# The Right Heart-Pulmonary Circulation Unit in Systemic Hypertension

Olga Vriz, MD, PhD[a,*], Yoshiki Motoji, MD[b], Francesco Ferrara, MD, PhD[c], Eduardo Bossone, MD, PhD[c], Robert Naeije, MD, PhD[b]

**KEYWORDS**

• Systemic hypertension • Pulmonary hypertension • Arterial stiffness • Right ventricle • Right heart failure

**KEY POINTS**

- Hypertension is a cause of altered right ventricular function and increased pulmonary vascular resistance.
- Exercise stress testing discloses increased pulmonary vascular reactivity and decreased aerobic exercise.
- Altered right ventricular function occurs in the presence of increased pulmonary vascular resistance and left ventricular hypertrophy.
- The clinical relevance of altered function of the The Right Heart– Pulmonary Circulation Unit in Systemic Hypertensionis not known.

## INTRODUCTION

Hypertension has long been known to affect the pulmonary circulation and the right heart. As early as in the late 1940s, Werkö and Hagerlof[1] mentioned that patients with hypertension had somewhat higher pulmonary artery pressure (PAP) than healthy controls. In their review of hypertension and the heart in 1974, Cohn and colleagues[2] noted that right ventricle (RV) in hypertension seems impaired, with a tendency to increased right atrial pressure (RAP) but a normal or slightly decreased stroke volume (SV). In 1977, Atkins and colleagues[3] found a positive correlation between systemic vascular resistance (SVR) and pulmonary vascular resistance (PVR) in 110 hypertensive patients and wondered if there could be a causal relationship. In 1978, Olivari and colleagues[4] reported on depressed RV function and increased PVR in patients with hypertension, without this related to left ventricular (LV) dysfunction, pulmonary blood flow, lung mechanics, or arterial $P_{O_2}$, $P_{CO_2}$, or pH. In 1980, Ferlinz[5] measured a depressed cineangiographic RV ejection fraction (EF) together with high-normal mean normal PAP (mPAP) and wedged PAP (PAWP) in patients with uncomplicated hypertension.

Thus, the idea that systemic hypertension is associated with abnormal RV and pulmonary vascular function without this explained by diastolic or systolic LV failure has been floating around in the literature for decades. The purpose of this review is to refresh this knowledge with input of recent advances and clinical relevance.

Disclosure Statement: The authors have nothing to disclose.

[a] Adult Cardiology Consultant, Heart Centre Department, King Faisal Hospital and Research Center, P.O. Box 3354 Riyadh, Saudi Arabia; [b] Department of Cardiology, Erasmus University Hospital, Campus CP 604, 808 Lennik Rd., 1070, Brussels, Belgium; [c] Department of Cardiology, Cava de' Tirreni and Amalfi Coast Hospital, University of Salerno, Via Giovanni Paolo II, 132, 84084 Fisciano, Salerno, Italy

* Corresponding author.

*E-mail address:* olgavriz@yahoo.com

Heart Failure Clin 14 (2018) 247–253

https://doi.org/10.1016/j.hfc.2018.02.002

## THE PULMONARY CIRCULATION IN HYPERTENSION

Hypertension is a cause of LV hypertrophy and eventual failure, which in turn is a cause of upstream transmission of increased LV end-diastolic pressure, increased pulmonary vascular pressures, pulmonary vasoconstriction, and vascular remodeling ending up in RV failure in a proportion of these patients.[6,7] When increased PVR and decreased RVEF are observed in patients with hypertension, it is, therefore, essential to explore the left heart with help if needed of fluid challenge and exercise stress tests. At the moment of evaluation, patients with left heart failure may present with a normal PAWP in the context of optimized therapy and bed rest. On the other hand, reevaluation after several weeks or months of normalized left heart filling pressures may be needed to observe abnormally increased PVR return to normal.[6,7] Exclusion of heart failure in hypertensives with altered RV function and/or increased PVR may be challenging.

The first comprehensive study on the pulmonary circulation in uncomplicated hypertension was reported by Olivari and colleagues.[4] They investigated 16 hypertensives with LV hypertrophy and 17 hypertensives without LV hypertrophy and compared the results to 10 controls. The diagnosis of LV hypertrophy was based on electrocardiographic and echocardiographic criteria. On average, PVR was double of that of controls (160 dyne·s/cm$^{-5}$ vs <80 dyne·s/cm$^{-5}$) whereas RAP and PAWP were increased but mostly within limits of normal. The increased PVR was unrelated to LV filling pressures, pulmonary blood flow or volume, pleural pressure, and arterial blood gases. The investigators believed their findings could be due to shared mechanisms of vascular structure and tone by the pulmonary and systemic circulations in hypertension.

Guazzi and colleagues[8] reported on pulmonary hemodynamics in 36 patients with hypertension and confirmed the findings of Olivari and colleagues.[4] Their patients had also increased PVR, which was correlated with SVR but unrelated to PAWP, cardiac output, lung mechanics, and blood gases. Calcium channel blockade with nifedipine brought PVR and SVR back to normal, which suggested to the investigators a common calcium-dependent mechanism for both increased PVR and SVR in hypertension.

Fiorentini and colleagues[9] tested the effects of arithmetics or cold exposure as adrenergic stimuli in 26 patients with early-stage hypertension without increased LV filling pressures compared with 10 healthy controls. Mental stress increased cardiac output and heart rate and decreased SVR. Cold exposure stress was associated with an increased SVR and almost no change in cardiac output and heart rate. Patients with hypertension had a higher baseline PVR than the controls. Both mental and cold pressor tests increased PVR in the hypertensives by 42% and 29%, respectively, whereas PVR did not change in the controls. The investigators concluded that abnormal pulmonary vascular tone in hypertension may be the consequence of increased sympathetic nervous system activity.

Guazzi and colleagues[10] investigated the effect of hypoxic breathing (17%, 15%, and 12% of oxygen in nitrogen, respectively) in 43 hypertensives and 17 controls. Hypertensives had a lower threshold and increased pulmonary vascular reactivity to hypoxia. This pattern was not related to differences in severity of the hypoxic stimulus, plasma catecholamine concentration, hypocapnia, or respiratory alkalosis induced by hypoxia. Calcium channel blockade with nifedipine was able to almost abolish hypoxic pulmonary vasoconstriction in both the normotensives and the hypertensives. The $\alpha$-adrenergic blocker phenoxybenzamine increased cardiac output and decreased PVR with no change in PAP in both groups as well. The investigators concluded that increased pulmonary vascular reactivity in hypertension was explained by altered calcium-dependent regulation of pulmonary vascular tone rather than by sympathetic over-reactivity.

The finding of increased PVR in uncomplicated hypertension has not been universal. Fagard and colleagues[11] reported a PVR, on average, of 0.65 Wood units, well within the normal range, in patients with hypertension who were included in a trial on the hemodynamic effects of labetalol. The same investigators subsequently reported on a PVR, on average, of 0.63, which was related to age but not to PAWP or systemic blood pressure in 16 patients with mild to moderate hypertension.[12] In the same study, refined PVR assessments by multipoint pulmonary vascular pressure plots during exercise were within normal limits as well. The investigators concluded that the pulmonary circulation is normal in uncomplicated hypertension.

These discrepancies might be related to selection biases of small series of patients with perhaps underdiagnosed left heart problems and report of only moderate increases in PVR, below the cutoff value of 3 Wood units, which is diagnostic of pulmonary hypertension.

The clarify the issue, the pulmonary circulation was investigated using Doppler echocardiography in 113 patients with early uncomplicated stage I or