Effect of Balloon Inflation Volume on Pulmonary Artery Occlusion Pressure in Patients With and Without Pulmonary Hypertension

Adriano R. Tonelli, MD; Kamal K. Mubarak, MD, FCCP; Ning Li, PhD; Robin Carrie, ARNP; and Hassan Alnuaimat, MD

Background: Pulmonary artery occlusion pressure (PAOP) is used to differentiate patients with pulmonary hypertension (PH) associated with left-sided heart disease from other etiologies. Technical errors in the measurement of PAOP are common and lead to incorrect classification of the etiology of PH. We investigated the agreement among PAOP measurements obtained from both pulmonary arteries with balloon full (1.5 mL) and half (0.75 mL) inflation in patients undergoing right-sided heart catheterization for suspected PH.

Methods: Thirty-seven patients suspected or known to have PH who underwent right-sided heart catheterization were included. Seventy-six percent had PH (mean pulmonary arterial pressure > 25 mm Hg). The validity of the measurements was assessed by using five preestablished criteria based on hemodynamic, fluoroscopic, and gasometric data. For each patient, the measurement that most likely represented the left atrial pressure was labeled “best PAOP.”

Results: Seventy percent of all the PAOP measurements met at least four of the five preestablished criteria for validity. In patients with PH ($n = 28$), the mean $\pm$ SE PAOP was 23.1 ± 2 and 19.1 ± 2 mm Hg for balloon full and half inflation, respectively, in the right pulmonary artery and 23.54 ± 2 and 19.07 ± 2 mm Hg for balloon full and half inflation, respectively, in the left pulmonary artery ($P = .05$). Bland-Altman analysis revealed lower bias and narrower limits of agreement with balloon half inflation. Wedge angiography showed that some balloon inflations failed to occlude upstream flow, whereas others had collateral vessels draining after the occlusion.

Conclusions: PAOP can be falsely elevated in patients with PH according to the balloon inflation volume. Balloon half inflation was safe and correlated with higher precision and lower bias in the PAOP measurements.

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Abbreviations: LAP = left atrial pressure; PA = pulmonary artery; PAC = pulmonary artery catheter; PAOP = pulmonary artery occlusion pressure; PAP = pulmonary arterial pressure; PH = pulmonary hypertension; RHC = right-sided heart catheterization

Pulmonary hypertension (PH) is defined as a resting mean pulmonary arterial pressure (PAP) of ≥ 25 mm Hg.¹ Right-sided heart catheterization (RHC) is required to confirm this diagnosis.^{2,3} RHC

also provides prognostic information, tests the vaso-reactivity of the pulmonary circulation, and measures pulmonary artery occlusion pressure (PAOP). This last measurement helps to differentiate PH associated with left-sided heart disease (group 2 of the

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Affiliations: From the Pulmonary Vascular Disease Program (Drs Tonelli, Mubarak, and Alnuaimat and Ms Carrie), Division of Pulmonary and Critical Care, Department of Medicine, and Department of Epidemiology and Biostatistics (Dr Li), University of Florida, Gainesville, FL.

Correspondence to: Adriano R. Tonelli, MD, Health Science Center, PO Box 100225, 1600 SW Archer Rd, Rm M452,

Gainesville, FL 32610-0225; e-mail: Adriano.Tonelli@medicine.ufl.edu

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clinical classification of PH; from the 4th World Symposium on PH held in 2008 in Dana Point, California) from other conditions.⁴ Patients with PH associated with left-sided heart disease usually have a PAOP > 15 mm Hg and a transpulmonary gradient (difference between mean PAP and PAOP) $\leq$ 12 mm Hg.²

PAOP is the pulmonary artery catheter (PAC)-derived measurement that is subject to the greatest error in measurement and interpretation.^{5,6} This measurement represents the pressure in the medium to large pulmonary veins at the confluent point where the postcapillary veins supplied by the occluded artery become confluent with veins derived from nonoccluded pulmonary arteries (PAs). It closely approximates the left atrial pressure (LAP) because there are no resistance vessels beyond the confluent point.⁷ The correlation between PAOP and LAP is very good in most studies,^{8,9} but as PAOP increases, the correlation with LAP is subject to considerable error.¹⁰

In patients with PH, several factors complicate the measurement and interpretation of PAOP, reducing the clinical utility of PAOP in both diagnosis and treatment.¹¹⁻¹⁴ We hypothesized that the difficulty in the measurement of PAOP in these patients is due to the distortion of the proximal pulmonary vasculature, which prevents complete occlusion of the vessels by the PAC balloon.^{15,16} In certain cases, therefore, it might be possible to overcome this anatomic difficulty by reducing the volume of air injected in the PAC balloon, allowing an occlusion of a more distal and less-distorted vessel. We sought to determine the agreement among the PAOP measurements when obtained in both PAs with balloon full and half inflation.

MATERIALS AND METHODS

After obtaining institutional review board approval from the University of Florida (Study ID: H-280-2009), all subjects who underwent RHC for evaluation of PH from September 2009 to March 2010 were invited to participate. Informed consent was obtained from all subjects before enrollment. During RHC, patients were supine in a steady state, relaxed, and breathing room air or oxygen to maintain pulse oximetry > 90%. We cannulated preferably the right internal jugular vein with a 7F introducer using minimal local anesthesia. We inserted a 7F balloon-tipped PAC (Model 131HF7; Edwards Lifesciences; Irvine, California) and advanced it by fluoroscopic guidance to the pulmonary circulation.¹⁷ We used the Transpac (Hospira Inc; Lake Forest, Illinois) disposable pressure transducers that were zeroed at the left atrial level (fourth intercostal level at the midaxillary line) and checked carefully for air bubbles and loose connections. We recorded pressure tracings on a paper strip and obtained hemodynamic measurements by averaging several breathing cycles at end expiration.

We measured the PAOP on both left and right PAs with balloon full (1.5 mL of air and balloon diameter of 1.3 cm) and half (0.75 mL of air and balloon diameter of ~0.9 cm) inflation. In all but three patients, the PAC spontaneously entered the right PA. After obtaining the PAOP measurements with balloon full and half inflation, the catheter was withdrawn and advanced to

the contralateral PA. In only 20% of patients in whom the catheter initially went to the right PA, catheter manipulation alone was successful in leading it to left PA. In the remaining patients, we used a Safe-T-J (Cook Inc; Bloomington, Indiana) curved guidewire (diameter, 0.025 in) to guide the PAC to the desired location.

Blood draws from the distal port of PAC for oximetry analysis were attempted during each of the four PAOP measurements. When blood was withdrawn, the initial 10 to 15 mL were discarded (vascular dead space). Oxygen saturation was measured using Avoximeter 1000E (ITC; Edison, New Jersey).

Two nonblinded authors evaluated the validity of each of the four PAOP measurements by analyzing five preestablished criteria: (1) PAOP is less than the diastolic PAP, (2) the tracing is compatible with the atrial pressure waveform, (3) the fluoroscopic image demonstrates a stationary catheter after inflation, (4) free flow is present within the catheter, and (5) highly oxygenated blood (capillary) is obtained from the distal port while the catheter is in occlusion position.¹² In every patient, we recorded the number of criteria present (one to five) in each of the four PAOP measurements. In addition, we identified in all patients the measurement with the highest number of criteria present that most likely reflected the LAP (namely, "best PAOP") in order to assess for agreement in the PAOP measurements between left and right PAs with two different balloon inflation volumes.

In some instances, when the PAOP measurement did not meet at least four of the preestablished criteria for validity, we performed wedge angiography using 5 mL of iohexol (Omnipaque 350; GE Healthcare Inc; Princeton, New Jersey). Wedge angiography is a technique that enables a very high concentration of contrast material distal to the PAC balloon.¹⁸ We did not routinely measure left ventricular end-diastolic pressure because this approach would increase the risks and costs of the procedure and cause increased pain and inconvenience to our patients.

Statistical Analysis

Statistical analysis was performed using SPSS, version 17 (SPSS Inc; Chicago, Illinois) and MedCalc, version 10.3.0.0 (MedCalc Software; Mariakerke, Belgium). We presented the results as mean $\pm$ SD. For comparison of categorical values, we used χ^2 test. Mann-Whitney test was used for comparison of continuous values. Because the four measurements were obtained from different occlusion sites and correlated within patients, linear mixed-effects models were used to evaluate the PAOP measurement effects. A random intercept was considered to capture the within-patient correlations. We examined the distribution of the outcome variables before we fit the models to ensure normality of the data. We evaluated the PAOP measurement effects within each stratum defined by PH condition and tested for the interaction effect between PH and PAOP measurement for each outcome variable. Agreement between PAOP measurements and what we called best PAOP was analyzed by Bland-Altman analysis. A $P < .05$ was considered significant.

RESULTS

A total of 37 patients suspected or known to have PH were included in this study. Mean age was 58.1 ± 15 years, and 86.5% were women (Table 1). Twenty-eight (75.7%) patients had PH (mean PAP > 25 mm Hg). Of the patients with PH, 46.4% had a PAOP > 15 mm Hg, and 71.4% had a pulmonary vascular resistance of ≥ 3 Wood units.

Table 1—Patient Demographic and Hemodynamic Characteristics

Characteristic	Value
Total sample, No.	37
Age, y	58.1 ± 15
Women, %	86.5
Reasons for RHC, %	
Unexplained dyspnea with high RVSP on echocardiogram	22
IPAH	19
Collagen vascular disease PH	19
Portopulmonary hypertension	11
Left ventricular diastolic dysfunction	11
CTEPH	5
Other	13
RA pressure, mm Hg	10.5 ± 6.5
Right mean PAP, mm Hg ^a	39.7 ± 17.5
Left mean PAP, mm Hg ^a	39.7 ± 17.1
PAOP	15.2 ± 7.5
Cardiac output, L/min	5.9 ± 2.2
Cardiac index, L/min/m ²	3.1 ± 1
Pulmonary vascular resistance, Wood units	5.1 ± 4.6
Mixed venous oxygen saturation, %	68 ± 7.8

Data are presented as mean ± SD, unless otherwise indicated. CTEPH = chronic thromboembolic pulmonary hypertension; IPAH = idiopathic pulmonary arterial hypertension; PAOP = pulmonary artery occlusion pressure; PAP = pulmonary artery pressure; PH = pulmonary hypertension; RA = right atrial; RHC = right-sided heart catheterization; RVSP = right ventricular systolic pressure.

^a*P* = .94 for the comparison.

Of a total of 148 recorded measurements, 1.4%, 8.1%, 14.9%, 18.2%, 39.9%, 17.6% met none, one, two, three, four, or five of the preestablished criteria for a valid PAOP, respectively. All the patients had at least one PAOP measurement that met four or five criteria. Forty-five percent of the patients had at least one PAOP measurement that met all five preestablished criteria. In patients with PH, blood return was obtained in 2.6 ± 1.1 of the four PAOP measurements in contrast with 3.4 ± 0.7 of the four measurements in patients without PH (*P* = .036).

PAOP in All Patients

We observed a trend toward a significant difference among the four PAOP measurements (*P* = .057) (Table 2). Bland-Altman analysis showed greater bias and limit of agreement with balloon full vs half inflation in both the right and the left PA (Fig 1). In multivariate analysis, mean PAP had a significant effect on the PAOP measurement, with an estimated ± SE increase in PAOP of 0.38 ± 0.1 mm Hg for every 1 mm Hg increase in mean PAP (*P* < .001). Similarly, mean PAP had a significant effect on difference between PAOP and best PAOP, with an estimated ± SE increase in the difference of 0.28 ± 0.09 mm Hg for every 1 mm Hg increase in mean PAP (*P* = .003).

Of all the PAOP recordings (*n* = 148), 57.5% met at least four of the preestablished criteria for a valid measurement. When only one PAOP measurement

met four or more criteria on the right PA (*n* = 12), 75% of them required a balloon full inflation and 25% a balloon half inflation. In 16% of the cases, PAOP measurements with three or fewer criteria were obtained for right-side pulmonary circulation, thus requiring catheterization of the left PA to obtain a reliable PAOP.

PAOP in Patients With and Without PH

In patients with PH, the right PA mean ± SE PAOP was 23.14 ± 2 mm Hg and 19.14 ± 2 mm Hg with balloon full and half inflation, respectively. In the left PA, the PAOP was 23.54 ± 2 mm Hg and 19.07 ± 2 mm Hg with balloon full and half inflation, respectively (*P* = .05 for the comparison of all four PAOP measurements) (Fig 2, solid circles).

In patients with PH, Bland-Altman analysis demonstrated greater bias and limits of agreement with balloon full vs half inflation in both the right and the left PA. With balloon full inflation, the variation between the measurements (*y*-axis) correlated with the magnitude of measurements (*x*-axis) (Fig 1, solid squares).

In patients without PH, Bland-Altman analysis revealed smaller bias and narrower limits of agreement than in patients with PH (Fig 1, open squares). In this group of patients, the comparison among PAOP measurements was not significant (*P* = .99, for both comparisons) (Fig 2, open circles). Of 112 and 36 PAOP measurements obtained in patients with or without PH, respectively, 50% and 81% met four or five of the criteria for validity (*P* = .002).

DISCUSSION

In the present study, we observed significant variability in the PAOP measurements in patients with PH, depending on the volume of air used to inflate the balloon of the PAC. We demonstrated that in some instances, the use of balloon inflation volumes <1.5 mL may help to better position the PAC in a smaller pulmonary vessel, allowing a more complete occlusion. In addition, balloon half inflation correlated with higher precision and lower bias than balloon full inflation.

We observed that it is not always possible to reliably measure PAOP in patients with PH by using fixed volumes of balloon inflation (eg, 1.5 mL) and directing the catheter to one PA (Fig 3). This finding is in accordance with the sentinel study by Swan et al¹⁹ that used a balloon inflation of 0.8 mL and had a success rate in the measurement of PAOP of 72%. Failures in the PAOP measurements generally occurred in patients with PH.

Table 2—PAOP Measurements in All Patients (N = 37) Obtained From the Right and Left Pulmonary Arteries With Two Different Balloon Inflation Volumes

Measurement	Right PA (1.5 mL)	Right PA (0.75 mL)	Left PA (1.5 mL)	Left PA (0.75 mL)	P Value
PAOP, mm Hg	19.95 ± 1.7	16.95 ± 1.7	20.27 ± 1.7	16.92 ± 1.7	.057
PAOP measurements with four or five criteria, % ^a	73	57	43	57	.08
Measurements ± 5 mm Hg of the best PAOP, % ^b	73	86.5	70.3	83.8	.165
PAOP – best PAOP, mm Hg ^b	4.78 ± 1.25	1.76 ± 1.25	5.08 ± 1.25	1.78 ± 1.25	.058

Data are presented as mean ± SE, unless otherwise indicated. PA = pulmonary artery. See Table 1 legend for expansion of other abbreviation.

^aThe criteria for validity of the measurement (range, 1–5) were based on hemodynamic, fluoroscopic, and gasometric data.

^bBest PAOP was defined as the PAOP measurement that most likely reflects the left atrial pressure.

Investigators have reported several technical problems in the measurement of PAOP, such as damped tracing, poor dynamic response (absent oscillation, low frequency, or inadequate duration of oscillations after a sudden pressure drop from 300 mm Hg to vascular levels), overinflation, and partial PAOP.²⁰ Morris et al^{12,20} described that PAOP could not be measured in 12% of the attempts, and technical difficulties were noted in

20% to 33% of the measurements. Some of these difficulties were resolved by manipulation or flushing of the PAC. Leatherman and Shapiro¹³ described several cases of partial occlusion of the PA by the PAC balloon that led to intermediate pressure readings between the mean PAP and the diastolic PAP. Interestingly, the authors corrected this error in the measurement by reducing the PAC balloon inflation.

FIGURE 1. A–D, Bland-Altman plots comparing best PAOP measurements with PAOP. Bland-Altman plot of PAOP measurements obtained from the right and left pulmonary artery (PA) with 1.5 mL and 0.75 mL PA catheter (PAC) balloon inflation compared with best PAOP, a value selected from all patient measurements that most likely represents the left atrial pressure. In each plot, the solid line represents the mean (bias) and the dashed line the limit of agreement (± 1.96 SD). Solid and open squares represent patients with and without pulmonary hypertension, respectively. L = left PA; PAOP = pulmonary artery occlusion pressure; R = right PA.

FIGURE 2. PAOP in patients with and without PH. Mean and 95% CI of PAOP according to the four PA occlusion positions studied. The difference among the PAOP measurements was only significant in the stratum of patients with PH ($P = .05$). PH = pulmonary hypertension. See Figure 1 legend for expansion of other abbreviations.

In our study, all the patients met at least four of the five preestablished criteria used to define PAOP as valid in at least one of the four recorded PAOP measurements (right and left PA with balloon full or half inflation). The two most common reasons for not meeting all the preestablished criteria were the impossibility to obtain blood from the distal tip of the PAC in the occlusion position (approximately one-quarter of the measurements) and the relatively low oxygen saturation in a significant number of samples (only one-third of our samples yielded blood with an oxygen saturation $> 90\%$). The relatively low oxygen saturation is likely due to aspiration of less volume of blood (10–15 mL) than the one contained in the PA dead space, which usually varies between 15 and 40 mL.^{7,21,22} Both technical errors were observed more commonly in patients with PH.

FIGURE 3. Hemodynamic tracings and oxygen saturation measurements obtained from the right and left PAs with 1.5-mL and 0.75-mL PAC balloon inflations. Right and left 1.5-mL tracings correspond to partial PAOP (intermediate waveform between pulmonary arterial pressure and PAOP) (black arrows). The L 0.75-mL waveform is damped and had poor dynamic response (unsatisfactory pressure oscillations after step changes in pressure) (gray arrow). *In this patient, the R 0.75 mL was the only reliable PAOP measurement (20 mm Hg). SO_2 = oxygen saturation. See Figure 1 legend for expansion of other abbreviations.

In these technical errors, wedge angiography revealed appropriate balloon occlusion, but the tip of the catheter usually was positioned close to the vessel wall, and during suction, the wall became adherent to the distal tip of the PAC, occluding its lumen. Other investigators have reported similar findings. Brewster and McIlroy²³ observed that in several patients, blood could not be obtained from a “wedged” catheter. Similarly, Morris et al²⁰ described 12 PAOP measurements without technical problems that were associated with an inability to aspirate blood from the distal tip of the PAC.

With wedge angiography, we identified other possible explanations for technical errors in the measurement of PAOP. In several cases, we noted washout of the contrast injected in the distal lumen of the PAC by the inflow of uncontrasted blood from the vessel before the occlusion (Figs 4A, 4B). In addition, we saw clearing of contrast by a collateral pulmonary vessel draining after the balloon occlusion (Figs 4C, 4D) and the impact of the PAC balloon in an arterial branch point with full opacification of one branch and partial opacification of the other (Figs 4E, 4F).

Our current approach is to first obtain a PAOP measurement in the right PA with balloon inflation of 1.5 mL and, if not reliable, use an inflation of 0.75 mL. If the PAOP measurement does not meet at least four of the five criteria, we advance the PAC to the left PA using a balloon inflation of 1.5 mL and, if necessary, 0.75 mL. In our hands, this sequential approach improved the yield of obtaining a reliable PAOP measurement from 73% to 84% to 95% to 100%, respectively. The modest yield observed when only one PAOP measurement is obtained may help to partly explain the discrepancies in the measurements observed between PAOP and left ventricular diastolic pressure by Halpern and Taichman.¹¹

In patients without PH, all four PAOP measurements were similar and had high precision and low bias. In addition, the PAOP measurements obtained in these patients met a significantly higher number of preestablished criteria for validity than the ones recorded in patients with PH.

One reasonable concern is about the safeness of using balloon half inflation because the tip of the catheter may not be fully protected by the balloon. With balloon half inflation, the tip barely protrudes from the balloon, which would limit its potential for vascular damage. In our study, balloon half inflation was safe, and no complications were observed.

The study had several limitations. First, left ventricular end-diastolic pressure was not measured. Second, only 10 to 15 mL of blood were discarded before obtaining blood for oxygen saturation analysis in the PA occlusion position. Third, we were not blinded; thus, interrater variability could not be

FIGURE 4. A, B, Technical difficulties in the measurement of PAOP. Intermittent flow of noncontrasted blood is seen proximal to the balloon occlusion (0.75 mL balloon inflation) (arrow). C, D, Noncontrasted flow is seen from a collateral pulmonary vessel emptying after the balloon occlusion (1.5 mL balloon inflation). Arrows show a meniscus that corresponds to the collateral vessel. E, F, The balloon, located in a vessel bifurcation (0.75 mL balloon inflation), is completely occluding one segmental artery but partially a more medial one (arrows), where the tip of the catheter is located. In all of these situations, nonreliable PAOP measurements were obtained. Arrowheads delineate the PAC balloon. See Figure 1 legend for expansion of abbreviation.

determined. Finally, only a few patients underwent wedge angiography.

In conclusion, we did not identify a specific site or balloon inflation that most likely provides a reliable PAOP measurement. In patients with normal PAP, no significant difference was noted among the PAOP measurements. However, in patients with PH, significant variation was noted among the measurements, a factor that can lead to misclassification of PH and inadequate treatment of the disease. The validity of the PAOP in patients with PH varied according to balloon inflation. Balloon half inflation was safe and correlated with higher precision and lower bias in the PAOP measurements.

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Dr Mubarak: contributed to the study design, interpretation of data, and writing and revision of the manuscript.

Dr Li: contributed to the statistical analysis, interpretation of data, and writing and revision of the manuscript.

Ms Carrie: contributed to the institutional review board application and writing and revision of the manuscript.

Dr Alnuaimat: contributed to the study design, institutional review board application, data collection, interpretation of data, and revision of the manuscript.

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