LEFT ATRIAL PRESSURE MEASUREMENT IN A RAT IS CURRENTLY IMPOSSIBLE DUE TO SIZE LIMITATIONS OF BALLOON OCCLUSION

CATHETER

To the Editor:

I would like to note that a balloon catheter small enough to measure pulmonary capillary wedge pressure or (pulmonary artery occlusion pressure) does not currently exist to perform the estimation of left atrial (LA) pressure in the rat. Models of rat pulmonary hypertension secondary to left heart disease (PH-LHD) are scarce in current scientific literature, so I read with great pleasure the concise report by Fujimoto and colleagues¹ addressing PH-LHD in a diligently performed animal study. Pulmonary hypertension was created by partially clipping the LA while carefully avoiding the circumflex artery. Because the LA is a complex structure, depending on clip position, blood flow redistribution might vary according to individual left or right pulmonary vein occlusion. Functional assessment of this novel hemodynamic model was provided by echocardiography at 2, 4, 6, and 10 weeks, with final acute right ventricular (RV) and left ventricular (LV) pressure-volume curves (PV) determined by open chest catheterization at 10 weeks to compare the animals with LA stenosis and a sham operation control group. This model, especially the hemodynamic part of it, has multiple data points that both show pathophysiologic correlations with echocardiography and Doppler flow imaging and later correlate it with the acute LV and RV PV data. Moreover, an interesting observation has been drawn by Fujimoto and colleagues¹ in the case of pulmonary vein progressive medial hypertrophy during PH-LHD. Two major findings of the study were that the LA stenosis group had double the LV inflow velocity and significantly thicker interventricular septa than the sham operated group. Presented RV and LV PV data in Table 1 of the article of Fujimoto and colleagues¹ are more or less in correlation with the presented

echocardiography. One outstanding question to be answered in further exploratory modeling of LA stenosis at the model end point is the electrocardiographic characteristics of PH-LHD with correlation to LV and RV PV catheterizations.

I partially agree with the Letter to the Editor of Katz and colleagues² about the article of Fujimoto and colleagues,¹ where they offer a pathophysiological explanation of the PH-LHD model. More research needs to be performed, however, for a full understanding of this model from both pathohemodynamic and pathomorphologic angles and draw conclusions. Although I agree with the requirement of Katz and colleagues² of measurement of pulmonary artery pressure (PAP) in this model as one of the pillars of the pathohemodynamic model description, I would like to add that the correct characteristics of LA pressure would be best determined by pulmonary capillary wedge pressure (or pulmonary artery occlusion pressure) as a surrogate for LA pressure and *not* the PAP. In the rat, however, this is currently impossible because of the limitations of making such a small balloon occlusion catheter. In the study limitation section of the original article, Fujimoto and colleagues¹ rightly point out this limitation, which was overlooked by Katz and colleagues.² By measuring only PAP, some impression of the pathohemodynamics can be characterized; however, these changes may not correlate with the pathomorphologic changes in pulmonary vein medial hypertrophy, because LA pressure cannot be currently measured. In addition, I would respectfully disagree with Fujimoto and colleagues³ in their response to the letter of Katz and colleagues² regarding the *size* of the catheter used for PAP measurement. Multiple users of pressure catheters were able to perform this open chest PAP measurement in a rat, furthermore the company in question has wide variability of pressure catheter sizing (from 1.2F and 1.6F suitable for such measurement). I believe that measurement may have nothing to do with the “thinner” size of the catheter shaft, as stated by Fujimoto and colleagues,³ and rather propose that the catheter's proper application might be desirable while accessing the pulmonary artery.

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References

1. Fujimoto Y, Urashima T, Kawachi F, Akaike T, Kusakari Y, Ida H, et al. Pulmonary hypertension due to left heart disease causes intrapulmonary venous arterialization in rats. *J Thorac Cardiovasc Surg*. 2017;154:1742-53.e8.

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.

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<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