

**THE TRANSPULMONARY PRESSURE GRADIENT FOR THE DIAGNOSIS OF
PULMONARY VASCULAR DISEASE**

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Abstract

The transpulmonary pressure gradient, defined by the difference between mean pulmonary artery pressure and left atrial pressure (commonly estimated by a pulmonary artery wedge pressure) has been recommended for the detection of intrinsic pulmonary vascular disease in left heart conditions associated with increased pulmonary venous pressure. In these patients, a transpulmonary pressure gradient of more than 12 mmHg would be diagnostic of an “out of proportion” pulmonary hypertension. This value is arbitrary, because the gradient is sensitive to changes in cardiac output and both recruitment and distension of the pulmonary vessels which decrease the upstream transmission of left atrial pressure. Furthermore, pulmonary blood flow is pulsatile, with systolic and mean pulmonary artery pressure determined by stroke volume and arterial compliance. It may therefore be preferable to rely on a gradient between diastolic and wedged pulmonary artery pressures. The measurement of a diastolic-to-wedge gradient combined with systemic blood pressure and cardiac output allows for a step-by-step differential diagnosis between pulmonary vascular disease, high output or high left heart filling pressure states, and sepsis. The diastolic-to-wedge gradient is superior to the transpulmonary pressure gradient for the diagnosis of “out of proportion pulmonary hypertension”.

Key words: pulmonary hypertension; pulmonary circulation; heart failure; pulmonary artery wedge pressure, pulmonary vascular resistance, pulmonary vascular compliance

Introduction

Pulmonary hypertension is defined by a mean pulmonary artery pressure (mPpa) ≥ 25 mmHg at rest (1,2). The diagnosis of pulmonary vascular disease relies on the invasive measurements of a mPpa ≥ 25 mmHg, a pulmonary artery wedge pressure (Ppw) ≤ 15 mmHg, a pulmonary vascular resistance (PVR) ≥ 3 Wood units, and a transpulmonary pressure gradient (TPG) ≥ 12 mmHg (1,2). The TPG is the difference between mPpa and left atrial pressure (Pla). Left atrial pressure is usually estimated by Ppw. The TPG is thought to be particularly useful to diagnose “out of proportion pulmonary hypertension” in patients with left heart failure or mitral stenosis (1). “Out of proportion” means that mPpa is higher than expected from an upstream transmission of Pla because of increased tone and/or structural changes. However, a TPG-derived diagnosis of “out of proportion pulmonary hypertension” may not always agree with clinical context.

How much pulmonary hypertension secondary to advanced left heart failure results is the passive consequence on an increase in Pla can be observed after cardiac transplantation. In patients with purely passive pulmonary hypertension, mPpa would decrease along with decreased Pla, while in those with out of proportion pulmonary hypertension, mPpa would remain unchanged, or decrease proportionally less than Pla. This was examined in 20 previously reported patients with pre- and postoperative hemodynamic measurements (3). Before transplantation, mPpa was 43 ± 2 mmHg (mean \pm SE), Ppw 29 ± 2 mmHg, PVR 604 ± 60 dyne/s/cm⁻⁵.m² and the TPG 14 ± 1 mmHg. After transplantation, mPpa was 25 ± 2 mmHg, Ppw 12 ± 1 mmHg, PVR 452 ± 50 dyne/s/cm⁻⁵.m² and the TPG of 12 ± 1 mmHg. In this series of patients, transplantation was followed by a proportional decrease in mPpa and Ppw, (by on average 18 mmHg and 17 mmHg respectively) suggesting purely passive pulmonary hypertension. Yet the initial TPG was on average higher than 12 mmHg, with a

range of values from 6 to 20 mmHg. Since transplantation did not always normalize mPpa, the data of the 12 of the 20 patients in whom mPpa decreased to below the value of 25 mmHg were reexamined. The pre-operative TPG was higher than 12 mmHg (range 12-20 mmHg) in 6 of them. Thus, in this limited series of patients, a TPG higher than 12 mmHg did not predict out of proportion pulmonary hypertension better than flipping a coin. How is this possible?

How left atrial pressure affects mean pulmonary artery pressure

The normal relationship between mPpa and Pla is described by the PVR equation rearranged as: $mPpa = PVR \times Q + Pla$, where Q is pulmonary blood flow. The inherent assumptions of the PVR equation are that the TPG-Q relationship is linear, crosses a zero pressure/zero flow value, and is therefore independent of the absolute value of Pla. Many studies have shown that the TPG-Q relationship may be reasonably well described by a linear approximation over a limited range of physiological flows, but that its extrapolated pressure intercept is most often positive, and that the slope of the mPpa-Pla relationship is less than the unity (4).

It has long been known that PVR decreases with increases in Q or Pla. This has been initially explained by a pulmonary circulation model of parallel collapsible vessels with a distribution of closing pressures (P_c) (5). In each of these vessels, flow is determined by a pressure gradient between Ppa and P_c whenever there is a $P_c > Pla$. A Pla lower than P_c is irrelevant to flow, like the height of a waterfall. Pla then becomes an apparent outflow pressure and P_c the effective outflow pressure of the pulmonary circulation, while the PVR equation remains valid provided Pla is replaced by P_c . When Pla is higher than P_c , the vessel opens and the driving pressure for flow becomes Ppa minus Pla, the effective outflow pressure of the pulmonary circulation is Pla, and the usual PVR equation can be used.

A P_c higher than P_{la} is typically observed in West's zones I and II in the upper parts of normal vertical lungs (6). Diseases associated with increased pulmonary vessel tone and/or alveolar pressure are associated with an increase in P_c . In these patients, $mPpa$ becomes less sensitive or even insensitive to changes in flow or P_{la} , and calculated PVR rapidly decreases with increased cardiac output (7). The presence of a closing pressure in the pulmonary circulation can be identified by a gradient between P_{la} and the extrapolated pressure intercept of the linear adjustment of a multiple $mPpa$ - Q coordinates measured at constant P_{la} . Further proof is brought about by the demonstration of a functional dissociation between P_c and P_{la} on $mPpa$ - P_{la} relationships in experimental preparations in which flow is kept constant (discussed in reference 3). A typical experiment in an intact animal preparation of oleic acid lung injury as a model of the acute respiratory distress syndrome is shown in Fig 1 (8). In this animal, the extrapolated intercept of linear $mPpa$ - Q plots revealed a P_c higher than P_{la} , and P_{la} had to be increased above that value to be transmitted upstream to $mPpa$.

The "waterfall model" of the pulmonary circulation does not take into account the natural distensibility of the pulmonary vessels. A sufficient number of $mPpa$ - Q coordinates, more than 4-5, shows a slight curvilinearity which is ignored by linear adjustment procedures. This curvilinearity is explained by the fact that high flow distends pulmonary resistive vessels, and is an important cause of decreased slope of $mPpa$ - Q relationships, or PVR along with increasing flow. High flow linear adjustments of multipoint $mPpa$ - Q relationships are therefore associated with spurious increase in P_c estimated from extrapolated pressure intercepts (9).

This difficulty is overcome by a mathematical model of the pulmonary circulation fitting multipoint mPpa-Q plots by an equation relating mPpa, Pla, Q, PVR and a distensibility coefficient α (9): :

$$mPpa = \frac{\left[(1 + \alpha Pla)^5 + 5\alpha R_0(Q) \right]^{\frac{1}{5}} - 1}{\alpha}$$

The normal value for α measured on in vitro mounted pulmonary resistive vessels is 2 % change in diameter per mmHg change in pressure, and is remarkably constant in a wide spectrum of animal species (10). It is interesting that the same distensibility α value of 2 %/mmHg has been recovered by the application of the distensibility model equation to either invasive (10) or noninvasive (11-13) measurements of pulmonary vascular pressures and flows. The distensibility factor α is higher in young healthy women compared to men (12), and decreases with aging (12) or with chronic hypoxic exposure (13).

The distensibility equation allows for the modeling of the effects of increased Q or Pla on mPpa at various levels of vascular distensibility and PVR. The results are shown in Fig 2 and 3. It is apparent that an increase in α decreases mPpa or TPG at any given level of flow (Fig 2 and 3) and also decreases the TPG along with an increase in Ppw (Fig 3) In other words, an increase in Q and/or Pla may falsely decrease the TPG that would be increased because of pulmonary vasoconstriction or remodeling.

Distensible models provide a satisfactory explanation for all possible normal or pathological pulmonary vascular pressure-flow relationships in fully recruited lungs. Pulmonary vascular de-recruitment is to take into account in low cardiac output or high alveolar pressure states. The slope of the mPpa-Pla relationship decreases with pulmonary vascular distension, but

may increase in de-recruited lungs. In that case, an increased TPG may falsely suggest pulmonary vasoconstriction or remodeling.

There is thus no good rationale for a stable cut-off value of 12 mmHg for the TPG as the measurement is sensitive to left atrial pressure-dependent changes in pulmonary vascular recruitment and distension

How left atrial pressure affects pulsatile pulmonary artery pressure

The above considerations do not take into account the natural pulsatility of the pulmonary circulation. Pulmonary flow reaches a maximum during systole, and is inappreciable at the end of diastole. Accordingly, in a normal pulmonary circulation, diastolic Ppa (dPpa) is approximately equal to Pla (14). It has been assumed that, taken into account errors of measurements of ± 1 -2 mmHg, 5 mmHg would be a reasonable upper limit of normal of diastolic-to-wedge pressure gradient (DPG). This is indeed what was established on the basis of invasive hemodynamic measurements in 44 healthy volunteers aged 17 to 83 years, at rest and at various levels of exercise in either recumbent and sitting positions associated with Ppw values up to 34 mmHg and cardiac outputs up to 25 to 30 L/min. (14). Systolic and mPpa at any given dPpa increase in a fixed proportion depending on stroke volume (SV) and pulmonary arterial compliance (Ca), which decreases along with increased Pla. Therefore systolic Ppa (sPpa) and mPpa can be predicted from dPpa using the following equations (14):

$$sPpa = 1.41 + 1.61 \text{ dPpa} + 0.09 \text{ SV}$$

$$mPpa = - 1.33 + 1.34\text{dPpa} + 0.05 \text{ SV}$$

Predicted mPpa and sPpa as a function of Ppw at various SV are illustrated in Fig 4 to 6.

It now appears that the TPG may remain unchanged if dP_{pa} increases less than P_{pw} , but increases if dP_{pa} increases by an equal amount or more than P_{pw} . On the other hand, the DPG decreases or remains unchanged as long as the upstream transmission of P_{pw} remains equal or less than the unity, which is expected in the absence of pulmonary vasoconstriction or remodeling.

The tight correlation between sP_{pa} , mP_{pa} and dP_{pa} was recently rediscovered, with similar prediction equations, which interestingly remained valid in pulmonary hypertension of various severities and etiologies (15-17). This is explained by the monotonous response of the pulmonary circulation to insults, leading to proportional inverse changes in Ca and PVR with an unaltered time constant $Ca \times PVR$ 0.6-0.7 s (18,19). There may be one noticeable exception: pulmonary hypertension on passive upstream transmission of increased Pl_a in left heart conditions. In these patients, Ca decreases proportionally more than the increase in PVR because increased Pl_a is a cause of both pulmonary arterial stiffening and decreased PVR. Accordingly, the time constant in pulmonary hypertension on left heart conditions is shorter than in other types of pulmonary hypertension (20). This spuriously increases the TPG, but does not affect DPG.

It must be reminded that Ca should not be confused with the distensibility coefficient α . Pulmonary arterial compliance Ca is a global calculation, influenced by proximal pulmonary arterial elasticity, while α strictly corresponds to the distensibility of small peripheral pulmonary resistive vessels.

Thus the disproportionate decrease in Ca in the presence of increased Pl_a may be a cause of increased TPG without any coexistent pulmonary vasoconstriction or remodeling. How this

may cancel off the decrease in TPG related to pulmonary vascular recruitment and distension is unpredictable.

Clinicians understandably like cut-off values for decision making based on hemodynamic measurements. We regret to have to tell them that a TPG of 12 mmHg cannot be used for that purpose. The DPG may be preferable because this gradient is less sensitive to changes in Ca, stroke volume, and absolute values Pla.

The DPG for the differential diagnosis of pulmonary hypertension

The DPG used to be implemented in assessment of cardiac versus pulmonary causes of acute respiratory failure in critically ill patients (21). Here we propose an adaptation of this DPG-derived decision tree to make it more generally applicable (Figure 7). The earlier decision tree rested on a cut-off value for Ppw of 10 mmHg. A Ppw of 12 mmHg, or a direct measure of left ventricular end-diastolic pressure of 15 mmHg would seem more reasonable cut-off values as extreme upper limits of normal, as used in diagnostic algorithms of diastolic heart failure (22). The next step is a DPG below or above 5 mmHg, to discern passive upstream transmission of Pla from increased PVR due to pulmonary vasoconstriction and/or pulmonary vascular structural changes. The last step is cardiac output, being normal or decreased in heart failure, or normal or increased in hypervolemia and/or increased venous return on low systemic vascular resistance in anemia, systemic shunts, or sepsis. The arterio-venous oxygen content difference ($DaVO_2$) can be used as a surrogate of cardiac output, as the Fick equation predict that both variables are inversely correlated at any given value of O_2 uptake (21). The $DaVO_2$ is a useful internal control to integrate in hemodynamic measurements at right heart catheterization, as errors on a measurement of cardiac output are always possible. Low

systemic blood pressure argues in favor of a septic complication. Cut-off values for cardiac output or blood pressure are not proposed because of insufficient evidence and the desire to propose a decision tree with sufficient flexibility to assist rather than impose clinical decision.

Conclusion and perspective

In 1971, Harvey, Enson and Ferrer noted: “The pulmonary circulation has been under intensive study by innumerable investigators for almost 30 years. From the vast amounts of carefully accumulated data, certain conclusions can be drawn”. More than 40 years later, there has been progress, but also some persisting misconceptions. A typical example is the reliance of the TPG for the differential diagnosis of pulmonary vascular disease. The present discussion shows how the TPG may over-diagnose or under-diagnose pulmonary vascular disease in left heart conditions associated with an increased pulmonary venous pressure, and that this is to a large extent avoided by the use of a diastolic-to-wedge pressure gradient, or “DPG”. The DPG combined with clinical probability assessment, absolute values of pulmonary artery wedge or left atrial pressure, cardiac output or $D_{av}O_2$ and blood pressure measurements appears to be more useful for the diagnosis of “out of proportion” pulmonary hypertension secondary to left heart conditions, and may help in the management of critically ill patients with sepsis or acute lung injury.

It is of course understood that the presently proposed diagnostic tree requires prospective validation. This could be undertaken along with TPG-based algorithms as all these measurements are done during diagnostic catheterizations anyway.

As a final word of caution, one should never forget that decision trees based on single measurements cut-off values are vulnerable. This was recently illustrated by a poor agreement between right and left heart catheterization measurements of Ppw and Pla in a large patient population (23), and persistent discussion on how optimally measure Ppw (24). The measurement of dPpa is more exposed than mPpa to motion artifacts and inadequate dynamic responses due to over-damping or under-damping (insufficient or excessive flushing of the manometer-fluid-filled catheter system). This may explain why Ppw higher than dPpa are sometimes observed (14), while this is physically impossible. Furthermore, diagnostic cut-off values do not necessarily coincide with upper limits of normal (1,2), and some uncertainty remains about the limits of normal of pulmonary hemodynamics with aging as the number of reported studies in old but healthy subjects remains limited (10-12,14). Thus the upper limit of normal of the DPG may have to be increased in older healthy subjects. Great care must be applied to quality control of the measurements, and cross check with clinical probability assessment and alternative imaging techniques whenever possible.

References

1. Galiè N, Hoeper M, Humbert M, Torbicki A, Vachiéry JL, Barbera J, Beghetti M, Corris P, Gaine S, Gibbs S, Gomez-Sanchez M, Jondeau C, Klepetko W, Opitz c, Peacock A, Rubin L, Zellweger M, Simonneau G. Task force for diagnosis and treatment of pulmonary hypertension of European Society of Cardiology (ESC); European Respiratory Society (ERS); International Society of Heart and Lung Transplantation (ISHLT). Guidelines for the diagnosis and treatment of pulmonary hypertension. *Eur Respir J* 2009;34:1219-1263.
2. McLaughlin VV, Archer SL, Badesch DB, et al ACCF/AHA 2009 Expert Consensus Document on Pulmonary Hypertension. A Report of the American College of

- Cardiology Foundation Task Force on Expert Consensus Documents and the American Heart Association. *Circulation* 2009; 119: 2250-2294.
3. Naeije R, Lipski A, Abramowicz M, Lejeune P, Mélot C, Antoine M, De Smet JM, Leclerc JL, Primo G. Nature of pulmonary hypertension in congestive heart failure. Effects of cardiac transplantation. *Am J Respir Crit Care Med*. 1994; 147: 881-887.
 4. Naeije R. Pulmonary vascular resistance: a meaningless variable?. *Intens Care Med* 2003; 29: 526-529.
 5. Permutt S, Bromberger-Barnea B, Bane HN. Alveolar pressure, pulmonary venous pressure and the vascular waterfall. *Med Thorac* 1962 ; 19: 239-260.
 6. West JB, Dollery CT, Naimark A. Distribution of blood flow in isolated lung: relation to vascular and alveolar pressures. *J Appl Physiol* 1964; 19: 713-724
 7. Zapol WM, Snider MT. Pulmonary hypertension in severe acute respiratory failure. *N Engl J Med* 1977 ; 296: 476-480
 8. Leeman M, Lejeune P, Closset J, Vachiéry JL, Mélot C, Naeije R. Nature of pulmonary hypertension in canine oleic acid pulmonary edema. *J Appl Physiol* 1990 : 69: 293-298.
 9. Linehan JH, Haworth ST, Nelin LD, Krenz GS and Dawson CA. A simple distensible model for interpreting pulmonary vascular pressure-flow curves. *J Appl Physiol* 1992 ; 73: 987-994.
 10. Reeves JT, Linehan JH and Stenmark KR. Distensibility of the normal human lung circulation during exercise. *Am J Physiol Lung Cell Mol Physiol*. 2005 ; 288: L419-25.
 11. Argiento P, Chesler N, Mulè M, D'Alto M, Bossone E, Unger P, Naeije R. Exercise stress echocardiography for the study of the pulmonary circulation. *Eur Respir J* 2010; 35: 1273-8.

12. Argiento P, Vanderpool RR, Mule M, Russo MG, D'Alto M, Bossone E, Chesler NC, Naeije R. Exercise stress echocardiography of the pulmonary circulation: limits of normal and gender differences. *Chest* 2012 epub ahead of print.
13. Groepenhoff H, Overbeek MJ, Mulè M, van der Plas M, Argiento P, Villafuerte FC, Beloka S, Faoro V, Macarlupu JL, Guenard H, de Bisschop C, Martinot JB, Vanderpool R, Penaloza D, Naeije R. Exercise pathophysiology in patients with chronic mountain sickness. *Chest*. Epub ahead of print..
14. Harvey RM, Enson Y, Ferrer MI. A reconsideration of the origins of pulmonary hypertension. *Chest* 1971; 59: 82-94
15. Chemla D, Castelain V, Humbert M, Hébert JL, Simonneau G, Lecarpentier Y and Hervé P. New formula for predicting mean pulmonary artery pressure using systolic pulmonary artery pressure. *Chest* 126: 1313-1317, 2004.
16. Syyed R, Reeves JT, Welsh D, Raeside D, Johnson MK, Peacock AJ. The relationship between the components of pulmonary artery pressure remains constant under all conditions in both health and disease *Chest*. 2008 Mar;133(3):633-9.
17. Chemla D, Castelain V, Provencher S, Humbert M, Simonneau G, Hervé P.. Evaluation of various empirical formulas for estimating mean pulmonary artery pressure by using systolic pulmonary artery pressure in adults. *Chest* 2009; 135: 760-768.
18. Lankhaar JW, Westerhof N, Faes TJ, Marques KM, Marcus JT, Postmus PE and Vonk-Noordegraaf A. Quantification of right ventricular afterload in patients with and without pulmonary hypertension. *Am J Physiol Heart Circ Physiol* 2006; 291: H1731-1737.
19. Saouti N, Westerhof N, Helderma F, Marcus JT, Boonstra A, Postmus PE and Vonk Noordegraaf A. Right ventricular oscillatory power is a constant fraction of total

- power irrespective of pulmonary artery pressure. *Am J Respir Crit Care Med* 2010; 182: 1315-1320.
20. Tedford RJ, Hassoun PM, Mathai SC, Girgis RE, Russell SD, Thiemann DR, Cingolani OH, Mudd JO, Borlaug BA, Redfield MM, Lederer DJ, Kass DA. Pulmonary capillary wedge pressure augments right ventricular pulsatile loading. *Circulation* 2012; 125: 289-297
21. Stevens PM. Assessment of acute respiratory failure: cardiac versus pulmonary causes. *Chest* 1975; 67: 1-2.
22. Paulus WJ, Tschöpe C, Sanderson JE, Rusconi C, Flachskampf FA, Rademakers FE, Marino P, Smiseth OA, De Keulenaer G, Leite-Moreira AF, Borbély A, Edes I, Handoko ML, Heymans S, Pezzali N, Pieske B, Dickstein K, Fraser AG, Brutsaert DL. How to diagnose diastolic heart failure: a consensus statement on the diagnosis of heart failure with normal left ventricular ejection fraction by the Heart Failure and Echocardiography Associations of the European Society of Cardiology. *Eur Heart J*. 2007; 28: 2539-50
23. Halpern SD, Taichman DB. Misclassification of pulmonary hypertension due to reliance on pulmonary capillary wedge pressure rather than left ventricular end-diastolic pressure. *Chest*. 2009;136:37-43.
24. Ryan JJ, Rich JD, Thiruvoipati T, Swamy R, Kim GH, Rich S. Current practice for determining pulmonary capillary wedge pressure predisposes to serious errors in the classification of patients with pulmonary hypertension. *Am Heart J* 2012; 163: 589-594.

Legends of the figures

Figure 1. Mean pulmonary artery pressure (Ppa) as a function of cardiac output (Q) at constant left atrial pressure (Pla), left panel, and Ppa as a function of Pla at constant Q, right panel, in an animal before (Base) and after induction of acute lung injury by the injection of oleic acid (OA). Before OA, Ppa-Q plots presented with an extrapolated pressure intercept equal to Pla, and any increase in Pla was transmitted upstream to Ppa. After OA, Ppa-Q plots presented with an extrapolated pressure intercept higher than Pla, and Pla was not transmitted upstream to Ppa below a pressure equal to that value (from ref 8). These observations suggest that OA-induced pulmonary hypertension is caused by an increase in the closing pressure of the pulmonary circulation

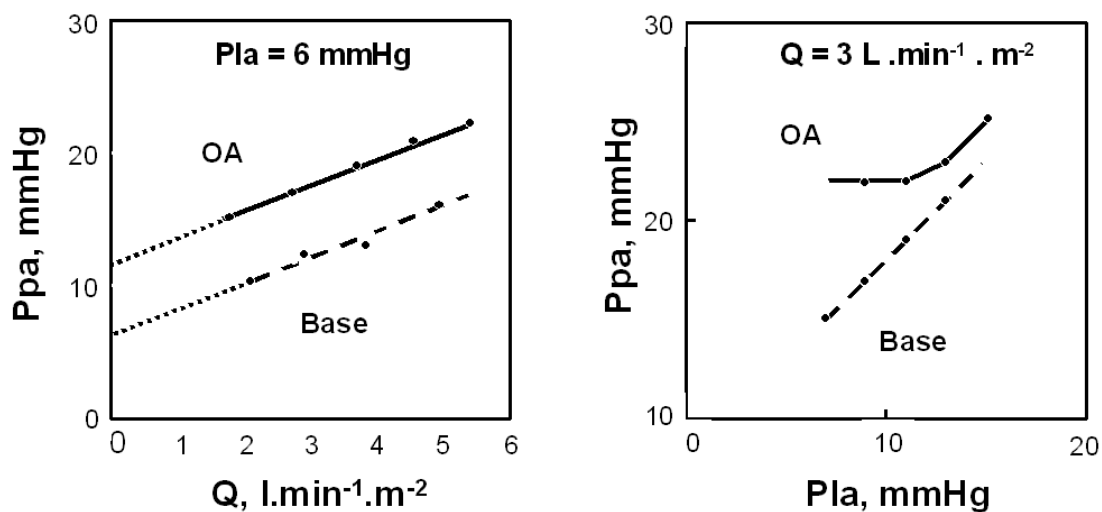


Figure 2. Mean pulmonary artery pressure (Ppa) as a function of cardiac output (Q- at two different levels of pulmonary vascular resistance (PVR). Increasing distensibility (α) decreases Ppa at any given level of Q. Thus pulmonary vascular distensibility results in a Ppa which is less than predicted by a linear model, that is the PVR equation.

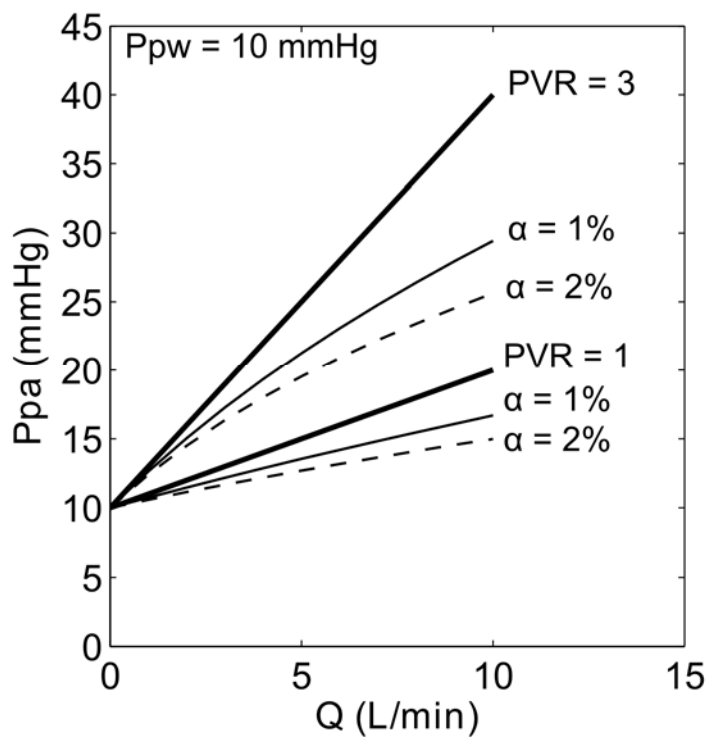


Figure 3. In the linear model, the transpulmonary pressure gradient (TPG) is only a function of flow rate (Q), left panel, and is not affected by pulmonary artery wedge pressure (P_{pw} , right panel) whatever the pulmonary vascular resistance (PVR). An increase in pulmonary vascular distensibility decreases the TPG is a function of Q as well as of P_{pw} .

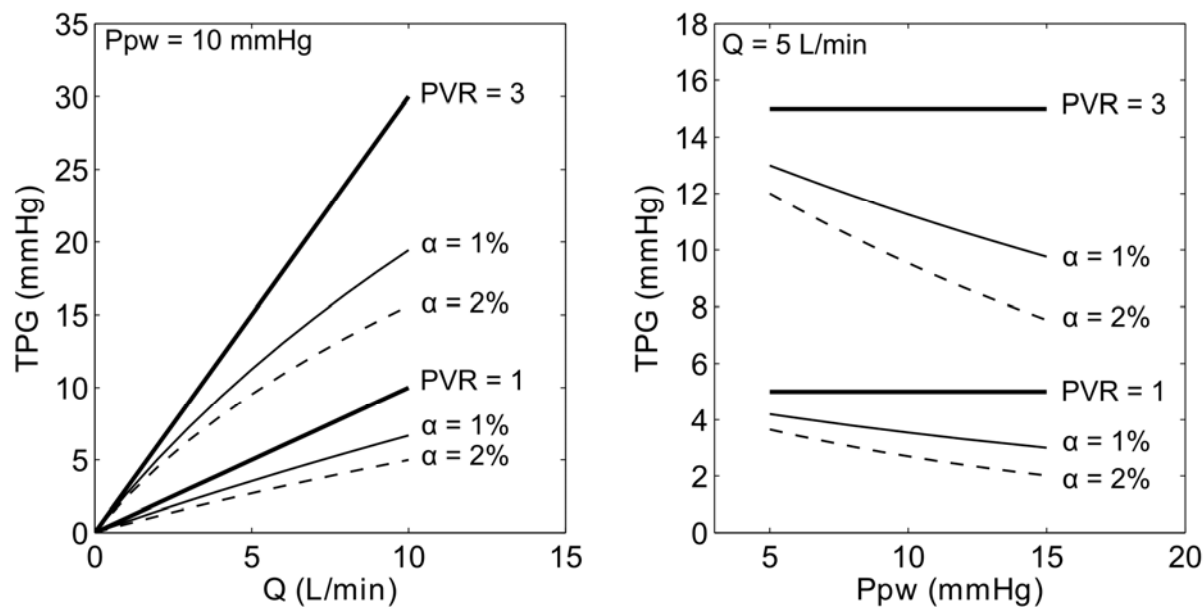


Figure 4. Effects of pulmonary artery wedge pressure (Ppw) and stroke volume (SV) on systolic, diastolic and mean pulmonary artery pressures (sPpa, dPpa and mPpa). If only a fraction of Ppw is transmitted to dPpa, the TPG is not a function of Ppw but increases proportionally to SV. The dPpa-Ppw gradient decreases with increased Ppw but independently of SV.

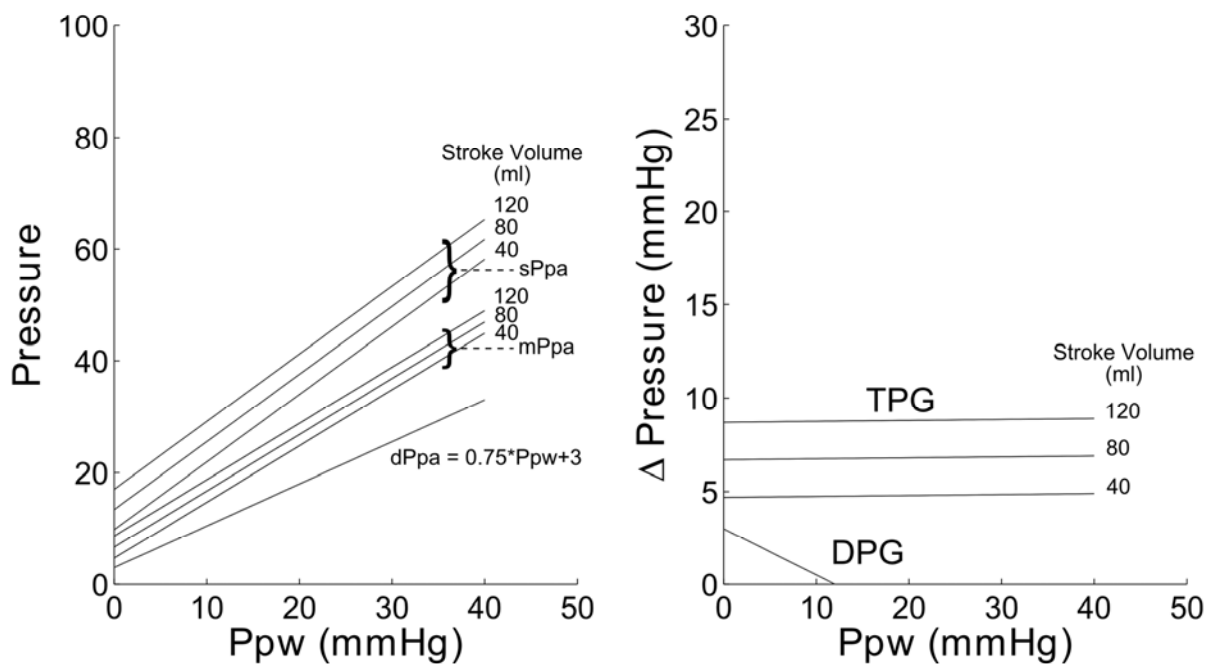


Figure 5. Effects of pulmonary artery wedge pressure (Ppw) and stroke volume (SV) on systolic, diastolic and mean pulmonary artery pressures (sPpa, dPpa and mPpa). If Ppw is directly transmitted to dPpa, there is an out of proportional increase in sPpa and mPpa depending on SV. The TPG increases, but the dPpa-Ppw gradient is independent of both Ppw and SV.

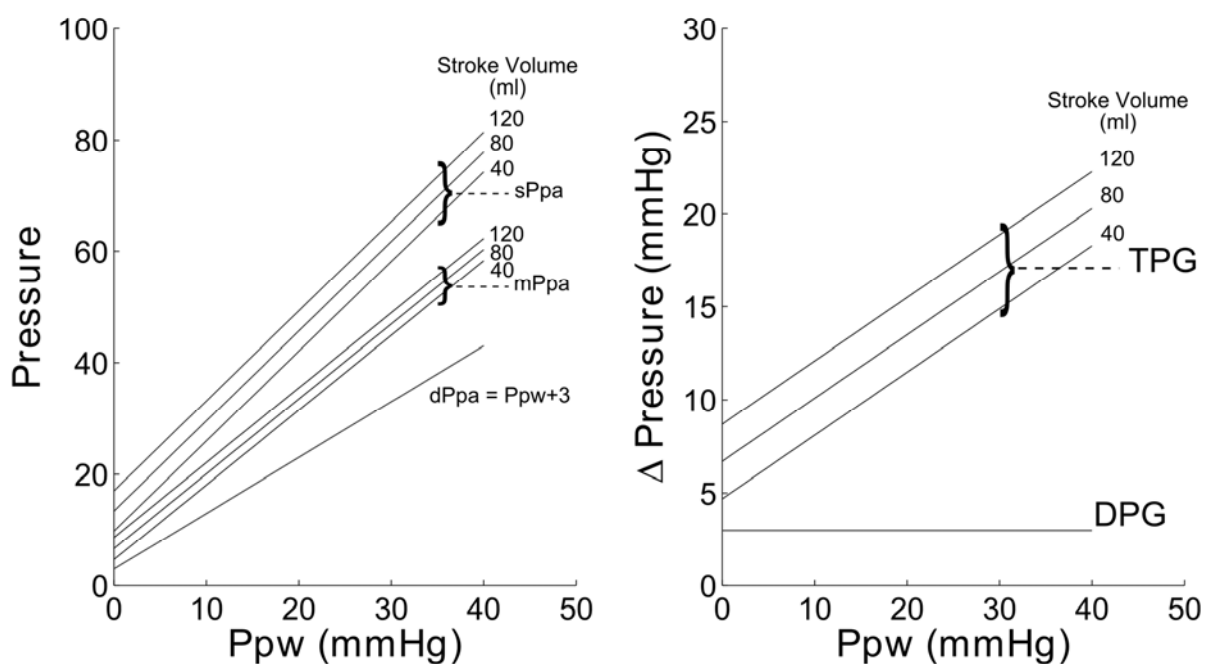


Figure 6. Effects of pulmonary artery wedge pressure (Ppw) and stroke volume (SV) on systolic, diastolic and mean pulmonary artery pressures (sPpa, dPpa and mPpa). If dPpa increases more than Ppw, there is an out of proportion increase in sPpa and mPpa that is a function of SV. The TPG increases. The dPpa-Ppw gradient increases linearly but slightly with Ppw but is independent of SV.

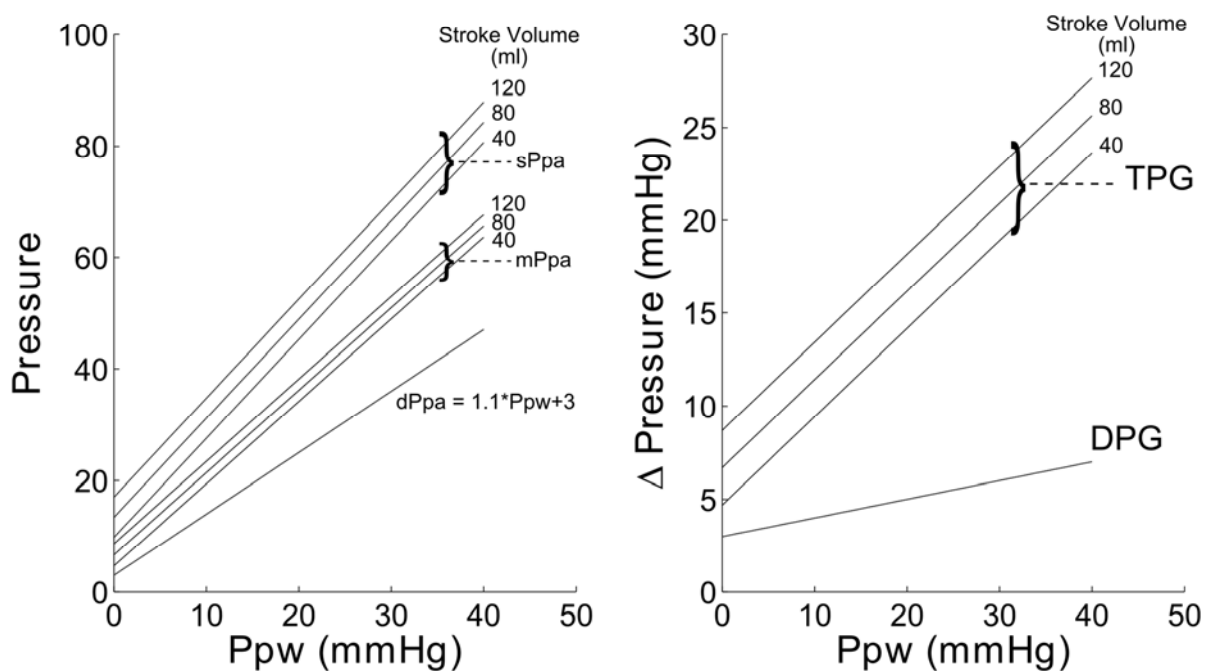


Figure 7.. Pulmonary artery wedge (Ppw)-derived algorithm for the diagnosis of heart failure (low or high output) versus intrinsic pulmonary vascular disease. A cut-off value of 12 mmHg is selected as true upper limit of normal of Ppw measured at right heart catheterization. If the cardiac catheterization is left, Ppw is replaced by left ventricular end-diastolic pressure, with a cut-off value of 15 mmHg. Ppa-Ppw is the diastolic-to-wedge pulmonary artery pressure gradient. Systemic hypotension is considered to make the decision tree applicable to septic shock. After ref 21.

