Prognostic Value of Cardiovascular Magnetic Resonance Imaging Measurements Corrected for Age and Gender in Idiopathic Pulmonary Arterial Hypertension

Swift et al: Corrected Cardiac MRI for Prognostication

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Abstract

Background—There is limited data on the prognostic value of cardiovascular magnetic resonance (CMR) measurements in idiopathic pulmonary arterial hypertension, with no studies investigating the impact of correction of CMR indices for age and gender on prognostic value.

Methods and Results—Consecutive patients with idiopathic pulmonary arterial hypertension (IPAH) underwent CMR imaging at 1.5T. Steady state free precession (SSFP) cardiac volumes and mass measurements were corrected for age, gender and BSA according to reference data and prognostic significance assessed. 80 patients with IPAH were identified, 23 patients died during the mean follow-up of 32 +/- 14 months. Corrected for age, gender and BSA, RV end-systolic volume (p=0.004) strongly predicted mortality, independent of WHO functional class, mean right atrial pressure (mRAP), cardiac index (CI) and mixed venous oxygen saturations (mVO2).

Conclusions—Consideration should be given to correcting CMR measures, for age, gender and BSA, particularly given the changing demographics of patients with IPAH. Corrected right ventricular end-systolic volume is a strong prognostic marker in IPAH, independent of invasively derived measurements, mRAP, CI and mVO2.

Key Words: pulmonary hypertension; prognosis; magnetic resonance imaging; right ventricle
Idiopathic pulmonary arterial hypertension (IPAH) is a progressive, incurable disease with high morbidity and mortality despite the development of effective treatment options. The emergence of goal orientated therapy has focused interest on prognostic markers that can both inform the clinician regarding disease severity at presentation and be used to follow-up response to therapy. Traditionally this is based on an assessment of the clinical status, exercise capacity and measures of right ventricular (RV) function.

Magnetic resonance (MR) imaging using steady state free precession (SSFP) provides accurate and reproducible information on cardiac morphology and function. The imaging modality has been proposed, as a non-invasive tool in the clinical assessment of patients with pulmonary hypertension. Van Wolferen et al showed that when indexed for body surface area (BSA), a large RV volume, low stroke volume (SV) and a small left ventricular (LV) volume strongly predicted mortality in IPAH. However, cardiac volumes, not only vary with BSA but also age and gender which are strong predictors of outcome.

In recent publications from the UK and Ireland pulmonary hypertension registry, the French and REVEAL registries patient age has been shown to be an important predictor of outcome in patients with PAH. How much this is related to the presence of comorbidities or a direct effect of age on for example how the right ventricle is able to cope with an increase in afterload, is not known. These studies have also demonstrated that the range and average age of patients has risen significantly over the last decade making adjustments for age and gender more relevant in the current era for accurate individual risk stratification. In particular age is a strong predictor of outcome and the inverse relationship between age and ventricular volume may influence the prognostic value of CMR measures.
The aim of this study was to establish the prognostic value of CMR derived ventricular measurements in patients with IPAH with correction for age, gender and BSA.

Methods

Patients
Consecutive treatment-naïve patients with IPAH who underwent MRI and right heart catheterisation (RHC), within 48 hours, were identified from a database of a large volume, nationally designated, PH referral centre from 1st of January 2008 to November 2011. A census was performed on the 17st of Dec 2012, providing a minimum of 1 year follow-up from scan date. Patients referred with suspected pulmonary hypertension underwent systematic evaluation as previously described in the ASPIRE registry, including lung function, exercise testing, HRCT and CT pulmonary angiography, CMR and MR angiography and RHC. This study was approved by our institutional review committee and informed consent was waived for this retrospective study.

CMR image acquisition
CMR imaging was performed using an 8 channel cardiac coil on a GE HDx (GE Healthcare, Milwaukee, USA) whole body scanner at 1.5T. Short axis cine images were acquired using a cardiac gated multi-slice balanced SSFP sequence (20 frames per cardiac cycle, FOV 48, matrix 256 x 256, BW 125 KHz/pixel, TR/TE 3.7/1.6 ms). A stack of images in the short axis plane with slice thickness of 8 mm (2mm inter-slice gap) were acquired fully covering both ventricles from base to apex. End-systole was considered to be the smallest cavity area. End-diastole was defined as the first cine phase of the R-wave triggered acquisition. Patients were in the supine position with a surface coil and with retrospective ECG gating.
Image analysis

Image analysis was performed on a GE Advantage Workstation 4.1 with the observer blinded to the patient clinical information, and cardiac catheter parameters. Right and left endocardial and epicardial surfaces were manually traced from the stack of short-axis cine images, using our MR workstation software to obtain RV end-diastolic (RVEDV) and end-systolic (RVESV), and LV end-diastolic (LVEDV) and end-systolic volumes (LVESV). From end-diastolic volume and end-systolic volumes, RV and LV ejection fraction (RVEF and LVEF) and RV and LV stroke volume (RVSV and LVSV) were calculated. Cardiac volumes but not RVEF and LVEF were indexed for BSA. For calculation of ventricular mass the interventricular septum was considered as part of the LV. The RV myocardial volume was calculated by multiplying the area of the RV wall on each slice by the inter-slice distance. The product of the sum total of myocardial slice volumes for the RV and the density of myocardium (1.05 g/cm³) gave an estimate of RV mass. Ventricular mass index (VMI) was defined as RV mass divided by LV mass, as previously described.7, 18.

RHC

RHC was performed using a balloon-tipped 7.5 Fr thermodilution catheter (Becton-Dickinson, USA). RHC was usually performed via the internal jugular vein using a Swan-Ganz catheter. Features at RHC required to define IPAH were mean pulmonary arterial pressure (mPAP) ≥ 25 mmHg at rest with a pulmonary capillary wedge pressure (PCWP) of ≤15 mmHg.19 Pulmonary vascular resistance index (PVRI) was determined as follows: PVRI = 80*(mPAP - PCWP)/Cardiac index (CI).
CMR volumetric measurements indexed for BSA were corrected for age and gender and presented as percentage (%) predicted. To establish predicted values for corrected cardiac volumes, regression equations were generated for age and gender from healthy volunteers based on previously published reference data\textsuperscript{10,11}, for example corrected RVEDVI (%) = RVEDVI/predicted RVEDVI x 100. The interval from evaluation with CMR until all cause death or census was regarded as the follow-up period. Log-log plots were produced for each variable to assess proportional hazards; continuous variables were dichotomised, with an even number of deaths in each group for this analysis. The prognostic value of CMR derived volumetric measurements, phase contrast indices, invasive haemodynamic measurements mPAP, mean right atrial pressure (mRAP), cardiac output (CO), PVRI, mixed venous oxygen saturation (SvO2), and patient age, gender and WHO functional class (dichotomised into WHO groups II and II versus WHO group IV) were assessed using univariate Cox proportional hazards regression analysis. Bivariate analysis was performed for right ventricular indices significant at univariate analysis (p<0.2), on significant covariates and a regressions of CMR indices on outcome adjusting for both age and gender was performed. Kaplan-Meier analysis was used to assess the prognostic value of CMR volumetric measurements using median threshold values. CMR variable rescaling was performed for secondary Cox proportional hazards analysis in order to improve ease of interpretation of Hazard ratios. Rescaling was performed by dividing individual CMR values by the standard deviation of the variable.

A p-value $< 0.05$ was considered statistically significant; the p-values are two-sided.

Statistical analysis was performed using SPSS 19 (SPSS, Chicago, Ill) and for presentation of the data GraphPad Prism 5.05 (GraphPad Software, San Diego, Calif) software was used.
Results

Patients

109 patients were identified fitting the diagnostic criteria for IPAH, 81 patients had undergone RHC and MRI within 48 hours and one patient was excluded as the imaging was of non-diagnostic quality and precluded volumetric analysis. Thus, 80 patients with IPAH were included in the study. During a mean follow-up of 32 months (standard deviation 14 months) 23 patients died. Baseline haemodynamic, demographic and CMR data for all patients, survivors and non-survivors are shown in Table 1.

Cox proportional hazards survival analysis

Demographics and haemodynamics

Age, WHO functional class, right atrial pressure, cardiac index and mixed venous oxygen saturation were all univariate predictors of mortality (Table 2).

CMR indices indexed for BSA

Table 3 presents Cox proportional hazards regression analysis results for scaled CMR indices. RVESVI and RVEDVI did not predict mortality when uncorrected for age and gender, p=0.140 and p=0.259 respectively. In addition, RVEF when uncorrected did not significantly predict adverse outcome (p=0.336) (Table 2). LVSVI was the only CMR measurement without correction for age and gender that predicted adverse outcome (p=0.022) at univariate analysis. We performed a regression of CMR indices indexed for BSA on outcome, adjusting for age and gender and found RVESVI and LVSVI to be significant predictor of adverse outcome (p=0.040) and (p=0.023), respectively.
CMR indices corrected for age, gender and BSA

RVESV when corrected was a CMR predictor of mortality (p=0.004). Corrected measurements of RVEDV (p=0.078) and RVEF (p=0.187) did not predict adverse outcome. Ventricular mass index was not of prognostic significance (p=0.960). Corrected LVSV was the only left ventricular measurement that predicted adverse outcome (p=0.048).

At bivariate analysis corrected RVESV was associated with mortality independent of WHO functional class (p=0.001), mRAP (0.041), CI (p=0.042) and mVO2 (p=0.018), see Table 4.

Kaplan-Meier analysis

Kaplan-Meier plots for CMR measurements corrected for age, gender and BSA and simply indexed for BSA are presented in Figures 1-4. Corrected RVESV above the median value of 292% predicted was associated with significantly worse outcome, log rank test: chi=9.44, p=0.002. When indexed for BSA, RVESV did not predict mortality at Kaplan-Meier analysis (chi=1.28 p=0.257). Corrected LV stroke volume less than the median value of 56% predicted was strongly linked to adverse outcome, log rank 7.35, p=0.007. However, LVEDV and LVESV measurements did not significantly predict adverse outcome (p=0.083; and log rank 0.493, p=0.356 respectively). VMI was not associated with adverse outcome (log rank 0.04, p=0.952).

Discussion

This study has shown that correction of CMR parameters for age and gender impacts on the prognostic value of right and left ventricular metrics. We have demonstrated that right ventricular end-systolic volume corrected for age, gender and BSA is strongly associated with adverse outcome in newly diagnosed patients with IPAH. We have also shown that the
prognostic significance of corrected RVESV is independent of invasive predictors of outcome namely, mRAP, CI and mVO2.

Van Wolferen et al studied the prognostic value of CMR measurements indexed for BSA in 64 patients with IPAH\(^9\). They found baseline RVEDV and progressive RV enlargement were associated with adverse outcome. Our study has corrected CMR measures for age and gender as recommended by Maceira et al\(^{11}\) and demonstrates that corrected RVESV is a stronger predictor of adverse outcome than RVEDV. Increased RVESV implies enlargement of the RV in combination with a loss of systolic function and may explain the greater prognostic significance of RVESV over RVEDV. Our findings are reflected in work by van de Veerdonk et al\(^{20}\), in which RVESV but not RVEDV measurements significantly predicted mortality at baseline in patients with PAH. These studies highlight the adverse prognostic impact of RV volumetric measurements in patients with PAH. Correction for age and gender when interpreting CMR volumetric measurements may be particularly important as the average age of patients with IPAH is significantly higher than in previous studies and a reduction in cardiac volumes with advancing years, may act to minimise the prognostic value of this measure\(^{21}\).

Several studies have highlighted the prognostic value of cardiac output and stroke volume in the evaluation of patients with pulmonary arterial hypertension\(^9\) \(^{22-25}\). The present study highlights the importance of making volumetric estimates of stroke volume from the left rather than right ventricle (Figure 4). Previous investigators have already suggested that left sided estimates of stroke volume are mandatory\(^ {26}\) although this is the first article to directly compare RV and LV volumetric measurements of stroke volume. Using RV volumetry to estimate cardiac output has been shown previously to be a poor marker of the forward flow from the RV in pulmonary hypertension possibly reflecting difficulties in accurate border
detection and RV trabeculations although the loss of forward contribution to cardiac output may also be important.

Low LV end-diastolic volume as a predictor of mortality at Kaplan Meier analysis was of borderline statistical significance (p=0.083). Previous studies have shown that low LV end-diastolic volume is a predictor of adverse outcome in IPAH and PAH cohorts, the likely mechanistic explanations include, underfilling of the LV due to reduced blood flow or compression of the LV cavity due to RV pressure overload.

Van de Veerdonk et al, has shown that baseline measurement of RVEF predicts mortality in a heterogeneous group of patients with PAH and an improvement in RVEF at follow-up has been associated with better outcome independent of pulmonary vascular resistance. In contrast Van Wolferen did not demonstrate any prognostic value of RVEF at baseline in IPAH. In our study RVEF when corrected for age and gender did not reach statistical significance (p=0.09). This possibly reflects the sample size and also the differing populations of patients included in studies.

The mechanisms underlying the impact of increasing age and gender on the outcome of patients with PAH and specifically how this may relate to RV modelling are not clear. An animal study has shown that the LV of female rats adapts more favourably to volume overload than males. In contrast to males, in female rats, volume overload leads to concentric left ventricular hypertrophy, yet there is minimal ventricular dilatation and no change in myocardial compliance, with females showing less frequent progression to heart failure. The ability of female rats to develop appropriate concentric hypertrophy is sufficient to maintain a stable compensated state preventing the development of ventricular dilatation and CHF.

Whether this is the case in the right ventricle is not known but clearly remains a possibility. Interestingly in patients with IPAH females are at higher risk of developing pulmonary hypertension, but women seem to have better right ventricular function and improved
survival compared to men with IPAH. Ventetuolo et al, in large study of patients with no
known cardiovascular disease have shown that higher levels of estradiol are associated with
better RV systolic function in postmenopausal women using hormone therapy. In addition,
higher levels of androgens are associated with greater RV mass and larger RV volumes in
men and postmenopausal women. There is very little data in the published literature on the
impact of age on RV function but one may postulate that the ventricle may have a reduced
ability to remodel in the setting of an increase in right ventricular afterload.

In stratifying patients within a population for disease severity, adjusting for important
variables such as age and gender may be helpful in more accurately identifying patients with
a poor prognosis who may benefit from more intensive therapy at the time of diagnosis. In
addition it may be helpful in making outcome comparisons between different pulmonary
hypertension centres where patient demographics may vary. However, the utility of the
presented corrected MR volumetric measurements will be minimised when using MRI to
follow up treatment response in an individual patient.

Limitations

The major limitation of this work are the comparisons to data from a reference normal
population and the relatively small number of subjects (n=120) from which the regression
equations were derived to allow correction for age and gender. However, in our view the
study by Maceira et al as a comparative cohort provides the most well defined normal
population in which we were able to derive regression equations to adjust for age and gender.
The absence of other comparable normal populations which have measured MR variables
using the same methodology as we have, particularly with regards to the inclusion or
exclusion of trabeculae in RV mass and volume measurements means that our reference
equation is based on a small albeit well defined reference population structure. More work to
establish a larger cohort of “normals” to improve the confidence of correction is required. Validation of our observations in prospective studies at other centres would be helpful. Given the small number of deaths we have used a bivariate rather than a multivariate Cox proportional hazards model. All data in this study was from the baseline assessment of patients with IPAH, further work studying MRI predictors at follow-up would be of value in future studies.

Conclusions

In patients with idiopathic pulmonary arterial hypertension corrected RV end-systolic volume predicts mortality more strongly than RV end-diastolic volume, and has prognostic value independent of mRAP, CI and mVO2. Adjusting volumetric cardiac magnetic resonance measurements for patient age, gender and body surface area should be considered given the changing demographics and increasing age at diagnosis of patients with IPAH.

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Disclosures

None.
References

pulmonary arterial hypertension: Results from the pulmonary hypertension registry of the united kingdom and ireland. Am J Respir Crit Care Med. 2012;186:790-796.
Table 1. Demographics, right heart catheter (RHC) and cardiac MRI values for survivors and non-survivors. Cardiac MR measurements are presented corrected for age, gender and BSA

<table>
<thead>
<tr>
<th>Demographics</th>
<th>All patients</th>
</tr>
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<tbody>
<tr>
<td>N=80</td>
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</table>

Demographics
- Age (years): 59 ± 17
- Gender (female/male): 48/32
- WHO functional class: IV (18), III (48), II (14)

RHC
- mPAP (mmHg): 53 ± 11
- mRAP (mmHg): 11 ± 5
- PCWP (mmHg): 10 ± 3
- PVRI (dyn.s.cm⁻³.m⁻²): 1449 ± 599
- CI (L/min/m²): 2.6 ± 0.8
- Mixed venous O₂ (%): 62.2 ± 8.7

CMR phase contrast
- PA stroke volume index (ml/m²): 35 ± 15
- PA cardiac index (L/min/m²): 2.7 ± 1.1

Corrected CINE cardiac MR
- RV EDV index (%): 136 ± 40
- RV ESV index (%): 301 ± 121
- RV EF (%)*: 45 ± 20
- RV SV index (%): 61 ± 38
- LV EDV index (%): 63 ± 17
- LV ESV index (%): 74 ± 28
- LV EF (%)*: 92 ± 15
- LV SV index (%): 58 ± 18
- VMI (ratio)*: 0.9 ± 0.3

*% predicted by age, gender. Eg. RVEDVI predicted by age and gender/RVEDVI*100

*RVEF, LVEF and VMI are not indexed for BSA
Table 2. Univariate Cox proportional hazards regression analysis

<table>
<thead>
<tr>
<th>Demographics</th>
<th>Cox proportional hazards analysis</th>
</tr>
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<tbody>
<tr>
<td></td>
<td>Overall</td>
</tr>
<tr>
<td></td>
<td>Univariate</td>
</tr>
<tr>
<td></td>
<td>Hazard Ratio (95% CI)</td>
</tr>
<tr>
<td></td>
<td>p-value</td>
</tr>
<tr>
<td>Age</td>
<td>1.078 (1.029 to 1.129)</td>
</tr>
<tr>
<td>Sex</td>
<td>1.833 (0.868 to 4.339)</td>
</tr>
<tr>
<td>WHO functional class</td>
<td>3.900 (1.715 to 8.869)</td>
</tr>
<tr>
<td>RHC</td>
<td></td>
</tr>
<tr>
<td>mPAP</td>
<td>0.993 (0.956 to 1.0030)</td>
</tr>
<tr>
<td>mRAP</td>
<td>1.101 (1.017 to 1.191)</td>
</tr>
<tr>
<td>PVRI</td>
<td>1.000 (1.000 to 1.000)</td>
</tr>
<tr>
<td>PCWP</td>
<td>1.081 (0.938 to 1.246)</td>
</tr>
<tr>
<td>CI</td>
<td>0.533 (0.292 to 0.972)</td>
</tr>
<tr>
<td>Mixed venous O2</td>
<td>0.956 (0.915 to 0.999)</td>
</tr>
<tr>
<td>CMR phase contrast</td>
<td></td>
</tr>
<tr>
<td>PA stroke volume index</td>
<td>0.953 (0.920 to 0.988)</td>
</tr>
<tr>
<td>PA cardiac index</td>
<td>0.510 (0.303 to 0.858)</td>
</tr>
<tr>
<td>CINE cardiac MRI indexed for</td>
<td></td>
</tr>
<tr>
<td>BSA</td>
<td></td>
</tr>
<tr>
<td>RV EDV index</td>
<td>1.006 (0.996 to 1.016)</td>
</tr>
<tr>
<td>RV ESV index</td>
<td>1.010 (0.997 to 1.024)</td>
</tr>
<tr>
<td>RV EF*</td>
<td>0.985 (0.956 to 1.015)</td>
</tr>
<tr>
<td>RV SV index</td>
<td>0.999 (0.977 to 1.021)</td>
</tr>
<tr>
<td>LV EDV index</td>
<td>0.973 (0.938 to 1.009)</td>
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<tr>
<td>LV ESV index</td>
<td>1.003 (0.948 to 1.062)</td>
</tr>
<tr>
<td>LV EF*</td>
<td>0.980 (0.943 to 1.018)</td>
</tr>
<tr>
<td>LV SV index</td>
<td>0.943 (0.896 to 0.993)</td>
</tr>
<tr>
<td>CINE cardiac MR corrected for</td>
<td></td>
</tr>
<tr>
<td>age, gender and BSA (%)</td>
<td></td>
</tr>
<tr>
<td>RV EDV corrected</td>
<td>1.006 (0.999 to 1.013)</td>
</tr>
<tr>
<td>RV ESV corrected</td>
<td>1.004 (1.001 to 1.006)</td>
</tr>
<tr>
<td>RV EF* corrected</td>
<td>0.986 (0.966 to 1.007)</td>
</tr>
<tr>
<td>RV SV corrected</td>
<td>1.000 (0.990 to 1.010)</td>
</tr>
<tr>
<td>LV EDV corrected</td>
<td>0.989 (0.963 to 1.015)</td>
</tr>
<tr>
<td>LV ESV corrected</td>
<td>1.007 (0.994 to 1.021)</td>
</tr>
<tr>
<td>LV EF* corrected</td>
<td>0.982 (0.957 to 1.008)</td>
</tr>
<tr>
<td>LV SV corrected</td>
<td>0.975 (0.951 to 1.000)</td>
</tr>
<tr>
<td>VMI*</td>
<td>1.038 (0.243 to 4.433)</td>
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</tbody>
</table>

*RVEF, LVEF and VMI are not indexed for BSA
Table 3. Presents the Cox proportional hazards analysis for scaled CMR volumes indexed for BSA, corrected for BSA and age and sex. Scaling was performed by dividing the mean by the standard deviation for each metric.

<table>
<thead>
<tr>
<th></th>
<th>Scaled and indexed BSA</th>
<th></th>
<th>Scaled and corrected Age, sex and BSA</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>HR</td>
<td>p-value</td>
<td>HR</td>
<td>p-value</td>
</tr>
<tr>
<td></td>
<td>(95% CI)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>RV EDV</td>
<td>1.213 (0.868 to 1.695)</td>
<td>0.259</td>
<td>1.318 (0.969 to 1.791)</td>
<td>0.078</td>
</tr>
<tr>
<td>RV ESV</td>
<td>1.315 (0.914 to 1.893)</td>
<td>0.140</td>
<td>1.551 (1.152 to 2.087)</td>
<td>0.004</td>
</tr>
<tr>
<td>RV EF*</td>
<td>0.823 (0.554 to 1.224)</td>
<td>0.336</td>
<td>0.783 (0.511 to 1.140)</td>
<td>0.187</td>
</tr>
<tr>
<td>RV SV</td>
<td>0.847 (0.060 to 11.858)</td>
<td>0.902</td>
<td>0.999 (0.676 to 1.476)</td>
<td>0.995</td>
</tr>
<tr>
<td>LV EDV</td>
<td>0.694 (0.431 to 1.118)</td>
<td>0.133</td>
<td>0.828 (0.532 to 1.288)</td>
<td>0.403</td>
</tr>
<tr>
<td>LV ESV</td>
<td>1.024 (0.680 to 1.540)</td>
<td>0.911</td>
<td>1.231 (0.837 to 1.811)</td>
<td>0.291</td>
</tr>
<tr>
<td>LV EF*</td>
<td>0.813 (0.549 to 1.205)</td>
<td>0.302</td>
<td>0.766 (0.519 to 1.132)</td>
<td>0.181</td>
</tr>
<tr>
<td>LV SV</td>
<td>0.588 (0.369 to 0.936)</td>
<td>0.025</td>
<td>0.631 (0.400 to 0.995)</td>
<td>0.048</td>
</tr>
</tbody>
</table>

*RVEF and LVEF corrected for age and sex only.
Table 4. Bivariate Cox proportional hazards regression analysis of scaled and corrected RVESV on covariates

<table>
<thead>
<tr>
<th>Bivariate analysis of RVESV</th>
<th>Hazard Ratio of RVESV with covariate</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>WHO functional class</td>
<td>1.513 (1.074 to 2.132)</td>
<td>0.018</td>
</tr>
<tr>
<td>mRAP</td>
<td>1.438 (1.014 to 2.037)</td>
<td>0.041</td>
</tr>
<tr>
<td>Cardiac index</td>
<td>1.417 (1.013 to 1.984)</td>
<td>0.042</td>
</tr>
<tr>
<td>mVO2</td>
<td>1.492 (1.084 to 2.053)</td>
<td>0.018</td>
</tr>
</tbody>
</table>
Figure Legends

**Figure 1.** Kaplan Meier plots showing the prognostic value of CMR right ventricular volume indices indexed for BSA alone (left) and corrected for age, gender and BSA (right).

**Figure 2.** Kaplan Meier plots showing the prognostic value of CMR left ventricular volume indices indexed for BSA alone (left) and corrected for age, gender and BSA (right).

**Figure 3.** Kaplan Meier plots showing the prognostic value of CMR left and right ventricular ejection fraction uncorrected (left) and corrected for age and gender (right).

**Figure 4.** Kaplan Meier plots showing the prognostic value of CMR left and right ventricular stroke volume indices indexed for BSA alone (left) and corrected for age, gender and BSA (right).
CMR indices corrected for body surface area only

RVEDV < 96 ml/m²

Log rank $\chi^2 = 2.89$, P = 0.089

RVEDV ≥ 96 ml/m²

CMR indices corrected for age, gender and body surface area

RVEDV < 131 % predicted

Log rank $\chi^2 = 7.290$, P = 0.007

RVEDV ≥ 131 % predicted

RVESV < 70 ml/m²

Log rank $\chi^2 = 1.283$, P = 0.257

RVESV ≥ 70 ml/m²

RVESV < 290 % predicted

Log rank $\chi^2 = 9.44$, P = 0.0020

RVESV ≥ 290 % predicted
CMR indices corrected for body surface area only

LVEDV > 45 ml/m²

LVEDV ≤ 45 ml/m²

Log rank $\chi^2 = 2.89$, P=0.089

Years since MRI

CMR indices corrected for age, gender and body surface area

LVEDV > 60 % predicted

LVEDV ≤ 60 % predicted

Log rank $\chi^2 = 0.300$, P=0.083

Years since MRI

LVESV > 17 ml/m²

LVESV ≤ 17 ml/m²

Log rank $\chi^2 = 0.537$, P=0.464

Years since MRI

LVESV > 69 % predicted

LVESV ≤ 69 % predicted

Log rank $\chi^2 = 0.493$, P=0.483

Years since MRI
CMR indices (RVEF and LVEF do not require correction for BSA)

- LVEF > 62%
- LVEF ≤ 62%

Log rank $\chi^2 = 0.731$, $P = 0.393$

Years since MRI

CMR indices corrected for age and gender

- LVEF > 91% predicted
- LVEF ≤ 91% predicted

Log rank $\chi^2 = 1.170$, $P = 0.280$

Years since MRI

- RVEF > 30%
- RVEF ≤ 30%

Log rank $\chi^2 = 1.364$, $P = 0.243$

Years since MRI

- RVEF > 45% predicted
- RVEF ≤ 45% predicted

Log rank $\chi^2 = 2.87$, $P = 0.090$

Years since MRI
CMR indices corrected for body surface area only

LVSV > 27 ml/m²

LVSV ≤ 27 ml/m²

Log rank $\chi^2 = 6.75$, $P=0.009$

Percent survival (%)

Years since MRI

CMR indices corrected for age, gender and body surface area

LVSV > 57 % predicted

LVSV ≤ 57 % predicted

Log rank $\chi^2 = 7.35$, $P=0.007$

Percent survival (%)

Years since MRI

RVSV > 27 ml/m²

RVSV ≤ 27 ml/m²

Log rank $\chi^2 = 0.053$, $P=0.819$

Percent survival (%)

Years since MRI

RVSV > 54 % predicted

RVSV ≤ 54 % predicted

Log rank $\chi^2 = 0.411$, $P=0.521$

Percent survival (%)

Years since MRI
Prognostic Value of Cardiovascular Magnetic Resonance Imaging Measurements Corrected for Age and Gender in Idiopathic Pulmonary Arterial Hypertension

Andrew J. Swift, Smitha Rajaram, Michael J. Campbell, Judith Hurdman, Steve Thomas, Dave Capener, Charlie Elliot, Robin Condliffe, Jim M. Wild and David G. Kiely

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