derived using 2D guided M-mode (Figure 3a), is simple and highly reproducible, and has been recommended by American Society of Echocardiography (ASE) guidelines as part of routine echocardiographic evaluation.[8] Normal values vary between 2.3 cm–2.6 cm, with a TAPSE of 2.0 cm likely representing the lowest acceptable normal value. Values in the range of 1.8 cm–2.0 cm, 1.6 cm–1.8 cm, and <1.6 cm are consistent with mild, moderate, and severe RV systolic dysfunction.[19] A significant limitation of TAPSE in PAH-CHD is that it is highly load dependent, such that it may become pseudonormalized in the presence of significant ventricular volume loading, such as with left to right shunting or severe TR.[22]

Tissue Doppler imaging. Analogous to TAPSE, systolic wave velocity by tissue Doppler imaging (TDI) is a measure of longitudinal myocardial contraction. Tissue Doppler imaging like TAPSE is load dependent and may become pseudonormal under conditions of increased ventricular volume loading. Mean value in normal controls is approximately 15 cm/s at the annulus, with a lower accepted reference limit of normal of 10 cm/s.[8]

Fractional area change. A more quantitative approach of assessing RV function is to measure the RV functional area change (FAC), [(end-diastolic area – end-systolic area)/end-diastolic area] $\times$ 100, which has demonstrated a close correlation with RVEF by MRI.[23] It is obtained by tracing areas of the RV at end diastole and end systole from the apical 4-chamber view beneath the trabeculations. Unfortunately, incomplete visualization of the RV cavity, especially when the RV is dilated, as well as difficulties in endocardial definition lead to relatively poor reproducibility, thus making it an unreliable tool for serial assessment.

Myocardial performance index. The myocardial performance index (MPI), also known as the Tei index, provides a

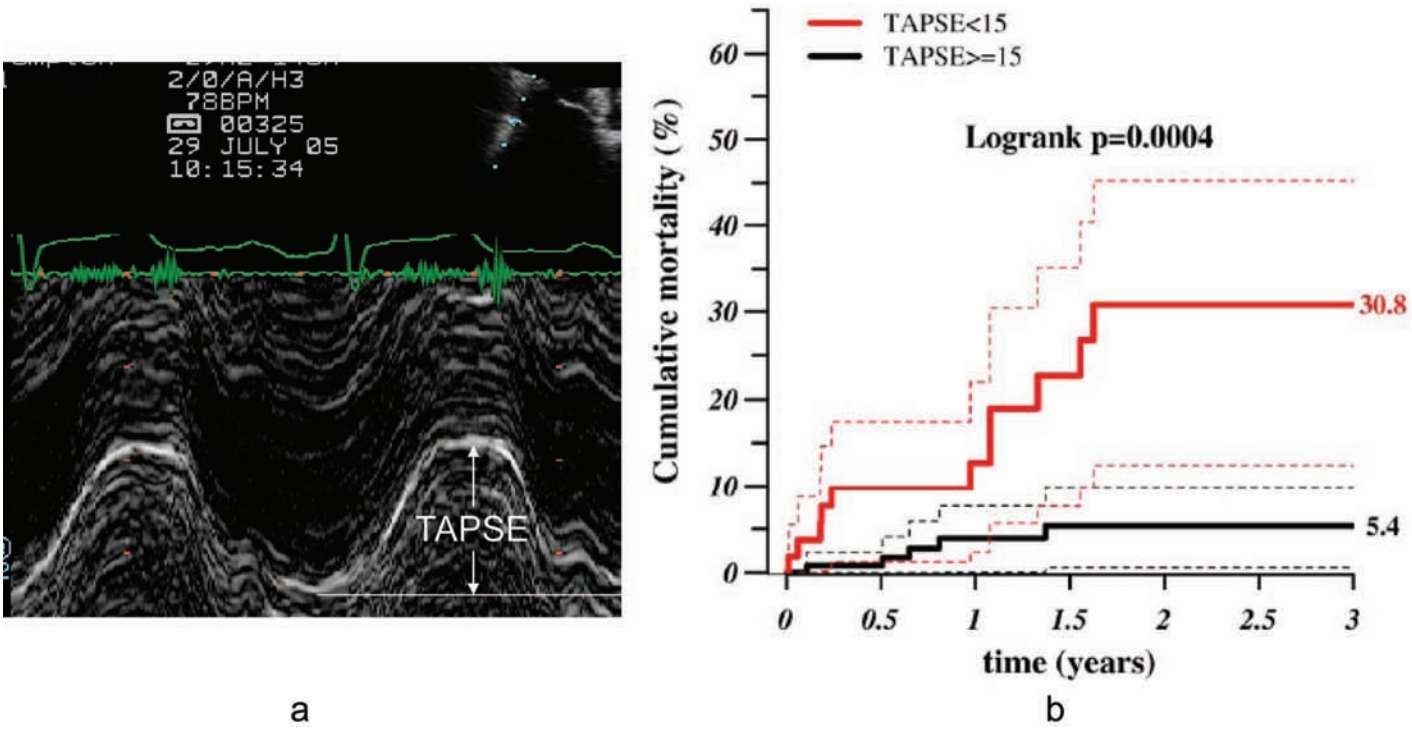


Figure 3: (a) TAPSE by M-mode recording. (b) Kaplan-Meier curve for TAPSE. Patients with TAPSE <15 mm had higher mortality rates than patients with TAPSE ≥15 mm. (Reprinted with permission from Moceri P, Dimopoulos K, Liodakis E, et al. Echocardiographic predictors of outcome in Eisenmenger syndrome. *Circulation*. 2012;126:1461-1468.)

global assessment of both RV systolic and diastolic function. It can be calculated either from Doppler imaging (apical 4-chamber view for the tricuspid inflow pattern and the parasternal short-axis RVOT view for the determination of ejection time) or from TDI (single image from the lateral annulus of the tricuspid valve), according to the formula: MPI = (isovolumic contraction time + isovolumic relaxation time)/RV ejection time.[24]

Values greater than 0.40 by pulsed-wave Doppler or greater than 0.55 by tissue Doppler signify RV dysfunction.[8] It has a good reproducibility, does not rely on geometric assumptions, and can be applied even in the presence of a suboptimal acoustic window. On the other hand, it is relatively load dependent and unreliable when RA pressure is elevated. Right ventricular ejection time, a component of MPI, has been shown to increase on targeted therapy for PAH.

Total isovolumic time. The total isovolumic time (t-IVT), which represents the sum of both isovolumic relaxation time (IVRT) and isovolumic contraction time (IVCT), can be calculated by subtracting filling time and ejection time from RR interval. It can be expressed as seconds per minute when calculated using the following formula: t-IVT=60 – [(ejection time × heart rate/1000) + (total filling time × heart rate/1000)].

Total isovolumic time is the time during the cardiac cycle heart neither ejecting nor filling. It is the total wasted time. In patients with increased pulmonary artery pressure, reduced pulmonary artery compliance will limit RV ejection time and prolonged tricuspid regurgitation duration will result in shortened filling time. Therefore, t-IVT will be significantly prolonged, and as a consequence stroke volume and hence cardiac output decreases.[18,25] Total isovolumic time can be used for monitoring disease progression and assessing prognosis.

Advanced right ventricular imaging. Speckle tracking—strain and strain rate examine the deformation and rate of deformation of the myocardial segments. These represent a method of assessing intrinsic RV myocardial contractility that is less load dependent, but currently remain outside the standard echocardiographic protocols due to the lack of normative data and high interobeserver variability.[26]

Real time 3-dimensional echocardiography can overcome the limitations of 2D echo in the assessment of RV volumes and EF. Three-dimensional echocardiographic RV volumes are comparable to those derived by MRI, although little data exist for significantly dilated or dysfunctional ventricles.[27] Technologies, able to create a 3D model of the RV by a post-processing analysis of anatomical landmarks identified in any 2D view, are currently under investigation in an ongoing study in PAH.[28]

Echocardiographic Predictors of Clinical Outcome

Different echocardiographic variables have been demonstrated to yield prognostic information that may guide clinical management. From the current literature, and according to the European Society of Cardiology (ESC) guidelines, the echo-

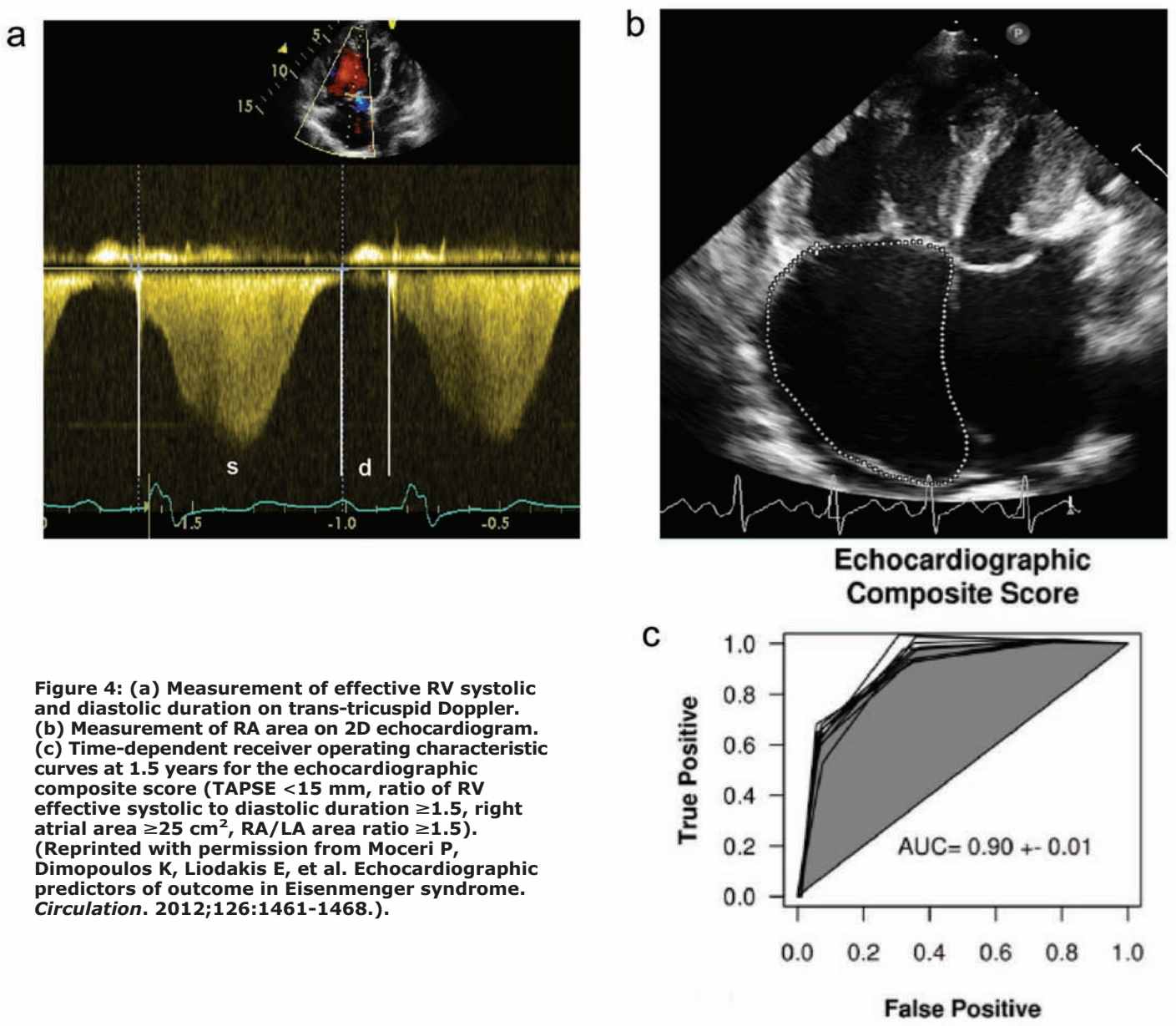


Figure 4: (a) Measurement of effective RV systolic and diastolic duration on trans-tricuspid Doppler. (b) Measurement of RA area on 2D echocardiogram. (c) Time-dependent receiver operating characteristic curves at 1.5 years for the echocardiographic composite score (TAPSE <15 mm, ratio of RV effective systolic to diastolic duration ≥1.5, right atrial area ≥25 cm^2, RA/LA area ratio ≥1.5). (Reprinted with permission from Moceri P, Dimopoulos K, Liodakis E, et al. Echocardiographic predictors of outcome in Eisenmenger syndrome. *Circulation*. 2012;126:1461-1468.).

cardiographic indices most closely associated with unfavorable outcome, including RA area index, diastolic eccentricity index, pericardial effusion, MPI, and TAPSE, are all indicators of RV decompensation.

However, prognosis is significantly affected by the etiology of PAH. Patients with Eisenmenger syndrome exhibit a better prognosis compared with idiopathic PAH and connective tissue disease–associated PAH. Patients may survive decades after the initial diagnosis of PAH-CHD, even before the advent of advanced targeted PAH therapy. As mentioned before, the difference in outcome is thought to be related to better adaptation of the RV to systemic or high pulmonary artery pressure. In support of this view, we have recently demonstrated that the longitudinal function of the RV is preserved or mildly impaired in the majority of patients with Eisenmenger syndrome, and that even though RV dilation was prevalent, it was less severe than that described in idiopathic PAH and was not related to adverse outcome.[29]

Right ventricular long axis function (TAPSE). Right ventricular longitudinal contraction in Eisenmenger patients has been shown to be an independent prognostic factor, both in our cohort, where even small reductions in TAPSE were associated with adverse outcome (Figure 3b), and in another recent prospective study from Van De Bruaen and colleagues where TAPSE <15.9 mm was predictive of lower event-free survival and higher all-cause mortality.[30]

Ratio of RV effective systolic to diastolic duration. The duration of TR, a marker of impaired adaptation to pressure overload and of RV failure, is strongly related to outcome. In fact, in these cir-

cumstances RV filling time is limited by prolongation of TR in presystole and/or early diastole, and cardiac output may consequently decrease. In order to improve the diagnostic power of echo in Eisenmenger patients, a ratio of RV effective systolic to diastolic duration can be calculated (Figure 4a). Durations of systole and diastole can be measured from the clearest Doppler signal of TR from the apical view. Effective systolic duration is measured from the onset to the end of TR. Effective diastolic duration is measured from the end of TR to the onset of the subsequent TR signal. A ratio ≥1.5 is an independent predictor of outcome.[29]

Right atrial area and ratio of RA to LA area. Parameters reflecting high central venous pressure have also been shown to predict mortality in PAH. Right atrial dilation is a reflection of long-standing pressure overload and ensuing heart failure. Quantitative assessment of RA size is performed from the apical 4-chamber view (Figure 4b). Right atrial measurements are obtained at the end of ventricular systole, when chamber size is maximal. Right atrial area is usually measured, as it has been reported to predict adverse outcome in the setting of PAH. Eisenmenger patients with pre-tricuspid shunts, who are thought to have a worse prognosis compared with those with post-tricuspid shunts,[31] are expected to have larger atria because of the long-standing shunt at the atrial level. Right atrial dilation, beyond being a marker of right-sided overload and possibly stiffness of a hypertrophied RV, is also a predisposing factor for arrhythmias. Mortality risk is significantly increased when RA area is ≥25 cm^2 or RA/LA ratio is ≥1.5.[29]

All the parameters discussed above have their limitations when used in isolation. Comprehensive assessment with a combination of multiple parameters provides the most accurate prognostication.

In our cohort, a composite score based on these strong echocardiographic predictors of outcome (TAPSE <15 mm, ratio of RV effective systolic to diastolic duration ≥1.5, RA area ≥25 cm^2, and RA/LA area ratio ≥1.5) identified patients with more than 3-fold increased risk of death at 1.5 years, with a very high area under the curve on receiver operating curve (Figure 4c).

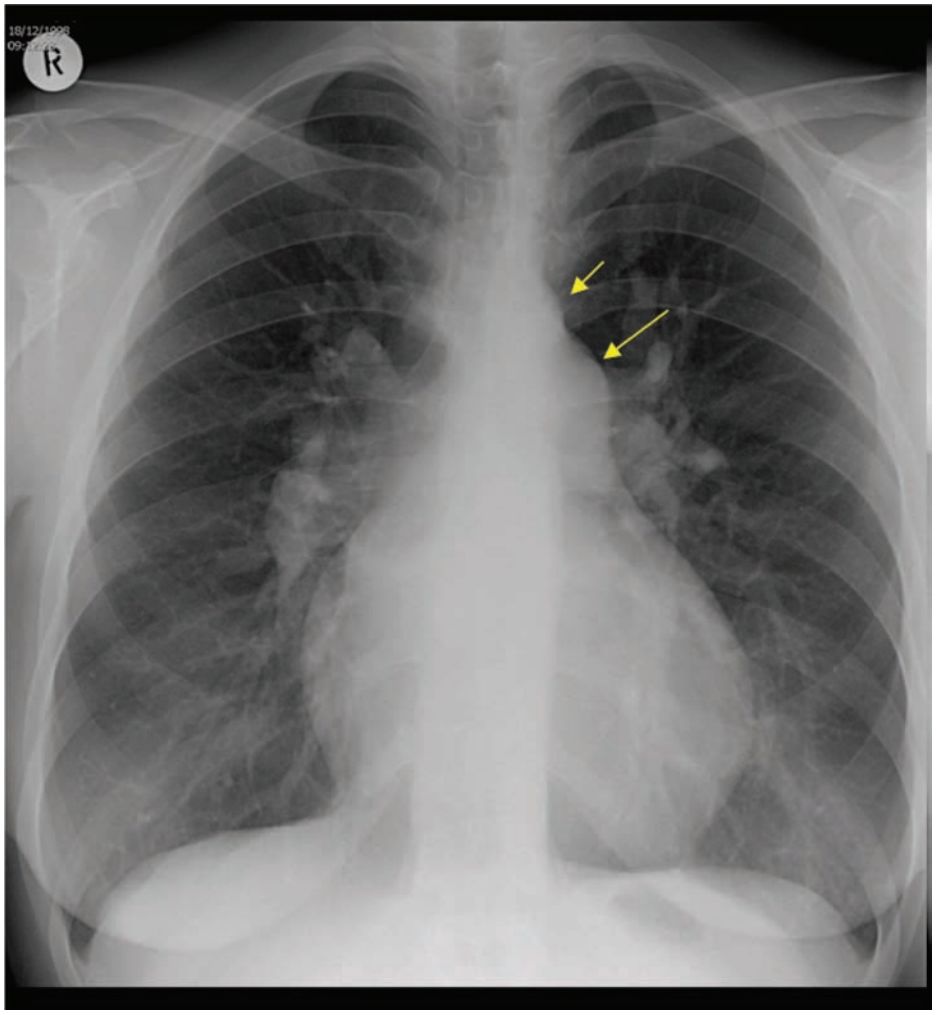


Figure 5: Chest x-ray of a patient with ASD and PH. The main pulmonary artery (long arrow) and its main branches are enlarged, and the peripheral pulmonary vessels by comparison are "pruned." The heart is enlarged and the shape suggests right heart enlargement. The aortic knuckle (short arrow) is small—a feature typical of ASD.

CHEST RADIOGRAPHY AND CARDIAC COMPUTED TOMOGRAPHY

A plain chest x-ray provides a record of cardiac size, which in the CHD population as a whole carries prognostic significance.[32] The typical changes of PAH on the chest x-ray are enlargement of the central pulmonary arteries with relative pruning of the distal vessels. There may also be signs of specific chamber enlargement or other features to suggest a particular underlying defect (Figure 5).

Although disadvantaged by the need for ionizing radiation and contrast, computed tomography (CT) has an important part to play in the investigation of PAH-CHD, as it provides information on cardiac chambers, great arteries, lung vasculature, and parenchyma and mediastinal structures in a single acquisition with high spatial resolution.[33] This is particularly the case when acoustic windows have been poor (limiting echocardiography), lung disease is present, or devices such as pacemakers prevent cardiovascular magnetic resonance (CMR) scanning.

Similar features of cardiac physiology associated with PAH described previously can also be identified using cardiac CT. Communications between chambers can be visualized and the direction of shunt inferred by the direction of contrast (Fig-

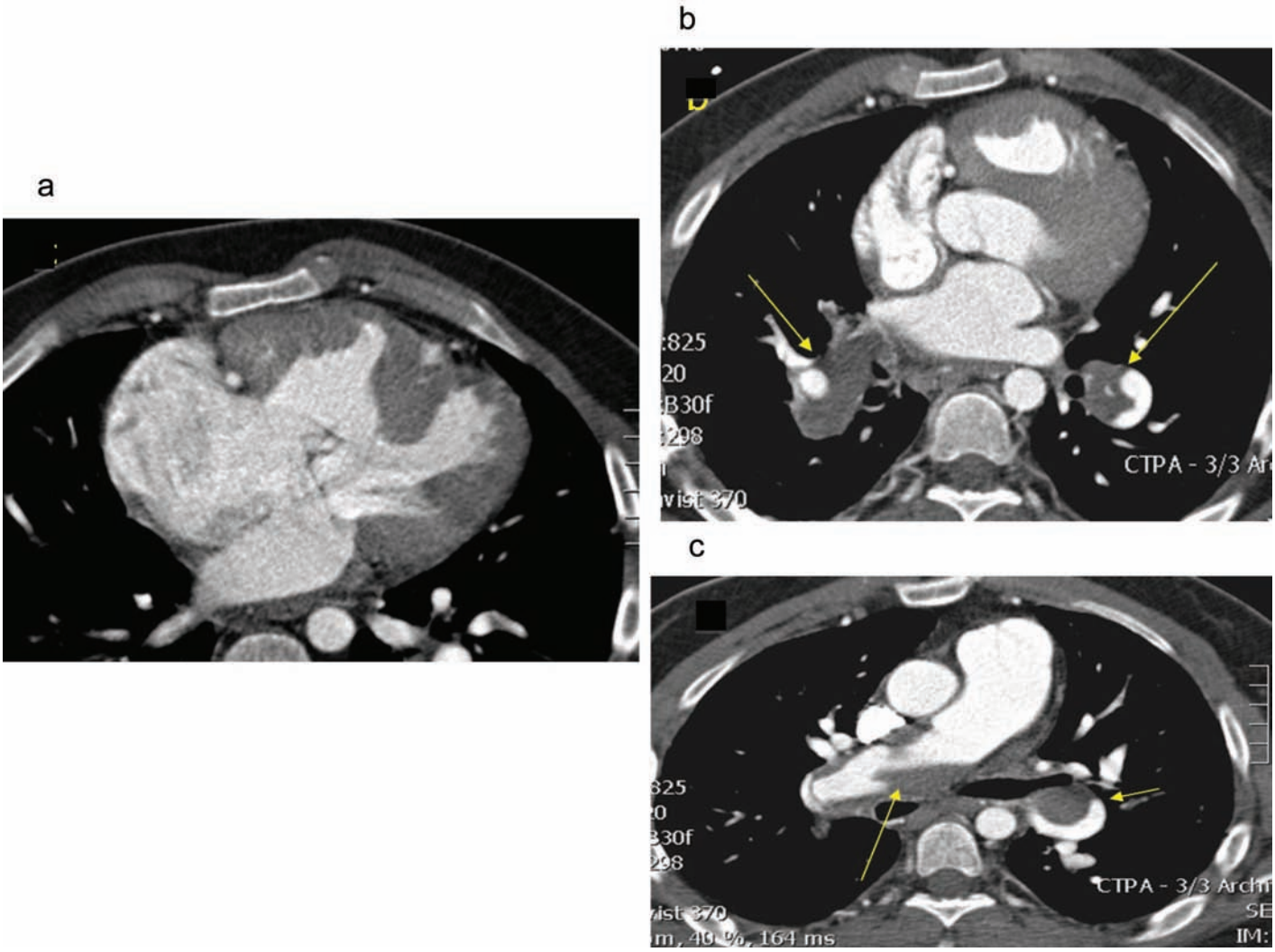


Figure 6: Computed tomography pulmonary angiograph of patient with AVSD and PAH. (a) The common AV valve and atrial and ventricular components of the AVSD are seen, the right atrium is dilated, and there is RV hypertrophy. (b) The main pulmonary artery is dilated and larger in cross-section than the ascending aorta. (b and c) Extensive thrombus is present in the branch pulmonary arteries (arrows).

ure 6a). Although excellent at providing anatomical detail, it is generally not the modality of choice for providing functional data. If necessary, biventricular function can be assessed, though this necessitates greater radiation exposure to capture information throughout the cardiac cycle.

The CT pulmonary angiogram is the test of choice to assess the proximal and distal pulmonary arteries noninvasively. In doing so, pulmonary artery dilatation can be identified as well as the presence of thrombus, which may form in situ due to sluggish blood flow in an inflamed pulmonary vascular bed rather than being embolic in origin (Figures 6b and c).

High-resolution CT scanning provides valuable information on lung parenchyma, which can be abnormal in patients with CHD because of bronchiectasis or hypoplasia. It may also detect parenchymal changes due to PAH, for example, ground glass changes, nodular opacities, and serpiginous intrapulmonary vessels. In those with chronic thromboembolic PH, it may also identify within the lung tissue hemorrhage, infarction, or a mosaic pattern (due to heterogeneous lung perfusion). High-resolution CT has a vital role in identifying patients with pulmonary veno-occlusive disease, where advanced therapies might be harmful. The key features of this rare entity on CT are interlobular septal thickening, ground glass shadowing, and adenopathy.

When contrast is enhanced, this technique is particularly adept in the assessment of extracardiac features, particularly native or surgically fashioned systemic to pulmonary shunts. Collateral vessels are readily identified. These include dilated bronchial arteries (a feature commonly seen in PAH) or bypassing vessels in cases of pulmonary venous occlusion.

An analytic technique called fractal analysis has been studied to determine whether the degree of branching within the pulmonary arteries of children and young adults with PAH, half of whom had CHD, could be used as a noninvasive

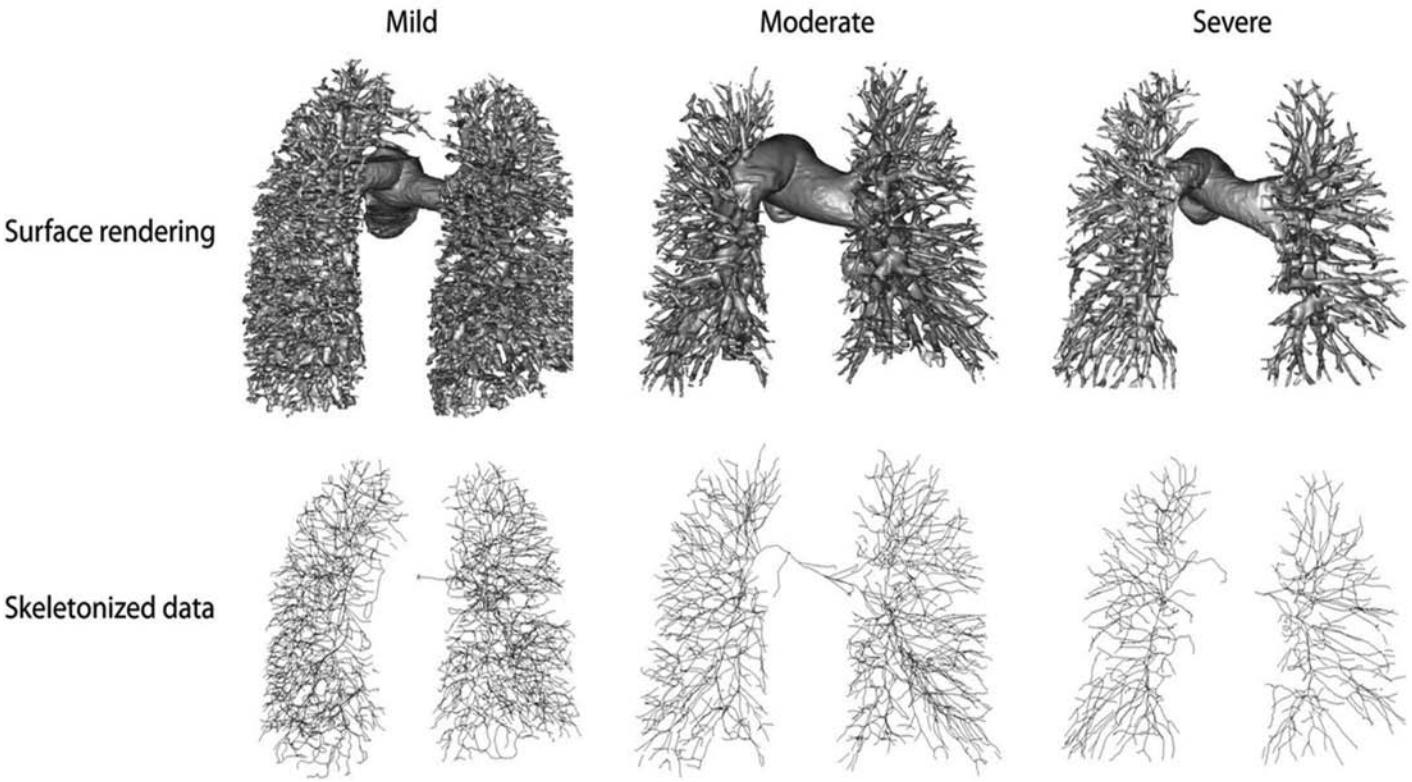


Figure 7: Representative examples of segmented pulmonary artery masks, and below them the derived skeletonized representations for patients with mild, moderate, and severe PH. (Reprinted with permission from Moledina S, de Bruyn A, Schievano S, et al. Fractal branching quantifies vascular changes and predicts survival in pulmonary hypertension: A proof of principle study. *Heart*. 2011;97:1245-1249.).

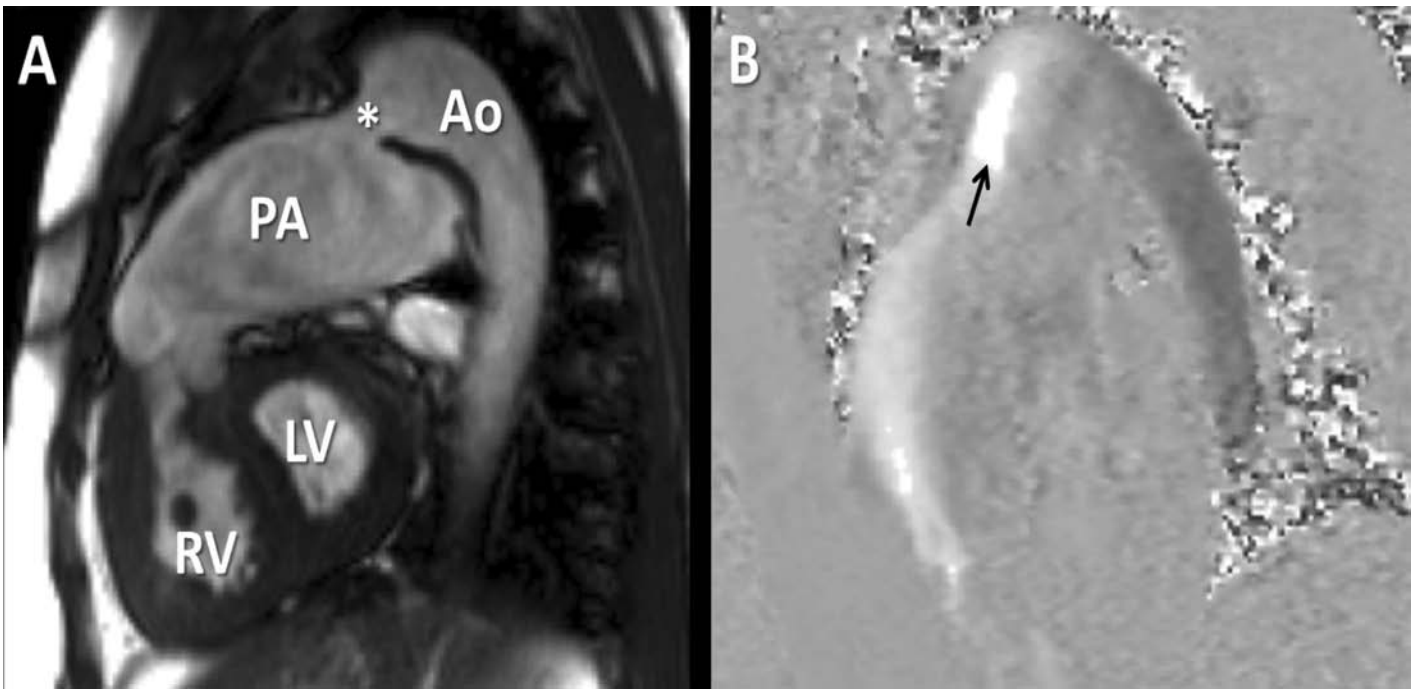


Figure 8: (A) Cardiovascular magnetic resonance still systolic frame from balanced steady-state free precession cine image demonstrating a large PDA (asterisk) measuring 13 mm diameter. The pulmonary artery is severely dilated with maximum diastolic diameter 50 mm. The RV is severely hypertrophied. (B) A corresponding in-plane phase velocity map is shown, and blood flow is demonstrated to be predominantly from the main pulmonary artery to the aorta in systole.

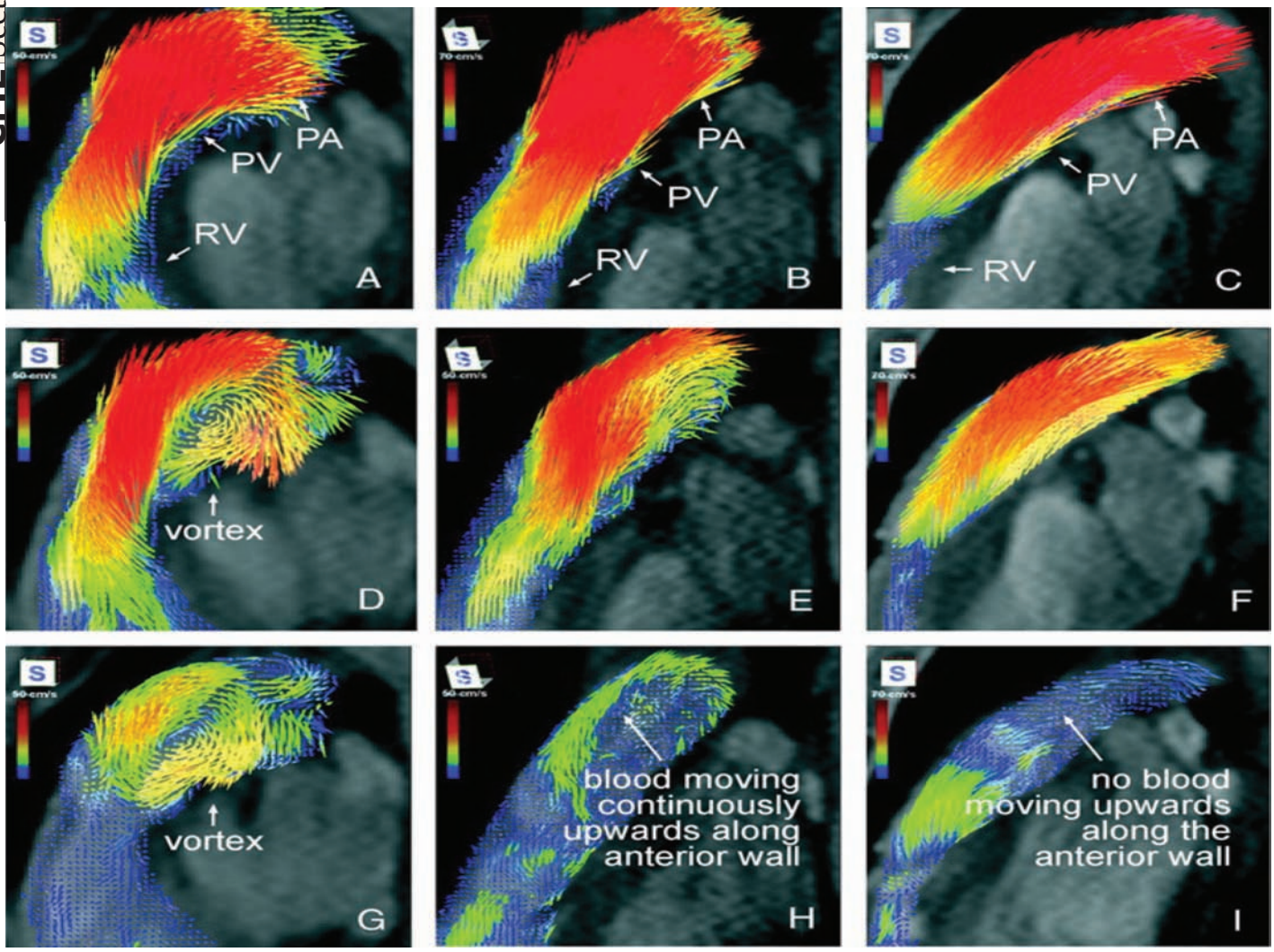


Figure 9: Typical flow patterns in the RVOT at different cardiac phases for a patient with manifest PH (A, D, and G), a patient with latent PH (B, E, and H), and a normal subject (C, F, and I). PA indicates main pulmonary artery; PV, pulmonary valve; and RV, right ventricle. At maximum outflow (A through C), flow profiles were distributed homogenously across the cross sections of the main pulmonary artery in the manifest PH group (A), the latent PH group (B), and the normal group (C). In later systole (D through F), a vortex was formed in the manifest PH group (D). No such vortex could be found in the latent PH group (E) or the normal group (F). After pulmonary valve closure (G through I), the vortex in the PH group persisted for some time. In all cases, continuous diastolic blood flow upward along the anterior wall of the main pulmonary artery could be observed. (Reprinted with permission from Reiter G, Reiter U, Kovacs G, et al. Magnetic resonance-derived 3-dimensional blood flow patterns in the main pulmonary artery as a marker of pulmonary hypertension and a measure of elevated mean pulmonary arterial pressure. *Circ Cardiovasc Imaging*. 2008;1:23-30.).

measure of PH (Figure 7).[34] This index compared well with conventional markers of disease severity such as functional class, 6-minute walk test distance, and indexed PVR, and predicted death among the cohort [HR 5.6 (95% CI 1.2 to 25; $P = 0.027$)].

CARDIOVASCULAR MAGNETIC RESONANCE

Cardiovascular magnetic resonance has the major advantage of being able to image in any plane with high spatial and temporal resolution without requiring ionizing radiation. As repeated examinations become common, the latter characteristic is particularly beneficial for patients with PAH-CHD.

In order to optimize image quality, breath holding is required. This may be problematic for some patients with PAH-CHD. In addition, pacemakers/devices currently represent a contraindication to routine CMR.

CMR acquisition and subsequent analysis of a stack of contiguous cine image covering the whole heart from base to apex provides the gold standard assessments of right and left ventricular size and function,[35] especially so for heavily trabeculated RVs. However, analysis remains operator dependent.

Using both cine imaging and in-plane flow mapping, intracardiac shunts can be easily identified and quantified. By comparing the ratio of flow through the pulmonary

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