# SAPHIRE : Stress and Pulmonary Hypertension in Rheumatoid Evaluation – A Prevalence Study

**Reeves G [1,2,3], Collins N [4], Hayes P [4], Knapp J [1,2,3], Squance M [1,2,3], Tran H [3], Bastian B [4].**

[1]Autoimmune Resource & Research Centre, NSW, Australia
[2] HNELHD, Immunology; NSW, Australia
[3] Pathology North, Clinical Chemistry; NSW Australia
[4] HNELHD, Cardiology; NSW, Australia

## Introduction

PAH is a rare disease that is diagnosed when medical tests reveal increased resistance to flow in the pulmonary artery, pulmonary vein, or pulmonary capillaries due to narrowing of the blood vessels running from the right-side of the heart to the lungs. This resistance is shown by elevated pulmonary artery pressure. The pulmonary arteries are major blood vessels that carry blood from the heart to the small blood vessels in the lungs where oxygen exchange takes place.

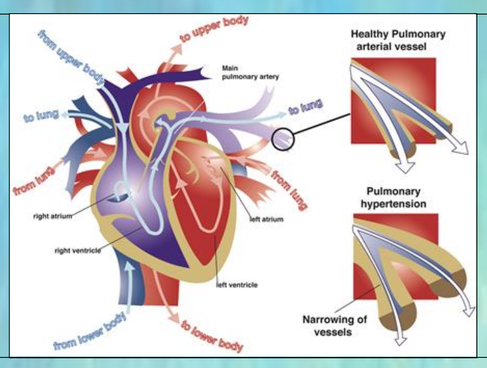


**Figure 1** Blood flow: heart and arterial vessels in PAH

PAH causes breathlessness and can potentially progress to right heart failure and death. PAH is more common in patients with autoimmune conditions, particularly scleroderma and its variants. Rheumatoid arthritis (RA) is another autoimmune condition, featuring symmetrical erosive polyarthropathy and may involve the vasculature, eyes, lungs and other organs. The shared pathogenesis between rheumatoid and other autoimmune conditions has raised the question of whether patients with RA may also display a heightened prevalence of PAH.

PAH is often silent, with the development of clinical symptoms often signalling the presence of advanced disease, associated with poor survival. With available therapeutic options (including phosphodiesterase inhibitors, prostacyclin analogues, and dual-receptor or single-receptor (ET-A) endothelin blockade), and given the irreversibility of advanced pathology associated with PAH, an impetus is provided for earlier detection of PAH in at-risk populations.

This study explores the prevalence of PAH in a population of unselected individuals with RA, using exercise echocardiography (EchoCG).

## Method

80 randomly-selected participants with RA were studied. They completed WHO functional class assessment, 6 minute walk distance (6MWD) testing, pulmonary function tests (including DLCO) and Doppler echocardiography (+ stress). Right heart catheterisation (RHC) occurred in the six patients who consented to it; the remaining 74 patients were assessed solely by echocardiography (Echocardiographically-derived elevation of pulmonary pressure (EDEPP): pulmonary artery systolic pressure (PASP) > 35 mmHg at rest or > 40 with exercise).

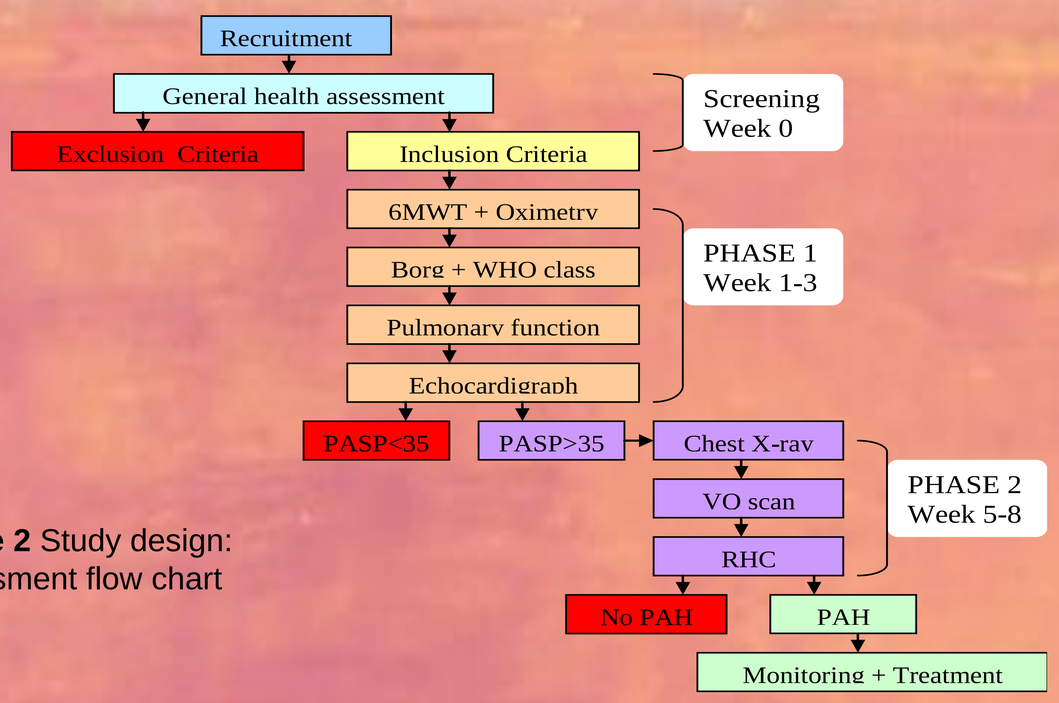


**Figure 2** Study design: assessment flow chart

## Results

Study population had a mean age of 60; gender ratio of 32 male:48 female; BMI 30.0 +/- 6.2; and were WHO Class II functional class dominated (96.2%).

Significant reductions in DLCO (78.8 vs 85.3% predicted, p = 0.04) and 6MWD (356.8 vs 441.3 m, p < 0.05) were noted in patients with (vs. without) EDEPP. PAH prevalence in these RA patients was 14% (resting PASP > 35 mmHg).

**Table 1** Patient characteristics by PAH status (n=80)

| | *PAH Determined by RHC (n=6)* | | | *PAH Determined by EchoCG (n=74)* | | |
|---|---|---|---|---|---|---|
| | *No PAH (n=4 [67%])* | *PAH (n=2 [33%])* | *P value* | *No PAH (n=56 [76%])* | *PAH (n=18 [24%])* | *P value* |
| *Age* | *62.3 ± 9.3* | *58.0 ± 12.7* | *0.66* | *60.0 ± 9.8* | *60.6 ± 11.3* | *0.82* |
| *WHO Class II* | *4* | *2* | - | *56* | *15* | - |
| WHO Class III | *0* | *0* | - | *0* | *3* | - |
| BMI (kg.m-2) | *32.5 ± 5.2* | *45.7 ± 7.3* | *0.06* | *29.0 ± 5.6* | *31.1 ± 5.7* | *0.16* |
| CRP (mg.L-1) | *20.2 ± 20.0* | *4.1 ± 0* | - | *32.7 ± 57.3* | *23.5 ± 21.0* | *0.55* |
| CCP (U.L-1) | *223.3 ± 158.1* | *312 ± 0* | - | *111.8 ± 123.4* | *110.8 ± 115.9* | *0.98* |
| PASPr * | *31.8 ± 4.5* | *37.5 ± 14.8* | *0.47* | *25.5 ± 3.3* | *40.8 ± 20.4* | *<0.05* |
| PASPe ** | *48.8 ± 15.7* | *51.5 ± 9.2* | *0.84* | *28.2 ± 5.0* | *42.5 ± 5.8* | *<0.05* |
| REEP *** | *17 ± 12.2* | *14 ± 5.7* | *0.77* | *3.1 ± 4.5* | *6.3 ± 21.3* | *0.31* |
| DLCO (% predicted) | *80.8 ± 14.2* | *92 ± 14.1* | *0.41* | *85.3 ± 13.3* | *78.8 ± 14.2* | *0.04* |
| 6MWD (m) | *382.8 ± 19.2* | *290 ± 12.7* | *0.18* | *441.3 ± 105.8* | *356.8 ± 92.7* | *<0.05* |

* PASPr - resting, mmHg
** PASPe - exercise, mmHg
*** REEP - rise in exercise-echo pressure, mmHg

**Table 2** PAH prevalence in RA (n=80)

| | |
|---|---|
| *Elevated mean PAP (RHC)* | *2 / 6 (33%)* |
| *Elevated resting PASP (EchoCG)* | *11 / 80 (14%)* |
| *Elevated exercise PASP (EchoCG)* | *17/80 (21%)* |

## Conclusions

The high prevalence of EDEPP in this population (14%) suggests that RA may be a risk factor for PAH. This warrants further replication and, ideally, exploration via RHC. Patients with RA may represent another autoimmune population for whom PAH screening with non-invasive tools such as EchoCG is justified.

## Acknowledgements

Gabor Major, Stephen Oakley, Stuart Turner, Patrick Diu, David Mathers, Siva Ratnarajah, John Glass, John van der Kallen, and Laurent Quiqueree.

RA patients of ARRC and the Rheumatology clinics of JHH

Morgan Penkae Williams – GriphonGraphics

arrc@hnehealth.nsw.gov.au
www.autoimmune.org.au