



The use of magnetic resonance imaging in pulmonary hypertension: why are we still waiting?

Jeroen N. Wessels , Frances S. de Man and Anton Vonk Noordegraaf

Affiliation: Dept of Pulmonary Medicine, Amsterdam Cardiovascular Sciences, Amsterdam UMC, Vrije Universiteit Amsterdam, Amsterdam, Netherlands.

Correspondence: Anton Vonk Noordegraaf, Dept of Pulmonary Medicine, Amsterdam UMC, Location Vumc, De Boelelaan 1117, 1081 HV Amsterdam, The Netherlands. E-mail: a.vonk@amsterdamumc.nl

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Cardiovascular magnetic resonance imaging is an important modality in pulmonary hypertension for diagnostics, evaluation of treatment response and prognostics. It can replace other modalities at follow-up and serve as an end-point in large clinical trials. <https://bit.ly/3hfSKN8>

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Pulmonary hypertension (PH) is a complex disease requiring a detailed assessment of haemodynamics, functional analysis and identification of the underlying cause. A typical patient with a suspicion of PH will undergo several noninvasive and invasive tests including right heart catheterisation before a definitive diagnosis can be made. Some of these tests, such as 6-min walking distance or N-terminal pro-brain natriuretic peptide can provide information on treatment response and prognosis. However, the extent of right ventricular (RV) adaptation to the increased afterload is the main determinant of outcome [1]. Because of this, there is a clear need for a test which provides us with detailed information on RV function at baseline and during follow-up. Cardiovascular magnetic resonance imaging (MRI) is the gold standard for functional and morphological assessment of the right ventricle [2]. It not only allows accurate quantification of RV volumes and mass, it also provides information on the other cardiac chambers (atria and left ventricle) and the pulmonary artery dimensions.

In this issue of the *European Respiratory Review*, ARYAL *et al.* [3] give a detailed description of the value of cardiovascular MRI in PH, in comparison to other major imaging modalities. It has high spatial and temporal resolution and does not rely on favourable acoustic windows. Reproducibility is excellent and allows for a standardised assessment of RV function. ARYAL *et al.* [3] also describe how cardiovascular MRI can be used to distinguish between different causes of PH. Congenital abnormalities like aberrant pulmonary veins or intracardiac shunts may become apparent. Left ventricular hypertrophy, dilatation or left atrial dilatation strongly suggest PH due to left heart failure. In addition, magnetic resonance angiography and perfusion imaging can be used for the diagnosis of chronic thromboembolic PH and to assess operability [4]. Serial follow-up of patients before and after surgery with cardiovascular MRI can provide information on the vasculature, as well as cardiac remodelling. Beside diagnostics and evaluation of treatment response, several cardiovascular MRI parameters provide information on prognosis and risk assessment. Stroke volume and RV ejection fraction are strong predictors of prognosis, both at baseline and during follow-up and can be accurately assessed by means of cardiovascular MRI [5, 6]. Volumetric parameters can also be used for risk stratification. In a recent study, the authors were able to identify

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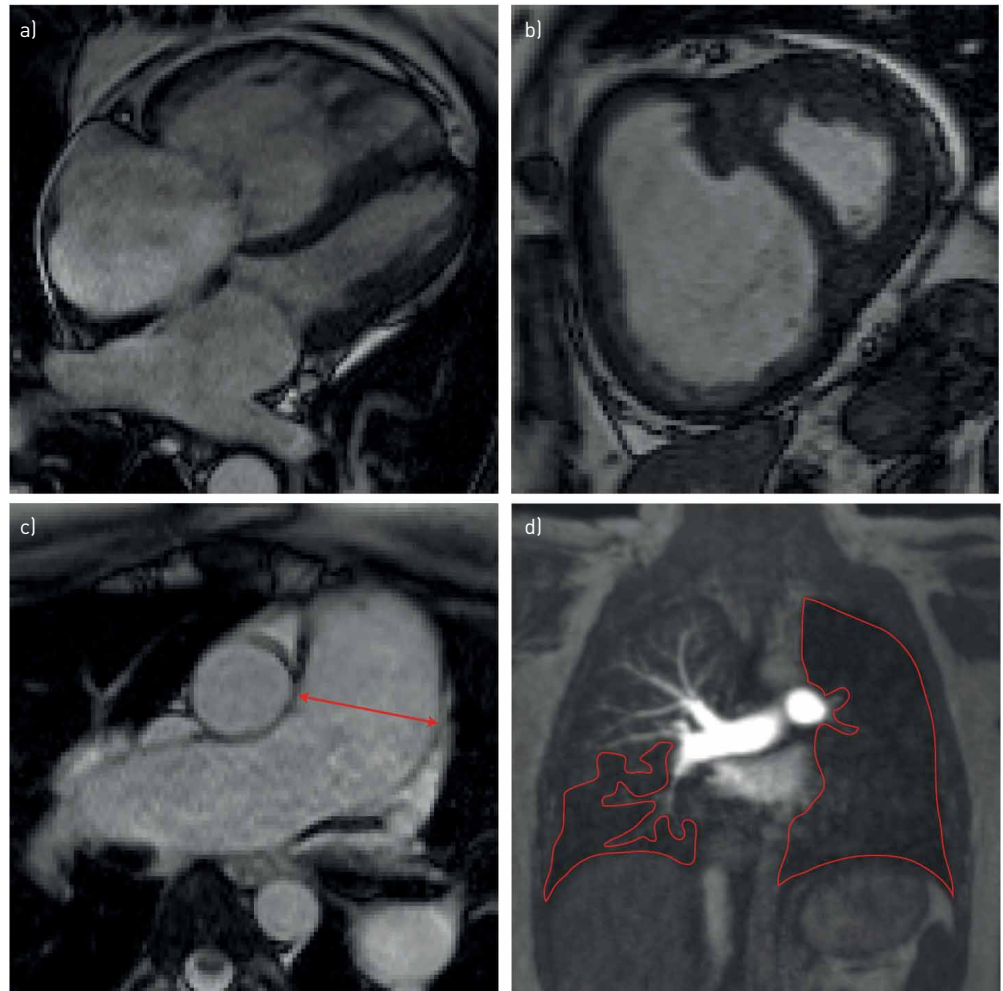


FIGURE 1 Versatile use of cardiovascular magnetic resonance imaging (MRI) in pulmonary hypertension (PH). These images show several of the important uses of cardiovascular MRI in PH. a) End-systolic 4-chamber view of a patient with pulmonary arterial hypertension. There is marked dilatation of the right ventricle and atrium, there is leftward septal bowing and hypertrophy of the right ventricular free wall and trabeculations. b) Short axis slice of the same patient. A stack of short axis slices enables quantification of volumes and mass. c) Pulmonary trunk in relation to the aorta. The pulmonary trunk and right pulmonary artery are dilated. d) Magnetic resonance angiography (coronal plane, slice thickness 10 mm) of a patient with chronic thromboembolic PH. There is normal perfusion of the right upper lobe, while there is hardly any perfusion of the right lower lobe. All lobar arteries of the left lung are occluded, causing an almost complete lack of perfusion.

thresholds of RV end systolic volume which improved risk stratification when added to current approaches [7]. In addition, although neglected for a long period of time, assessment of right atrial function has been shown to be of prognostic relevance [8]. This makes cardiovascular MRI an all-round technique (figure 1) that enables diagnosis, evaluation of treatment response and monitoring of disease progression.

If this technique has such a high potential, what is the reason that it is not part of standard care in PH expert centres? In 2007, NAGENDRAN and MICHELAKIS [9] described that cardiovascular MRI could be a one-stop shop for the comprehensive assessment of pulmonary arterial hypertension. Cardiovascular MRI has been knocking on our front door for years, its clinical value has been shown over and over again, but the doors to the PH centres remain shut.

Obvious reasons for this are poor availability, access and high costs. Although cardiovascular MRI is of essential value in the differential diagnosis of PH, it cannot fully replace techniques such as right heart catheterisation, pulmonary angiography, echocardiography and nuclear scintigraphy. A limitation of cardiovascular MRI in this respect so far, is its inability to reliably estimate pulmonary artery pressure. However, in a recent study the researchers could identify individuals with PH by using simple cardiovascular MRI metrics [10]. The detection of PH was very accurate with an area under the receiver

operating characteristic curve of 0.96. Still, this method is not widely used in clinical practice, probably because physicians prefer to directly measure pressures and resistance in the pulmonary circulation. Moreover, haemodynamic and imaging parameters are not linearly related to one another, making it difficult to determine whether cardiovascular MRI can substitute invasive catheterisation entirely. Pairwise measurement of haemodynamic and imaging parameters for a direct comparison is necessary to determine whether cardiovascular MRI performs as well as catheterisation. Recent advances in applying machine learning algorithms to cardiovascular MRI images in PH showed the incremental value of 3-dimensional cardiac motion for survival prediction [11]. These results need to be validated in different cohorts and machine learning algorithms standardised before its implementation in clinical practice. Future studies are needed to show that cardiovascular MRI is indeed able to replace current diagnostic tests and is essential for proper monitoring of PH. Fully using the potential of cardiovascular MRI as a one-stop shop and replacing other modalities will enable a reduction instead of an increase in cost.

Another reason for the limited use of cardiovascular MRI so far is the fact that cardiovascular MRI parameters have not been used as clinical trial end-points. Since cardiovascular MRI is not readily available in all centres it is often not considered as an end-point. Physicians will only start to believe in the value of cardiovascular MRI for evaluation of treatment response once this has been proven in large clinical trials. Therefore, the availability of cardiovascular MRI remains limited. This vicious circle needs to be broken in order to make full use of the potential cardiovascular MRI has in clinical trials. It is necessary to emphasise that cardiovascular MRI can be more cost effective than echocardiography and the fact that standardised protocols and high reproducibility of the measurements may reduce the number of subjects needed in a study [12]. It is currently unclear which cardiovascular MRI parameter is preferably used to assess treatment response. A recently unpublished multicentre phase 4 study showed that by using stroke volume as an end-point, the effect of treatment can be measured in a small group of patients [13]. Initiation of macitentan alone or in combination with a phosphodiesterase-5 inhibitor led to a relevant improvement of stroke volume. This improvement was already obvious at the interim assessment of just 42 patients. In the future these results should be extended to phase 2 and 3 trials to demonstrate the real value of cardiovascular MRI in drug discovery.

Even though cardiovascular MRI is knocking on the front door of every PH centre, it has not sufficiently been proven to be a one-stop shop for the comprehensive assessment of pulmonary arterial hypertension. Future robust multicentre studies using cardiovascular MRI parameters as end-points are required to open the doors, taking financial considerations and patient comfort into account. Important questions remain to be answered. Can cardiovascular MRI substitute other modalities during follow-up and become a complete, noninvasive follow-up measurement? What is the best cardiovascular MRI parameter to use as an end-point in clinical trials? What else is needed to allow cardiovascular MRI to become the standard of care in all PH centres?

Conflict of interest: None declared.

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