Dr Konecny is employed by Transonic Scisense Inc but has no direct or indirect financial relationships relevant to the contents of this letter to the Editor to disclose.

2. Katz MG, Fargnoli AS, Hajjar RJ, Hadri L. Pulmonary hypertension arising from left heart disease causes intrapulmonary venous arterialization in rats. *J Thorac Cardiovasc Surg.* 2018;155:281-2.
3. Fujimoto Y, Minamisawa S. Elusive mechanisms responsible for pulmonary hypertension. *J Thorac Cardiovasc Surg.* 2018;155:282.

<https://doi.org/10.1016/j.jtcvs.2018.04.093>

DIRECT MEASUREMENT OF LEFT ATRIAL AND PULMONARY ARTERY PRESSURE IN RATS WITH PULMONARY HYPERTENSION

Reply to the Editor:

We thank Dr Konecny for his comments and insightful remarks¹ concerning our recent letter to the Editor.² We would like to clarify some practical points concerning measurement of left atrial and pulmonary artery pressures in the rat model. In contrast to pulmonary arterial hypertension (PAH) arising from other etiologies, pulmonary hypertension due to left heart disease (PAH-LHD) is characterized by an elevated left atrial pressure (LAP; postcapillary pulmonary hypertension) with or without an additional precapillary component. The pathophysiology of PAH-LHD is complex, and a number of aspects remain incompletely understood. In most cases with PAH-LHD, the development of pulmonary hypertension is due to increased LAP and pulmonary venous congestion.

The calculation of pulmonary vascular resistance (PVR) is essential in the assessment of PAH. PVR is determined by the resistance of the pulmonary arteries on the basis of Poiseuille's law. Briefly, this states that resistance is inversely proportional to the fourth power of the radius of the blood vessel and directly proportional to the length of the blood vessel and viscosity of the blood. PVR is defined as the ratio of the transpulmonary gradient (difference between mean pulmonary artery pressure and LAP) over cardiac output.

It is well known that pulmonary capillary wedge pressure provides an indirect estimate of LAP. In clinical situations it is very feasible to measure pulmonary

capillary wedge pressure with a Swan-Ganz catheter, however not LAP without additional invasive means. With respect to the animal model however, it is a completely different situation in rats because of several challenges with scale and subsequent access through reliable instrumentation.

In our severe model of pulmonary hypertension, we routinely recorded invasive blood pressure via puncture access into the pulmonary arterial trunk. This point of access is located between the pulmonary valve and the bifurcation point of the right and left pulmonary arteries. Separately, we measure LAP directly through the left atrial appendage via sternotomy access before euthanasia. With this strategy, we obtain pulmonary artery pressure and LAP consistently. Just before the euthanasia and on the same day, we have cardiac output as well as full functional parameters derived from high fidelity small animal 7T magnetic resonance imaging.

We can understand how some groups find it very challenging to measure these pressures consistently. Initially, we successfully measured the pressure through a left thoracotomy in the 2 to 3 intercostal space in intermediate time points, however, most are acquired terminal.

Practical technical points that groups might find useful in executing these measurements are disclosed herein. Our routine terminal protocol is to open the chest and exposes the pulmonary artery (PA) and LAP catheterization access points for guiding a miniaturized 1.2-French pressure catheter. Anesthesia and proper ventilation are necessary criteria to ensure consistent measurements, because complications during these procedures can significantly alter blood pressures. Generally our guidelines are as follows: we maintain anesthesia (2.5% isoflurane, 1:1 O₂/air mix) via intubation (tube, 16-gauge) attached to a VentElite Harvard Apparatus (Holliston, Mass) unit. Typical ventilator settings: breathing frequency, 70 breaths per minute; tidal volume approximately 3.5 mL/min depending on the animal weight; and inspiratory/expiratory ratio, 1:1. PA and LAP pressures are then recorded by using a commercially available rodent pressure-volume catheter 1.2-French connected to an ADVantage PV System (Transonic Inc, London, Ontario, Canada). First, PA pressure is measured by introducing a 27-gauge needle into the pulmonary artery, then advancing the 1.2-French catheter directly generating a curve (Figure 1, A and B). Next, an access point is made into the left atrium. To achieve this, we place purse strings to lift the left atrial appendage. This is achieved with a 7-0 prolene purse suture. The actual puncture access is then achieved with the use of either a

Authors have nothing to disclose with regard to commercial support.

27-gauge needle or 22-gauge angiocath, which is inserted between the purse suture or puncturing the left appendage. The 1.2-French catheter is then advanced into the left atrium (Figure 1, C) with real time recording (Figure 1, D). After catheter withdrawal, the purse sutures are tightened. Typically we do not have any major issues with bleeding.

Analyses were performed when steady state was reached over an interval of at least 10 seconds.

We anticipate that our expanded discussion herein will help the research community understand the technical

aspects of conducting high-quality research in pulmonary hypertension with respect to logging critical pressures.

Michael G. Katz, MD, PhD

Anthony S. Fagnoli, PhD

Yassine Sassi, PhD

Roger J. Hajjar, MD

Lahouaria Hadri, PhD

Cardiovascular Research Center

Department of Cardiology

Icahn School of Medicine at Mount Sinai

New York, NY

Funded by the National Institutes of Health, National Heart Lung and Blood Institute (NHLBI) grants 7R01 HL083078, 5R01 HL133554.

FIGURE 1. A, Sternotomy of rat with pulmonary artery exposed (yellow arrow) featuring placement of pressure catheter (black). B, Main pulmonary artery pressure curve. C, Sternotomy of rat with left atrium exposed (yellow arrow). A 7-0 prolene suture was used to lift the left atrial appendage. Pressure catheter (black) was advanced as shown into the left atrium. D, Left atrium pressure curve.

References

1. Konecny F. Left atrial measurement in a rat is currently impossible due to size limitations of balloon occlusion catheter. *J Thorac Cardiovasc Surg.* 2018;156:1160-1.
2. Katz MG, Fagnoli AS, Hajjar RJ, Hadri L. Pulmonary hypertension arising from left heart disease causes intrapulmonary venous arterialization in rats. *J Thorac Cardiovasc Surg.* 2018;155:281-2.

<https://doi.org/10.1016/j.jtcvs.2018.05.026>