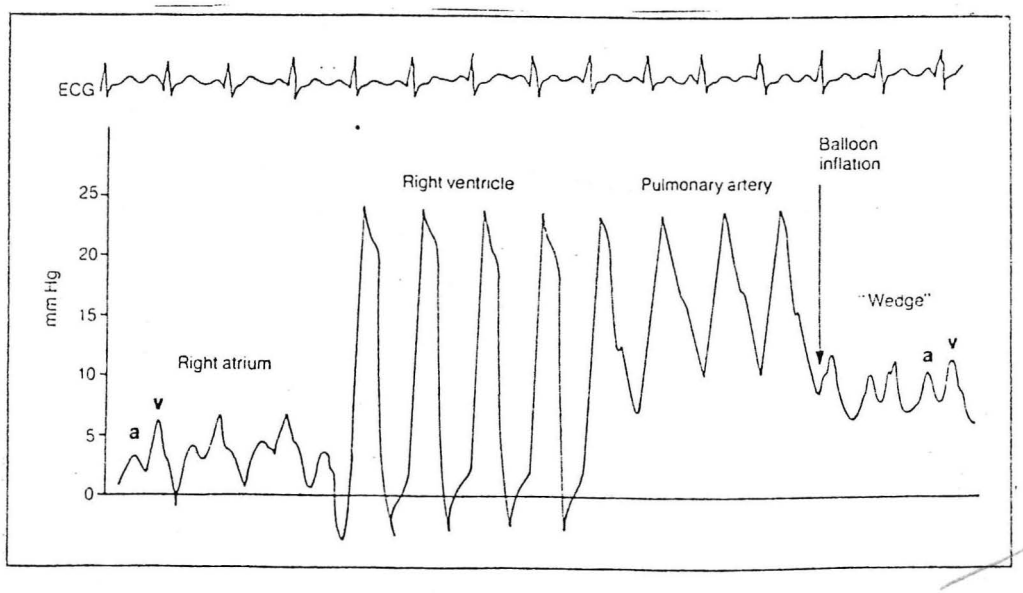
SELECTED TOPICS IN INTENSIVE CARE



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INTRODUCTION

The initial development of most of the basic techniques currently used in the respiratory intensive care unit began in the years prior to the development of the Salk vaccine. The fact that patients with complicated medical illness could survive an episode of respiratory failure was repeatedly demonstrated during polio epidemics. Essential principles of mechanical ventilation and airway care developed during this period include chest physiotherapy, postural drainage, tracheobronchial suctioning, humidification of inspired air, use of large bore flexible cuffed endotracheal tubes, and development of volume cycled ventilators (1). Intermittent pulmonary hyperinflations were empirically applied to overcome complaints of dyspnea that occurred despite clinically adequate oxygenation and ventilation. The essential physiologic role of sighing in preventing progressive atelectasis during shallow breathing was not established until as late as 1959 (2). Patients were weaned from ventilators by gradually reducing the number of assisted breaths as the ability to breathe spontaneously improved, a forerunner of present day intermittent mandatory ventilation. Measurement of arterial oxygen saturation was still the only clinically available method for assessing oxygenation. Adequacy of carbon dioxide elimination was checked by measurement of plasma bicarbonate. Systematic study of gas exchange and optimal ventilatory patterns was feasible when blood gas electrodes became available in the early 1960's.

With the advent of the Salk vaccine, polio became an increasingly rare disease. As polio oriented units were abandoned, most patients on ventilators were cared for on general hospital wards. Not unexpectedly, complication and mortality rates were high, largely due to mechanical failure of airway equipment and ventilators. This and the steady increase in both the variety of diseases and the numbers of patients in which mechanical ventilation was used prompted the reestablishment of intensive care units (3).

It is estimated that respiratory failure affects 25 to 50% of critically ill patients requiring intensive care (4). Hospital survival in patients requiring mechanical ventilation has increased largely because of the specialized nursing care and technology available in the intensive care unit (5). Respiratory function related morbidity and mortality rates are low in patients with ventilatory failure and minimal or no underlying pulmonary disease. Mortality rates have remained discouragingly high when respiratory failure develops secondary to direct pulmonary injury or in association with severe multisystem illnesses (6).

Mechanical ventilation is only one aspect of the care of patients with respiratory failure that has influenced survival. More effective antibiotics, improved management of cardiac problems, dialysis and hyperalimentation have also had a major impact. More recent developments in respiratory intensive care include new techniques for ventilatory support such as positive end-expiratory pressure (PEEP). One of the most notable developments during the last 10 years has been the ability to measure hemodynamic data at the bedside on an immediate and ongoing basis (7-9).

To put invasive hemodynamic monitoring into perspective, first I will review the indications and complications associated with the use of the Swan Ganz catheter and arterial line, briefly discuss measurement of the thermodilution cardiac output and review recent reports examining how invasive hemodynamic monitoring influences patient care. Second, I will discuss the clinical significance of mixed

venous oxygenation. Finally, I will review some clinical aspects of hemodynamic monitoring including the effect of spontaneous respiration, mechanical ventilation and PEEP on the interpretation of hemodynamic measurements.

HEMODYNAMIC MONITORING

A. Swan Ganz Catheterization

In 1970 Swan and Ganz reported the development of a new catheter designed to facilitate continuous bedside hemodynamic monitoring (10). It has been estimated that at least two million of these catheters have been used in the past decade. The total cost of bedside hemodynamic monitoring, including the purchase of the basic equipment is difficult to quantify, but obviously is of considerable magnitude. Direct costs of the insertion of a flow directed catheter including the cost of the catheter, disposable supplies and physician fees are currently in the range of $500.00. While costs incurred since the introduction of the Swan Ganz catheter are approaching one billion dollars (11), it has only been recently that their impact on patient management has been critically examined.

The Swan Ganz catheter is a technological advancement in that it is soft, flexible, and thus less likely to damage valves and endocardial surfaces if left in place for extended periods of time. In addition, the balloon tip provides flow direction to facilitate insertion at the bedside without flouroscopy. With the balloon inflated, the catheter tip is below the actual surface of the balloon so that forces ordinarily concentrated at the catheter tip are dispersed over a wide surface area. This probably accounts for a reduced incidence of arrhythmias during insertion. Subsequent modifications have extended the capability of these catheters to include a thermistor for measurement of thermodilution cardiac output and electrodes for transvenous cardiac pacing (7).

Indications for Swan Ganz Catheterization

The principal indication for Swan Ganz catheterization is the need for the physician to answer a specific question(s) about a patient that cannot be answered on the basis of the physical exam or less invasive means. In most instances, the decision to catheterize a patient is precipitated by a failure of therapy chosen on the basis of clinical evaluation. Like many other technical advances, the widespread use of the Swan Ganz catheter occurred before either the indications or benefits of its use were demonstrated by controlled studies. Four general indications for insertion are to:

1. Assess volume status and fluid management.
2. Measure right sided pressures.
3. Measure cardiac function.
4. Determine the choice and follow the results of therapeutic interventions.

A complete list of specific clinical situations in which catheterization may be indicated is beyond the scope of this presentation.

Table I. Prospective Evaluation of Complications

	Sise, et al (SICU)	Elliott, et al (MICU)
Total number of catheterizations	320	116
Total number of patients	219	81
Time catheterized (hours)	76 (range 1-403)	106 (range 24-336)
Patient age (years)	53 (range 16-84)	60 (range 17-91)
Overall hospital mortality	24%	48%
Indications		
Shock (volume status)	7%	41%
Fluid management	91%	-
Pulmonary edema	-	46%
Pre-op	-	10%
Suspected PE or MI	2%	3%
Insertions		
Subclavian	85%	93%
Internal jugular	12%	-
Antecubital	3%	7%
Complications*		
Cellulitis	16%	-
Pulmonary infarction	-	2%
Arrhythmias	11%	78%
Transient	10%	46%
V tach/treated	(1 death)	23%
Arterial puncture	1%	-
In situ thrombosis	0.3%	4%
Pneumothorax	2%	-
Bacteremia	8%	17%
Valve perforation	-	1/19 autopsies
Aseptic vegetations	-	4/19 autopsies
Technical "failures"	29%	?
Balloon related	15%	
Monitor/transducer related	9%	
Catheter clotting	5%	

*Expressed as percent of total catheterizations

Complications of Swan Ganz Catheterization

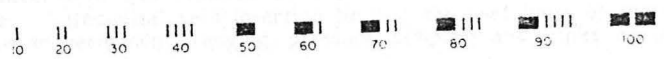
The relative ease of insertion and simplicity of design has inevitably resulted in a disregard of potential hazards by some physicians. Some of the complications related to catheterization are illustrated by two recent prospective studies (Table I). These reports provide interesting contrasts because one series is from an SICU (12) and the other an MICU (13). In general, the medical patients were older, had a higher overall hospital mortality and tended to be catheterized for longer periods of time.

Sise (12) reported 320 catheterizations in 219 patients. The principal indication for catheter insertion was fluid management in the post-operative period, particularly after cardiac surgery. Shock and suspected pulmonary embolism occurred in small numbers of patients. Elliott (13) reported 116 catheterizations in 81 patients. Principal indications for insertion included shock, ambiguous volume status in a hypotensive patient and management of cardiogenic pulmonary edema in patients with acute respiratory failure. Hemodynamic stabilization preoperatively and suspected pulmonary embolism or myocardial infarction occurred in smaller numbers of patients.

Catheter insertion in the large majority of patients in both series was accomplished without flouroscopy using a large central vein. The risk of additional radiation and the discomfort or difficulty of transporting a critically ill patient to a flouroscopy unit were considered to be reasons against its routine use. Specific indications for using flouroscopy include anomalous venous drainage, pulmonary hypertension and a large dilated right ventricle. Furthermore, if insertion is attempted without flouroscopy and serious arrhythmias develop or repeated insertion attempts are required, flouroscopy will often shorten total insertion time.

The catheter is designed so that its position in the vascular tree can be monitored without flouroscopy by using external markings at 10 cm intervals in combination with pressure tracings.

INSERTION ROUTE	DISTANCE TO RA
Internal jugular	15 cm
Subclavian	15 cm
Right Antecubital	40 cm
Left Antecubital	50 cm
Femoral	30 cm



For example, if right ventricle (RV) is not reached from the right atrium (RA) by an additional 15-20 cm, it is likely that a coil has formed in the RA or the catheter has passed down the inferior vena cava. Similarly, if the pulmonary artery (PA) is not reached from the RV by an additional 15 cm it is likely a coil has developed in the ventricle. Once the catheter is positioned in the pulmonary artery there is a tendency for it to migrate peripherally and wedge permanently.

Percutaneous catheterization of a large central vein is the most common approach in most series and is generally considered to be superior to a peripheral venous approach when local complications are evaluated. For example, Nehme retrospectively evaluated the complications associated with three insertion techniques in 189 catheterizations (14).

Local Complications of Swan Ganz Catheterizations

	Venous Cutdown Antecubital (n=76)	Percutaneous Antecubital (n=32)	Percutaneous Central (n=81)
Arterial Puncture	3%	-	1%
Transient neuropathy	3%	-	-
Cellulitis	25%	13%	5%
Thrombophlebitis	11%	9%	-
Bacteremia	11%	9%	7%
Catheter failure:			
Wedging	8%	6%	1%
Damping & kinks	25%	38%	-
Withdrawal	7%	3%	1%

Fifty seven percent of the catheters were inserted without flouroscopy at the bedside; 60% by percutaneous cannulation of a central or peripheral vein and 40% by antecubital venous cutdown. Duration of catheterization was similar for both groups. Obtaining access to the circulation required 10 minutes for percutaneous cannulation compared with 25 minutes for a cutdown. Average time from patient preparation to taping the catheter in place was 111 minutes by antecubital venous cutdown compared to 31 minutes by subclavian route.

Catheters inserted using antecubital veins were associated with a significantly greater incidence of cellulitis and thrombophlebitis, particularly after venous cutdown. Bacteremia was related to the duration of catheterization not the insertion site. Antecubital vein insertion limited the usefulness of the catheter in 45 patients due to permanent wedging, pressure damping and kinks or inadvertent withdrawal.

Despite its apparent advantages, there are specific considerations that limit insertion via a central vein. Absolute contraindications include severe coagulopathy, planned thrombolytic therapy, anticoagulated patients and a clotted vein. Relative contraindications include severe bullous emphysema or upper chest wall deformities, both of which are associated with an increased risk of pneumothorax.

A wide variety of complications were associated with catheterization in both of the prospective series in Table I (12,13). Arrhythmias occurred more frequently in the MICU. Critera for reporting arrhythmias were not described for either study so the difference between the groups is unexplained. It may be that in addition to age, patients in the MICU were more seriously ill and at a greater risk. Arrhythmias tended to be transient and usually resolved without specific therapy in both groups. One patient in the SICU died despite catheter withdrawal, antiarrhythmic therapy and resuscitation.

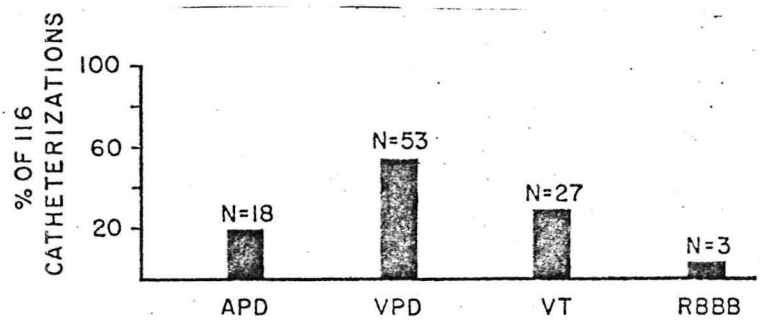
Cellulitis was a significant problem in the SICU (12), generally after an average catheterization of 108 hours. The occurrence of cellulitis did not automatically imply bacteremia which was generally noted after an average catheterization of 103 hours. Both the incidence of cellulitis and bacteremia increased with the duration of catheterization. For example, cellulitis was noted in less than 5% of catheterizations at 3 days, 10% at 4 days and 15% at 5 days.

In contrast, cellulitis was not a problem in the MICU and the reason for this difference is unclear. Cellulitis occurs frequently in other respective studies as the length of catheterization increases (7,14). Despite the absence of cellulitis in the MICU patients, positive blood cultures occurred in more catheterizations. Because most patients had multiple lines that could have been the source, the Swan was considered to be the sole cause of bacteremia in only 2 patients (1.7%). Sise did not consider whether other lines contributed to the incidence of bacteremia in their patients.

Although Elliott did not describe catheter malfunction, one assumes this occurred and was corrected, but not reported. The experience of Sise would seem to more closely approximate the incidence of catheter problems to which we are accustomed. Catheter malfunction rates increased dramatically after 72 hours and almost half of the technical failures required the reinsertion of a new swan for correction. The 15% incidence of balloon related failure includes 10 catheters proven to be defective before insertion. Pneumothorax occurred in 2% of catheterizations in the SICU. None were reported in the MICU despite no apparent difference in the frequency of central venous insertion. Elliott also reported the results of 19 autopsies including evidence of pulmonary infarction in 2 cases, 4 cases of aseptic vegetations and 1 case of pulmonary valve perforation in a patient who had 3 catheters over a period of 27 days.

The experience of Sise, particularly in terms of infection and catheter failure supports current recommendations that catheters should be routinely changed after 72 hours. A relatively low rate of serious morbidity during insertion and a 0.3% mortality suggests this can be done safely. On the other hand, the experience of Elliott which include incidence of infection that may be as low as 1.7%, negligible catheter malfunction and cellulitis suggests that the decision to change catheters can be made on a case by case basis. Most catheters were used for just three days in both series.

Specific complications of catheterization deserve much closer scrutiny. Arrhythmias are the most frequent complication with an incidence varying widely from 11-78% (12,13).



Arrhythmias during 116 pulmonary artery catheterizations. Each bar represents the percentage of catheterizations during which the arrhythmia was recorded. Numbers above the bars denote the number of catheterizations in which the arrhythmia was identified. APD—atrial premature depolarization; VPD—ventricular premature depolarization; VT—ventricular tachycardia; RBBB—right bundle branch block.

Premature ventricular contractions are most commonly reported and usually resolve when the catheter is pulled back into the right atrium. Risk of ventricular tachycardia is increased in patients with hypothermia, acidosis, and hypoxemia. The rare occurrence of transient RBBB suggests that a temporary pacemaker should at least be considered before a catheter is inserted in patients with LBBB (15). Catheters should only be inserted with continuous electrocardiographic monitoring and an intravenous line for access should antiarrhythmic medications be needed.

An underrecognized and completely avoidable complication is pulmonary infarction due to permanent wedging of the catheter. A true incidence is difficult to determine since infarctions are usually small, assymptomatic and only noted as a small infiltrate in the area of the catheter tip, but it may be as high as 7%. The catheter should be pulled back if the tip is more than 5 centimeters from the mediastinum on CXR (17). In addition, the balloon should never be inflated for more than 15 to 30 seconds to obtain a wedge.

Risk of pulmonary embolism due to thrombi in and around the catheter is poorly defined. Foote (16) reported that 9 of 25 patients catheterized following a myocardial infarction had clinical evidence of pulmonary ischemic lesions. In seven patients this was the result of permanent wedging. Catheter associated thrombi were convincingly demonstrated in only 2 patients with either axillary or subclavian thrombosis. Assymptomatic internal jugular thrombosis was noted following catheterization in 66% of patients studied using venography (18). This high incidence of thrombosis compared to retrospective studies suggests that clinical evaluation is inadequate to diagnose catheter associated thrombosis and that it is

usually of little clinical significance. Patients with thrombi had a significantly lower cardiac index and a longer period of hemodynamic compromise (shock) than patients without thrombi (4.9 vs 44 hours) (18).

Hoar reported that 100% of catheters inserted in patients before cardiac surgery had external catheter thrombi when examined 24 hours later at the time of right atriotomy (18).

Duration of Catheterization, Thrombus Formation, and Measurement Problems with 10 Heparin-Bonded and 10 Non-Heparin-Bonded Pulmonary-Artery Catheters.

Type of Catheter	Time from Insertion to Inspection *	Catheters with Adherent Thrombi	Weight of Thrombus Removed *	Measurement Problem	
				dampened tracing	variable cardiac output
	hr	*no.*	*mg*	*no. of catheters*	
Non-heparin-bonded	19.8±2.1	10	174.7±69.7	5	2
Heparin-bonded	24.0±2.2	1	6	0	0

*Mean ±S.E.M.

Heparin bonding of the external surface of the catheter almost completely prevented thrombi formation. Efficacy of heparin bonding beyond 24 hours is unknown and it has not been shown that prevention of thrombus accumulation on a catheter also prevents in situ thrombosis of the vein or distal embolization. These uncertainties and additional catheter cost do not support the routine use of heparin bonded catheters. Heparin bonding may yet prove to be useful in low flow states and right ventricular failure (18).

Many infrequent but no less serious complications have also been reported. For example, it is possible to tie a knot in a catheter (20). This generally occurs due to the overinsertion of a smaller (5 Fr) catheter and formation of a coil in the right ventricle. If a knot is formed, it may be possible to use a guidewire for intracardiac unknotting (21). Failing this, the catheter is withdrawn and a venotomy performed at the insertion site.

Balloon rupture is rare and usually assymptomatic, one possible exception being patients with a right to left shunt. To avoid coronary or cerebral air embolization in these patients, it has been recommended that the balloon should be inflated with carbon dioxide. Most reports of balloon rupture were at a time when catheters were reusable and it is felt that the process of resterilization weakened the balloon (10). Balloon difficulties currently tend to arise as a result of malfunction of the stopcock or valve mechanism for inflation. The balloon should never ever be inflated with a liquid.

One of the most serious complications of catheterization is pulmonary artery perforation or rupture. Patients at risk to rupture tend to be older (>60) or have pulmonary hypertension. The immediate cause for rupture is felt to be overinflation of the balloon, particularly if the catheter tip has migrated peripherally. The balloon should always be inflated slowly until a pulmonary

capillary wedge tracing is observed or undue resistance develops. If the volume of air needed to wedge is less than that used when the catheter was initially inserted, the catheter in all likelihood has migrated peripherally. To avoid dangerous overinflation, the catheter should be pulled back or the inflation volume recorded so that everyone inflating the balloon is aware of the volume limit. Symptoms of rupture are variable and include hypotension, hemoptysis and the rapid development of an infiltrate or effusion. If pulmonary artery rupture is suspected, the catheter should be pulled immediately. In some patients bleeding stops spontaneously, but patients with hemoptysis or an effusion generally require surgery. Mortality in reported cases is in excess of 50% with most deaths occuring within 6 hours (22).

Catheter insertion using a central vein is associated with pneumothorax (23). A chest x-ray should be obtained after any attempt to insert a Swan regardless of success or failure. Inexperience with insertion techniques is also associated with a risk of inadvertent carotid or subclavian arterial puncture; as high as 13% in some studies (23-25). Remarkably, this is rarely associated with subsequent cardiovascular or neurologic sequelae. Patients should always be in the trendelenburg position during insertion to avoid venous air embolism.

Most reports suggest that the incidence of catheter related sepsis is low (13), but the incidence of catheter contamination or colonization varies from 19 to 33% (26-28). It is difficult to interpret the literature due to variations in accounting for underlying sepsis, concomitant antibiotic use, multiple catheters, catheter duration, frequency of surveillance cultures and the exclusion of patients who die with catheters in place (Table II).

Positive catheter tip cultures in these 3 studies were considered to be either contamination during insertion and replacement or colonization during transient or persistent bacteremia. Contamination is defined as organisms cultured from the catheter tip and no other site. Colonization is when an organism cultured from the tip was cultured previously from some other site. It is possible that some cases classified as contamination may be the result of colonization by flora that subsequently changed during antibiotic treatment.

Table II. Positive Pulmonary Artery Catheter Tip Cultures

(Ref)	Number of Cases	Colonization	Contamination	Sepsis
26	152	24	21	1
13	92	5	25	2
27	153	17	12	0
Total	397	46 (12%)	58 (15%)	3 (1%)*

* All staph aureus

Michel (27) demonstrated that the incidence of catheter tip infection was strongly influenced by the presence of a persistent foci of infection. Cultures were positive in 35% of cases with a known focus of infection before catheter insertion, but only in 9% of cases without a known focus ($p<0.005$). In addition, catheters with positive cultures had been used significantly longer ($p<0.05$).

Factors Associated with Positive Catheter Tip Cultures

	% of patients	Catheter, Days Indwelling (mean±SEM)
Focus of Infection known before insertion:		
Catheter negative	65%	3.7±0.4
Catheter positive	35%	4.9±0.6
Focus of Infection unknown before insertion:		
Catheter negative	91%	3.1±0.2
Catheter positive	9%	5.2±1.1

Catheter sepsis is defined as a positive culture from the tip and the blood without previous isolation of the organism from another focus. Based on this definition, catheter related sepsis probably occurs in less than 1% of cases (Table II). This may be an underestimation since patients frequently die with catheters in place without catheter tip cultures. It is more important to recognize that a colonized or contaminated catheter may become a source of bacterial seeding. For this reason, consideration should be given to changing or removing pulmonary artery catheters after 3 days, particularly in patients with sepsis or a known focus of infection.

Incidence of catheter infection can be kept low by not repeatedly manipulating or advancing the catheter. A catheter should never be inserted through an area of inflammed or infected skin or in close association with a contaminated wound. Similarly, a cutdown site should not be reopened and used for catheter reinsertion (28).

Incidence of colonization and contamination in association with a known underlying focus of infection or sepsis suggests that both gram positive and gram negative organisms will be cultured. If the possibility of catheter related sepsis is considered, broad spectrum antibiotics (including staph coverage) are indicated until an organism is identified. In patients with multiple lines, the exact role of the Swan Ganz catheters in causing sepsis can only be defined if all lines are removed and cultured.

B. Arterial Line

Indications for an Arterial Line

Many patients who undergo Swan Ganz catheterization also undergo cannulation of a systemic artery (29). There are 2 basic indications for an arterial line:

1. Systemic pressure monitoring.
2. Systemic arterial access.

Not infrequently a major consideration for insertion is to avoid excessive patient discomfort from repeated arterial punctures over an extended period of time. Deciding to use an arterial line in this situation is a matter of clinical judgement because the safety or efficacy of using an arterial line instead of repeated sampling has not been studied.

Complications of an Arterial Line

Catheterization of an artery may be done percutaneously (30) or by direct cutdown (31). The radial artery is used most frequently because it is accessible and easy to cannulate. Insertion times average approximately 3 minutes and over 90% of insertions are successful during the first attempt. Complications during insertion include pain, hematoma formation and very rarely bradycardia and hypotension attributable to a vasovagal response. Hematomas also develop in up to 10% of patients after catheter removal, but rarely require surgical attention (32).

Potentially the most serious complication of using an arterial line is vascular occlusion. An exact incidence is unknown because most occlusions are assymptomatic and thus go undetected, but it has been estimated to occur in 40-60% of cases (33-35). After just 24 hours, catheter dysfunction as evidenced by dampening of the pressure contour or difficulty aspirating blood occurs in up to 20% of patients with a 20 gauge cannula (predominantly due to kinking) and in 13% with an 18 gauge cannula (predominantly due to thrombosis) (35). In long term studies (1-14 days), 60% of patients develop thrombus and occlusion, especially after 4 days (33).

Vessels felt to be occluded on the basis of the physical exam generally do contain significant quantities of thrombi on arteriography. Smaller vessels are especially vulnerable to thrombus formation and also take the longest time to recanalize (35). Most obstructed radial arteries eventually do regain patency so a complete recovery is likely if ischemia occurs and tissue necrosis can be prevented. Patients with radial artery occlusion generally do not have clinical evidence of distal ischemia or embolization. The actual incidence of tissue necrosis is 0.2 to 0.5% (36).

Factors increasing the risk of ischemic complications include advanced age, history of Raynaud's phenomenon, constricting dressings, vasoconstricting drugs, hypothermia and hypotension. To limit ischemic complications, it is recommended that nothing larger than 20 gauge catheters should be used. In addition, an arterial line should never be inserted without first performing the Allen's test. This simple maneuver demonstrates that the superficial arches may be incomplete in 22% of

patients while in 2-3% the deep arches are absent and the hand is totally dependent on radial artery flow (37).

Risk of infection of an arterial catheter is generally considered to be the same or less than a venous catheter. For example, Gardner has reported that four percent of 200 arterial catheter tip cultures were positive, all as a result of contamination or colonization. The average duration of catheterization of patients with positive cultures was 5.9 days compared to an average of 3.4 days for all 200 patients (34).

Band reported a higher incidence of infection in a prospective evaluation of 95 patients (130 lines). Eighteen percent developed local infection and 4% had sepsis. Risk of infection increased with catheter duration >4 days, cutdown insertion (risk increased x9) and local inflammation (x12). Use of antibiotics did not decrease the risk of infection, but did change the flora cultured (31).

Arterial cannulization for more than 3 days must be weighed cautiously against an increased risk of complications. Catheters should be removed if a red or discolored area develops over the catheter tip or if areas remain blanched after flushing. Arterial catheters should never be hand flushed with a syringe because as little as 3 ml of solution may force emboli from the wrist retrograde into the central circulation (38).

C. Thermodilution Cardiac Output

Thermodilution cardiac output is widely used in the intensive care unit because it uses a physiologic fluid as an indicator, does not require a withdrawal system and successive determinations can be made at short time intervals. In general the method can be used accurately and reproducibly if it is applied systematically and potential sources of error are controlled.

The principle of detecting blood flow by thermodilution is similar to that of other dilution techniques (39). Cardiac output is determined by injecting a known amount of indicator (negative heat) into the right atrium and integrating the temperature change of the blood measured by a thermistor at a fixed point downstream in the pulmonary artery. Most currently available cardiac output computers can complete these calculations within 15-30 seconds. The shape of the thermodilution curve is of fundamental importance in confirming the accuracy of measurements. Lack of a visual representation of these curves is a major limitation of the cardiac output computers available in our hospitals.

There are many technical considerations that influence the reliability of measurements as well as many myths and prejudices about proper technique (40). For example, the choice of D5W or NS as the injectate does not appear to be technically important, but may be clinically important in terms of volume status or electrolyte abnormalities. Positive end expiratory pressure does not directly change thermodilution values. It has been suggested that thrombus formation on the catheter increases the variability of readings by decreasing thermistor sensitivity, but the exact effect of external catheter thrombi is unknown (41).

Use of the pulmonary artery thermistor has all but eliminated errors due to inaccurate measurement of baseline body temperature. However, the temperature

of pulmonary artery blood does fluctuate with respiration, especially during deep spontaneous breathing, forced respiratory effort or attempted breathing against a ventilator (42). Because cardiac output computers determine baseline temperatures for a brief instant just prior to injection, ability to time injections with the respiratory cycle may be important. Wood noted that successive cardiac outputs varied 0-6.7% when measured at the same point in the respiratory cycle, but deviated by up to 14% when measured out of phase by half a cycle (43). If possible, injections should always be made at end expiration.

Either iced or room temperature injectate can be used. Room temperature injectate requires a higher recording sensitivity and is generally not recommended when it is necessary to use less than a 10 cc injectate volume, in patients with very high cardiac outputs or significant respiratory fluctuations (44). Forty five to 60 minutes are required for room temperature D5W in plastic syringes to achieve a steady state temperature (0-3°C) after being placed in an ice bath. When using iced injectate, rewarming of the syringe following manual contact is unimportant if contact time does not exceed 30 seconds (40). The optimum time interval between injections has not been determined. Importance of timing probably depends more on the interval during handling of the syringe and the respiratory cycle than the time between injections (40). Swan and Ganz determined that measurements are independent of injection rate as long as 10 ml is injected as smoothly as possible over 2-4 seconds (39).

There is some disagreement concerning the clinical importance of heat recirculation (40,45). Heat exchanged between iced saline and the catheter is returned to the circulation 5-35 seconds after injection. Heat exchanged between the blood vessel wall and blood occurs over a period of up to 75 seconds. Recirculation may be significant at low flows, but is unlikely to affect successive determinations if a sufficient time interval lapses to restore a steady state. It has been suggested that any effect of recirculation can be minimized if blood is withdrawn into the catheter immediately after an iced injection is finished (46).

Measurements should always be done in triplicate and a source of error in technique should be considered if differences between serial values exceed 10%. The coefficient of variation of measurements has been reported to be 4.74% over a wide range of outputs from 0.68 to 11.4 l/min; ranging from 4.20% at high outputs to 5.45% at low outputs. A somewhat greater variability (5.60%) is observed if room temperature injectate is used (47).

Reproducibility of Thermodilution Cardiac Output (47)

$\dot{Q}$ (l/min)	Mean±SD	Coefficient of Variation $\frac{S \cdot 100}{\bar{x}}$
<1.0-2.99	2.17±.12	5.45
3.0-4.99	4.13±.16	3.94
5.0-6.99	6.53±.29	4.46
7.0-7.99	7.63±.29	3.90
8.0-10.01	9.00±.38	4.20
$\bar{x}$ CO (n=111)	5.32±.25	4.74

Clinical studies have shown that there is good correlation between cardiac output determined by thermodilution and either Fick (48) or dye dilution techniques (49,50). Thermodilution values may be as much as 7.7% higher than dye dilution measurements when the cardiac output exceeds 4 l/min. Fick outputs are probably the most accurate at very low outputs. Regardless of the method, it should be remembered that the overall biologic error of most clinical methods of cardiac output determination may be in the range of 15-20% (40).

Fick cardiac outputs ($\dot{Q}$) are measured using the simultaneous collection of both a Douglas bag to determine oxygen consumption ($\dot{V}O_2$) and arterial and mixed venous blood samples to determine arteriovenous oxygen difference (ΔavO_2).

$$\dot{Q} = \dot{V}O2/\Delta aVO2$$

Fick cardiac outputs can be easily measured in patients spontaneously breathing room air. However, its usefulness in an intensive care unit is limited because higher F_IO_2 and mechanical ventilation introduce unacceptable measurement errors.

The Fick equation can also be used to calculate oxygen consumption by substituting thermodilution measurements of cardiac output.

$$\dot{V}O_2 = \dot{Q} \text{ thermo} \times \Delta aVO_2$$

When $\dot{V}O_2$ is calculated in this manner, sudden changes in $\dot{V}O_2$ that are not associated with changes in the patients clinical condition or extremely high or low values that are inconsistent with clinical evaluation should suggest possible errors either in the determination of thermodilution cardiac output or measurement of PvO_2 due to rapid aspiration of a wedged blood sample (51).

Calculation of $\dot{V}O_2$ can also be used to monitor the effects of therapy. For example, up to 24% of total body $\dot{V}O_2$ in some patients is attributable to the work of breathing (52). Intubation and controlled ventilation decreases the work of breathing and may thus make more oxygen available to other vital organs in patients with clinical evidence of tissue hypoxia. The difference between the $\dot{V}O_2$ calculated before and after instituting mechanical ventilation may quantitate this effect in some patients. The need to decrease the $\dot{V}O_2$ of respiration as a percentage of nonrespiratory $\dot{V}O_2$ has recently been suggested as a justification for early intubation in hypoxemic patients in cardiogenic shock. In animal models of respiratory failure and lactic acidosis, intubation results in significantly less lactic acid production and improved survival (53). Similar physiologic considerations may apply to early extubation or an overly aggressive use of intermittent mandatory ventilation in hypoxic patients (54).

Oxygen consumption in the normal resting human is approximately 4 ml/min/kg or 125 ml/min/m^2. It is unlikely that a steady state level of oxygen consumption exists in critically ill patients due to multiple factors such as nutritional state, variable muscular activity and fever. Cardiac outputs estimated by assuming a level of oxygen consumption based on body weight should NOT be used to make therapeutic decisions in clinically unstable patients. On the other hand, if factors

influencing the level of oxygen consumption appear to be controlled, cardiac outputs estimated in this manner can help confirm the validity of thermodilution values.

D. Summary: How does hemodynamic monitoring effect patient care?

In a recent prospective study, Connors evaluated 62 patients (mean age 56.3 years) without myocardial infarction undergoing right heart catheterization in a university medical center (55). Clinical indications for a Swan included hypotension (63%), respiratory failure (60%), congestive heart failure (47%), sepsis (47%), pulmonary edema (45%), renal insufficiency (34%) and coma (24%). In general, only rapidly deteriorating patients or patients not responding to therapy were cathed. Hospital mortality was 57% and complications included frequent arrhythmias, and rarely hematoma and vena caval thrombosis.

Before catheterization, physicians recorded a plan for therapy to be followed if cath data was unavailable and predicted the cardiac index, right atrial, mean pulmonary artery and pulmonary capillary wedge pressure.

Accuracy of Prediction of Hemodynamic Variables in Various Disease States.*

	No. of RHCs	Percentage of Accurate Predictions			
		PRA	PPA	PPCW	CI
Pulmonary edema					
Cardiogenic	12	50.0	63.3 †	16.7 †	46.7
Noncardiogenic	16	41.7	55.5	55.5	37.5
Left ventricular dysfunction					
PPCW >18 mm Hg	21	52.8	40.7	35.2	52.9
CI <2.2 liters/min/m^2	18	57.5 †	41.5	39.4	55.0
Both	10	72.2 †	47.4	47.4	72.2 †
Sepsis					
Suspected	29	47.8	43.5	46.8	41.5
Confirmed	18	44.6	46.8	45.0	39.1
Coma	15	27.5 †	35.0	42.4	36.1
Respiratory failure	37	36.1 †	46.4	36.7	37.6
All catheterizations	62	*42.7*	*44.0*	*42.0*	*44.0*

*RHC denotes right heart catheterization, PRA mean right atrial pressure, PPA mean pulmonary artery pressure, PPCW pulmonary capillary wedge pressure, and CI cardiac index.

†Significantly different from the accuracy of prediction of all other catheterizations ($P<0.05$).

Incidence of accurate predictions was better than random, but the percentage of accurate predictions was low and ranged from 42 percent for pulmonary capillary wedge pressure to 44% for mean pulmonary artery pressure and cardiac index. In a similar study (56), the mean error of predictions was ±3 mmHg for right atrial pressure, ±9 mmHg for pulmonary artery pressure, ±6 mmHg for the wedge pressure and ±1.82 l/min for cardiac output.

Connors noted that predictions of cardiac index were significantly more accurate in patients with left ventricular dysfunction when the wedge pressure was >18 mmHg and cardiac index <2.22 l/min. Prediction of wedge pressure was significantly less accurate in patients with cardiogenic pulmonary edema. In the setting of respiratory failure, the accuracy of predictions of right atrial pressure

were particularly poor. To determine whether prediction errors were due to physician uncertainty or the judgement of a few inexperienced physicians, 30 cases in which 3 or more physicians were unanimous in their predictions were examined separately. The accuracy of predictions in these patients was not different from the overall accuracy for all cases. Information obtained by catheterization prompted a change of therapy in 48.4% of cases, including either starting or stopping a drug intended to alter hemodynamic status or changing fluid administration rates by more than 100 ml/hour in 21% each. Both drug and fluid therapy were altered in 6% of cases.

These data suggest that the hemodynamic status of critically ill patients without acute myocardial infarction is not accurately determined by routine clinical evaluation. Patients who responded to a trial of therapy did not get cathed so patients with straight forward hemodynamic alterations were excluded. The high frequency of incorrect predictions probably reflects this selection of the most severely ill patients.

Prospective studies do suggest that right heart catheterization is indicated in the evaluation of hemodynamically unstable patients, but it has never been shown that catheterization or changes in therapy resulting from catheterization significantly improves or alters the clinical outcome.

Post myocardial infarction hemodynamic measurements have proven to be useful in assessing short term and long term prognosis (58,59) and are sufficiently useful in directing therapy (60,61) that the risks associated with catheterization in these patients are thought to be warranted. There is also no evidence that right heart catheterization reduces the mortality of patients after myocardial infarction. In fact, at least one report of clinically good risk (Killip Class I) patients who underwent routine catheterization as part of a research protocol has been criticized for excess mortality (57).

CLINICAL SIGNIFICANCE OF MIXED VENOUS OXYGENATION

Oxygen tension of mixed venous blood (PvO_2) is influenced by many factors that may be simultaneously changing in critically ill patients both as the result of disease and therapeutic interventions. These factors include:

1. Alveolar oxygen tension (P_AO_2)
2. Arterial oxygen tension (PaO_2)
3. Oxygen consumption ($\dot{V}O_2$)
4. Shunt
5. Cardiac output ($\dot{Q}$)

In regions of lung with low ventilation to perfusion ratios (V/Q), the P_AO_2 may fall to levels at which little oxygen exchange occurs. Return of deoxygenated blood from these regions into the systemic circulation causes the PaO_2 to fall to a level determined by the amount of blood shunted (Qs/Qt). If oxygen consumption

or tissue oxygen extraction is relatively constant, this reduction in PaO_2 necessarily results in a lower PvO_2. PvO_2 will fall even further if total body oxygen consumption is increased, cardiac output falls or blood flow is shunted to tissues with a higher oxygen extraction (63). Return of this increasingly deoxygenated blood to the lung completes a cycle of worsening arterial hypoxemia. Thus, in the setting of severe V/Q mismatching the cardiac output and PvO_2 become major determinants of PaO_2 (64). Clinically, this cycle is frequently seen in patients with acute respiratory failure due to the Adult Respiratory Distress Syndrome (ARDS).

The clinical significance of the PvO_2 has recently become a focus of controversy particularly as it is used in the intensive care unit to:

1. Assess the adequacy of cardiac output.
2. Assess the adequacy of tissue oxygenation.

The Relationship between the PvO_2 and Cardiac Output

The Fick equation demonstrates the relationship between cardiac output and the level of oxygenation of mixed venous blood. If $\dot{V}O_2$ is relatively stable, a widening arteriovenous oxygen difference is typically due to a fall in mixed venous oxygenation and generally indicates a fall in cardiac output. Under these conditions, the PvO_2 does correlate with cardiac output (65,66). There are three important considerations in using the PvO_2 to assess cardiac output:

1. Clinical decisions based on the PvO_2 should be based on serial determinations.
2. Changes in PvO_2 are best interpreted in the context of the ΔaVO_2 and/or the thermodilution cardiac output.
3. Small changes in Q may result in small changes in PvO_2, but large changes in CvO_2.

Relationships between $\dot{Q}$, CaO_2 and $\dot{V}O_2$ also make the level of oxygenation of mixed venous blood helpful in choosing appropriate therapeutic interventions in critically ill patients.

$$\dot{Q} = \frac{\dot{V}O2}{CaO2 - CvO2}$$

$$CvO2 = CaO2 - \frac{\dot{V}O2}{\dot{Q}}$$

↑ CaO2	↓ $\dot{V}O_2$	↑ $\dot{Q}$
- ↑F_IO_2	- Treat fever	- Digitalis
- PEEP	- Sedate	- Fluids
- Diuresis	- Paralyze	- Dopamine
- ↑Hgb		- (?) Unloading
- Correct pH		
- Correct ↓PO4		

The clinical significance of any measurement of cardiac output is increased if it is related to the amount of oxygen delivered or transported to the tissue:

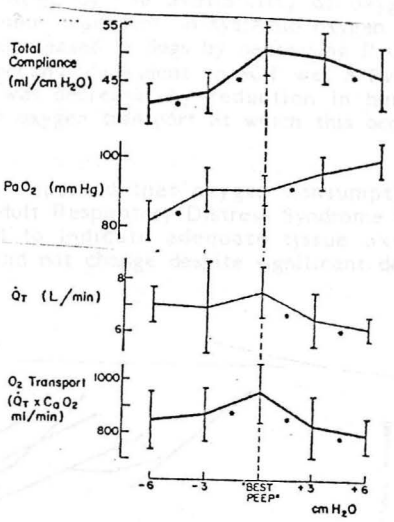
$$\text{Systemic Oxygen Transport} = \dot{Q} \times CaO_2$$

The physiologic significance of changes in $\dot{Q}$ and CaO_2 may be lost if considered alone. For example, positive end expiratory pressure (PEEP) generally increases PaO_2, but not infrequently decreases cardiac output. Calculation of SOT is useful to determine a level of PEEP at which these two parameters have a maximal effect on SOT (67).

	0 cm H_2O	5 cm H_2O	10 cm H_2O
Fraction of inspired oxygen	1.0	1.0	1.0
Arterial oxygen tension (mm Hg)	48	74	99
Arterial oxygen saturation (%)	80	95	98
Hemoglobin (gm/dl)	15	15	15
Arterial oxygen content (ml/100 ml)	16.1	19.1	19.7
Cardiac output (liters/min)	6.0	5.7	4.2
Oxygen transport (ml/min)	966	1089	827

In the above example, PaO_2 alone is inadequate to determine PEEP because it continued to increase as other parameters deteriorated. Similarly, considering only changes in cardiac output may have resulted in stopping short of a level of PEEP associated with maximal SOT. This concept is important because fluid administration (68) or cardiotonic agents can be used in some patients to maintain the cardiac output as higher levels of PEEP are attempted. Hypovolemia should ideally be corrected before PEEP is used, but if necessary fluids can usually compensate for small reductions in cardiac output at levels of up to 20 cm H_2O PEEP. Chronotropic support is usually not necessary unless myocardial function is depressed or >15 cm H_2O PEEP is used. The use of fluids to improve left ventricular filling is accomplished at the risk of increasing LVEDP, increasing pulmonary capillary hydrostatic pressure and worsening pulmonary edema (69). This may be compounded by fluid retention due to excess ADH activity in response to mechanical ventilation (70). Furthermore, while it is generally believed that PEEP reduces shunt (Qs/Qt) by alveolar recruitment, Dantzker has recently shown that shunt reduction may also result from decreases in cardiac output (71). In this case, increasing cardiac output (72) may paradoxically worsen arterial hypoxemia by increasing Qs/Qt (73,74).

Suter popularized the term "Best PEEP" for the level of PEEP at which hemodynamic parameters are at maximum levels (75). He determined that the highest level of total compliance measured using the ventilator correlated with optimal hemodynamic parameters measured by right heart catheterization.



These results have been criticized because each point is mean data from 15 patients and little attempt was made to maintain the cardiac output as PEEP was increased. However, the concept of "Best PEEP" is valuable because it focuses attention on the importance of considering SOT and not isolated gas exchange or hemodynamic measurements in the management of these patients. If there is a "Best PEEP" it must be systematically determined in every patient and reconfirmed after a patient's clinical condition changes significantly (76).

Relationship between the PvO_2 and Tissue Oxygenation

It is generally considered that a fall in PvO_2 is a warning that tissue oxygenation is impaired (77). The body responds to tissue hypoxia with a variety of compensatory mechanisms that make it difficult to use the PvO_2 to identify specific pathophysiologic abnormalities including: (78)

1. Increased cardiac output
2. Increased oxygen extraction (widened ΔavO_2)
3. Increased hemoglobin concentration
4. Altered affinity of hemoglobin for oxygen
5. Shunting
6. (?) decreased $\dot{V}O_2$

If tissue oxygen demand exceeds oxygen transport or these compensatory mechanisms begin to fail, tissue function can be maintained anaerobically until lactic acidosis results in death. At the point anaerobic metabolism begins aerobic

metabolism is controlled by the availability of oxygen. In other words, oxygen consumption may become dependent on systemic oxygen transport. Cain has shown that when SOT was decreased in dogs by decreasing PaO_2 (F_IO_2 of 9%) the critical point at which $\dot{V}O_2$ became dependent on SOT was a PvO_2 of 17 mmHg, but it was 45 mmHg when SOT was decreased by reduction in hemoglobin (Hct <10%) (79). The level of systemic oxygen transport at which this occurs clinically is very poorly defined.

Danek recently reported that oxygen consumption is dependent on SOT in patients with the Adult Respiratory Distress Syndrome (ARDS) despite PvO_2 values generally considered to indicate adequate tissue oxygenation (Fig. A) (80). Furthermore, PvO_2 did not change despite significant decreases in $\dot{Q}$ and SOT (Fig. B).

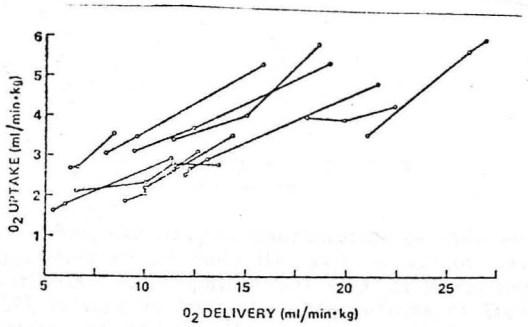


Fig. A

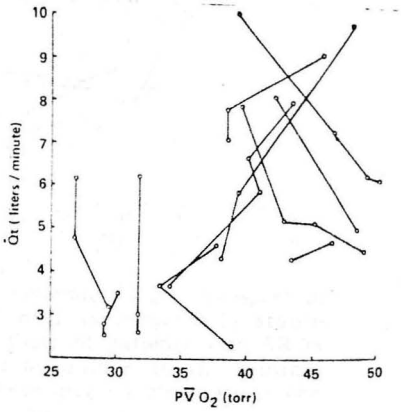


Fig. B

The concomitant increase in $\dot{V}O_2$ and SOT suggests that the oxygen needs of some tissues were never fully satisfied despite a wide range of SOT. None of the patients had clinical evidence of anaerobic metabolism. If the oxygen requirement of all tissues were satisfied by the compensatory mechanisms to hypoxia, $\dot{V}O_2$ would have been relatively constant at a level determined by the metabolic activity of the tissues and thus independent of changes in SOT. It was postulated that oxygen consumption may have been dependent on transport due to diffuse cellular dysfunction in peripheral tissues resulting in an inability to utilize available oxygen. This would be in keeping with a growing awareness that ARDS if frequently complicated by multiple organ failure.

This paper obviously presents a considerable challenge to our current understanding of the relationship between PvO_2 and cardiac output and tissue oxygenation. These results have been criticized because many of the patients were septic. Sepsis has been shown to interfere with peripheral vasoregulatory mechanisms resulting in preferential perfusion of tissues with low oxygen extraction (81,82). This would decrease $\dot{V}O_2$ and maintain a high PvO_2, even if cardiac output decreased. It is also known that PEEP causes changes in the distribution of blood flow to several tissue regions and may thus alter normal compensatory mechanisms

to optimize oxygen utilization (83-85). This effect may have been exaggerated due to the release of vasoactive substances secondary to stress, sepsis or tissue death (86).

In a second group of similar critically ill patients without ARDS Danek reported that compensatory mechanisms appeared to be intact (80). $\dot{V}O_2$ was maintained in the face of decreased delivery (Fig. A) primarily by increased tissue oxygen extraction (widened ΔavO_2). In these patients changes in PvO_2 reflected changes in cardiac output (Fig. B).

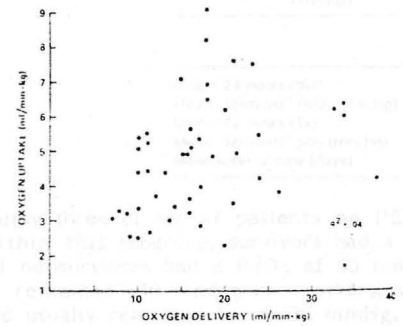


Fig. A

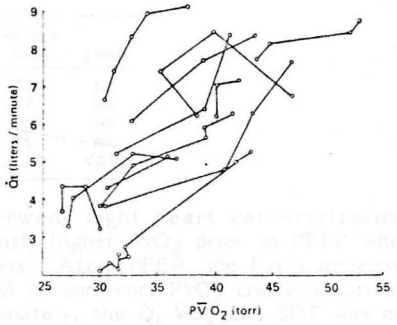


Fig. B

Because oxygen consumption is independent of systemic oxygen transport in this group of critically ill patients without ARDS as well as chronically stable patients with impaired SOT even at levels similar to those of patients with ARDS (87), it appears that the observations of Danek may be unique to the clinical setting of ARDS. More work is needed to confirm these original observations and further define the role of sepsis and peripheral shunt in these patients.

The controversy that this paper has caused has been valuable in that it refocused attention on the idea that the PvO_2 may not accurately reflect tissue oxygenation. Mixed venous blood is the combination of venous effluent from a wide variety of tissues with different metabolic rates (88). It is possible that a normal PvO_2 could be maintained even in the face of inadequate tissue oxygenation if areas of low oxygen extraction receive a higher proportion of blood flow. Widely disparate critical values of PvO_2 at which $\dot{V}O_2$ becomes dependent on SOT in Cain's experiments (79) strongly suggests that the PvO_2 correlates poorly with the adequacy of oxygenation in critical tissues. The use of the PvO_2 to follow the clinical response of patients may be misleading and thus should not be considered a therapeutic end point. At present, the most that can be said is that a low PvO_2 is bad, but a normal PvO_2 is not necessarily good.

Relationship between PvO_2 and Survival

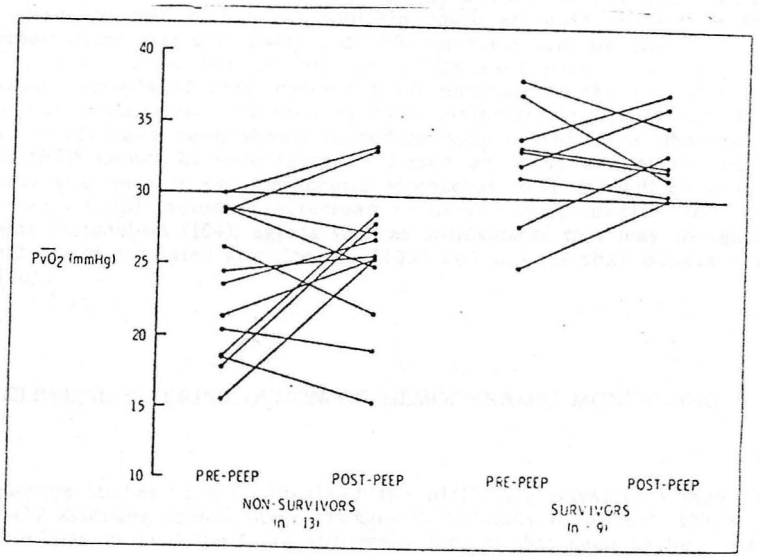
The level of oxygenation of mixed venous blood has also been correlated with patient survival both in stable chronic obstructive lung disease (89) and critically ill patients (90). For example, Springer retrospectively reviewed the hospital course of 78 critically ill patients with ARDS (90). Because the use of PEEP was just being

introduced in this type of patient during the time of the study (91), 60% of the patients were treated with PEEP and the remaining 40% received mechanical ventilation alone. Overall survival rate defined by hospital discharge was similar in the 2 groups, 60 and 55% respectively. The effect of PEEP was a prolongation in the length of survival; 9.2 days with PEEP and 4.2 days without. Virtually all patients in both groups with a PaO_2 <50 mmHg (on F_IO_2 1.0) eventually died.

Duration of Survival and Terminal PaO_2 in Patients Who Died With and Without PEEP Therapy

	PEEP (n-32)	No PEEP (n-23)	p Value
Died <24 hours (%)*	38	35	NS
Mean "terminal" PaO_2 (mm Hg)	39	37	NS
Died >72 hours (%)	62	65	NS
Mean "terminal" pO_2 (mm Hg)	76	75	NS
Mean survival time (days)	9.2	4.2	<0.05

Thirty three of the 47 patients on PEEP underwent right heart catheterization. Within this subgroup, survivors had a significantly higher PvO_2 prior to PEEP while all nonsurvivors had a PvO_2 of 30 mmHg or less. After PEEP, the PvO_2 increased or remained >30 mmHg in survivors, whereas in nonsurvivors PvO_2 changed variably and usually remained below 30 mmHg. Unfortunately, the $\dot{Q}$, $\dot{V}O_2$ and SOT was not reported in these patients to re-examine the relationship between the PvO_2 and tissue oxygenation and the cardiac output.



While this study didn't demonstrate any definite benefits of PEEP, it obviously hasn't precluded its widespread use. The results of this study have been criticized because it was retrospective and the two groups were different because hypotensive acidotic patients were rarely treated with PEEP. Furthermore, comparison of this report to other ARDS and PEEP studies is difficult due to a perponderance of postoperative cardiac patients, 14 patients were treated with PEEP without swan ganz catheterization and patients who decreased their cardiac output on PEEP were generally not treated with volume or chronotropic medications in an effort to maintain Q; rather PEEP was decreased. Good controlled prospective studies of PEEP have not been subsequently attempted.

Zapol has reported that survival in similar patients is related to the development of fixed pulmonary hypertension that occurs in the absence of systemic hypoxemia (92). Pulmonary vascular resistance was inversely related to pulmonary blood flow and was minimally reduced by diversion of up to one half of the cardiac output to an extracorporeal membrane oxygenator. Possible causes of this increase in PVR include active vasoconstriction, decreased lung volume, endothelial cell edema, diffuse microembolism or thrombosis, and microvascular obliteration by fibrosis and hemorrhage (92,93). While it is difficult to tell which of these may be clinically significant in any given patient, active vasoconstriction may be the one that is potentially the most reversible (94).

In animal models, the level of oxygenation of mixed venous blood appears to modulate pulmonary vascular tone, particularly in the setting of alveolar hypoxia (95). A low PvO_2 may act to increase PVR directly (96) or indirectly by reducing P_AO_2 to levels known to cause pulmonary vasoconstriction (97). Zapol did not examine whether low PvO_2 contributed to the increase in PVR (92), but it is an intriguing possibility that such a relationship could at least in part be the link between observations that both PvO_2 and PVR correlate with survival.

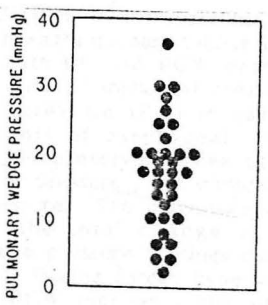
Clinical observations that patients with ARDS are hypoxemic out of proportion to measured amounts of lung water (98,99) emphasizes the potential role of circulatory abnormalities. Cyclo-oxygenase inhibitors (100,101) and narcotic antagonists (102) have been shown to reduce early hemodynamic abnormalities in sheep with ARDS caused by endotoxemia. Based on these and other reports, it seems likely that several new therapeutic approaches to ARDS will be tried in the next few years (103) including afterload reduction (94), specific inhibitors of arachidonate metabolism (104), agents such as antioxidants that may antagonize the injurious effects of activated granulocytes (105) and agents that oppose protease activity (106).

CLINICAL INTERPRETATION OF HEMODYNAMIC MONITORING

Prospective studies have emphasized the difficulty physicians may have in noninvasively assessing hemodynamic changes in critically ill patients (55,56). With hemodynamic data in hand there are still many factors that need to be considered

before proper clinical interpretation is possible.

In critically ill patients, right and left ventricular function may be so disparate that both the absolute central venous pressure (CVP) and changes in CVP are unreliable and often misleading estimates of left sided pressures (107-109).



Data from 33 patients, showing the wide range of pulmonary capillary wedge pressure values measured in the presence of normal central venous pressure (1-5 mm Hg).

There is normally very little difference between pulmonary artery diastolic (PAd), pulmonary capillary wedge (PCW), mean left atrial (LA), and left ventricular end diastolic (LVEDP) pressures. For this reason, the PCW and PAd are usually an accurate indirect measurement of LA and LVEDP (110,111). Pad can be used to estimate the wedge pressure in cardiac patients (excluding those with mitral disease) and patients in circulatory shock, if 3 criteria are met:

1) The PAd and PCW should be similar initially.
2) When clinical changes occur the PAd-PCW gradient should be rechecked.
3) PCW should be directly measured if pulmonary vascular resistance (PVR) is elevated or the heart rate is greater than 120 bpm.

A PAd-PCW gradient >5 mmHg correlates with an elevated PVR, but is not specific for a cause. Generally, even moderate degrees of hypoxemia increase PVR enough to make the PAd an unreliable guide of LA pressure.

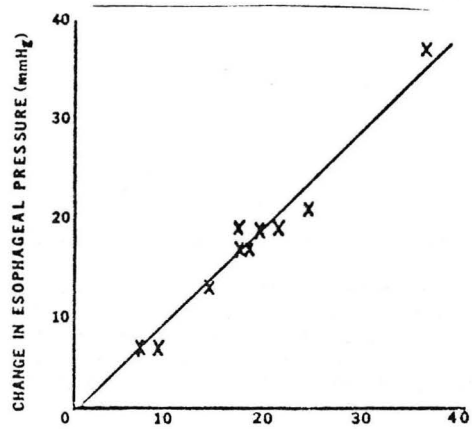
The equivalency of the PCW and LA is lost with obstruction or constriction of pulmonary veins, severe mitral valve disease and reduced left ventricular compliance or increased left ventricular volume or both. Left ventricular compliance or volume may be altered by ventricular hypertrophy, cardiomyopathies, chronic valvular disease, or myocardial infarction. In such cases up to 40% of the LVEDP may be due to atrial contraction, particularly when cardiac output is low. PCW may still reflect LA pressure in these patients, but may also underestimate LVEDP (110).

Because the PCW is used to indirectly assess left sided filling pressures in the ICU, the effect of mechanical ventilation on the accuracy of PCW determinations

deserves additional review. The focus of this review will be to determine how changes in intrathoracic pressure influence both the PCW itself and the equivalence between PCW and LA.

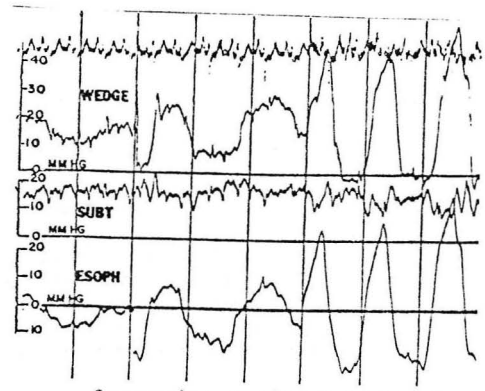
Alterations in the PCW due to Spontaneous Respiration

Significant respiratory variations in intravascular pressure measurements can develop during spontaneous breathing, particularly in patients with severe airflow obstruction (112). Changes in both PA and PCW pressures closely parallel these changes in intrathoracic pressure. Esophageal pressure (Peso) can be measured to indirectly estimate pleural pressure (P_{pl}) in patients with COPD and acute respiratory failure. Measurements of esophageal pressure are inexact and may underestimate both the net compressive forces of the lungs and the regional differences in the distribution of pressures, but clinically they are the least invasive means to measure pleural pressure. The magnitude of total changes in esophageal pressure correlate well with the total change in wedge pressure (Fig. A). Respiratory fluctuations in wedge pressure tracings can be minimized by subtraction of esophageal pressure (Fig. B). During forced hyperventilation, total respiratory fluctuation in the absolute PCW increases but subtraction of Peso from the measured PCW demonstrates that PCW does not change.



Total change in esophageal and wedge pressure in ten patients. Slope=1.04, r=0.98.

Fig. A



Segments of a tracing of a patient with simultaneous absolute wedge (*WEDGE*), esophageal pressure (*ESOPH*), with electrical subtraction (*SUBT*) recorded during quiet breathing and during hyperventilation.

Fig. B

It is difficult to measure Peso using an esophageal balloon in critically ill patients. It is possible to accomplish the same effect as measuring and subtracting Peso by routinely measuring the PCW at end expiration when airflow stops and the difference between P_{pl} relative to atmospheric pressure approaches zero. Equivalency of the PCW-LA is maintained at end expiration. In the event that an end expiratory pause may not be possible in tachypneic patients, the electronic

mean also serves to negate the effect of intrathoracic pressure. However, in the presence of both airways obstruction and loss of elastic recoil, marked positive intrathoracic pressures produced during active expiration can result in an elevated electronic mean. For example, Rice (112) demonstrated total intrathoracic pressure changes of greater than 20 mmHg resulted in significant differences between the electronic (113) mean and the effective pressure (PCW-Peso). This is compounded by the fact that the frequency response of most monitors is such that the digital readout lags behind changes in the patient's respiratory cycle (113). If the accuracy of the PCW is critical in such patients, a direct tracing is needed to more precisely measure at end expiration or the insertion of an esophageal balloon should be attempted.

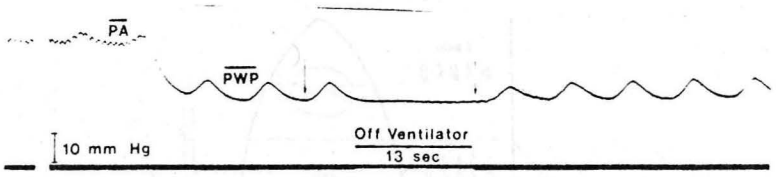
Three patients with total Pleural Pressure (P_{pl}) changes >20 mmHg with elevated electronic mean PCW in relation to (PCW - P_{pl})

Patient	Peak P_{pl} Inspiration/Expiration	Total P_{pl} Change	Difference Electronic Mean vs (PCW - P_{pl})
1	-7/+14	21	6
2	-6/+31	37	17
3	-10/+21	31	10

All pressures mmHg

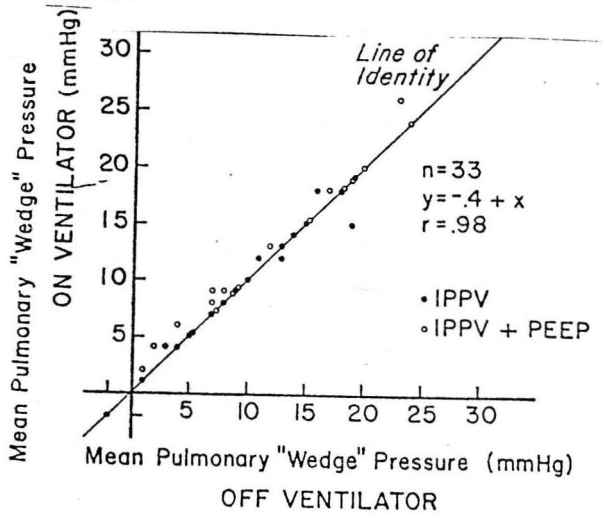
Alterations in the PCW due to Mechanical Ventilation

In contrast to spontaneous ventilation, pleural pressure rises with each inspiration during mechanical ventilation. The accuracy of the PCW during mechanical ventilation in patients with respiratory failure has been assessed using continuous recordings of the pulmonary wedge pressure during times when patients were briefly disconnected from the ventilator as part of their routine care (114).



Continuous recording of mean pulmonary wedge pressure (PWP) during discontinuation of mechanical ventilation. *Arrows* indicate points at which measurements of pulmonary wedge pressure were obtained for comparison. PA, Mean pulmonary arterial pressure.

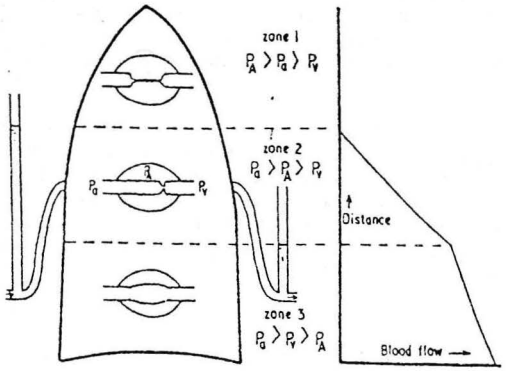
PCW will rarely vary by more than 1 mmHg off the ventilator as shown below if spontaneous respiratory effort is suppressed, PEEP is absent and measurements are made at end exhalation.



In certain clinical situations, positive pressure ventilation can directly alter hemodynamic measurements by:

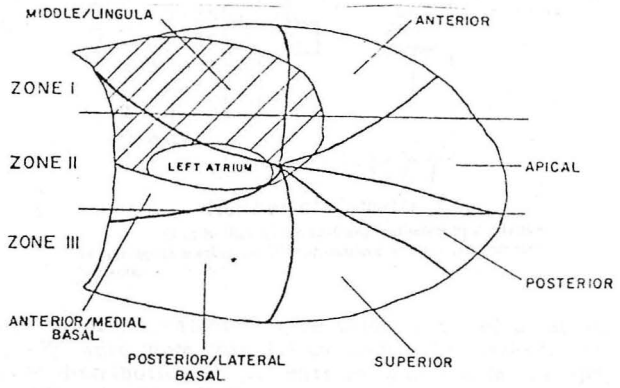
1. Direct pressure transmission to vessels and cardiac chambers.
2. Alterations of pulmonary blood flow.

The complex physiologic interactions of positive pressure breathing on cardiac output and pulmonary vascular resistance due to the direct transmission of pressure has recently been reviewed at these proceedings (69). The effect of positive pressure breathing on pulmonary blood flow is also complex. Regional lung perfusion is determined by the relationship between pulmonary arterial (P_{pa}), alveolar (P_{alv}) and pulmonary venous (P_V) pressure. Based on these pressures, West has divided the lung into 3 zones (115).



In regions where alveolar pressure exceeds the two vascular pressures (Zone 1) there is no blood flow. In Zone 2, pulmonary alveolar pressure exceeds pulmonary venous pressure but because it is less than pulmonary arterial pressure, perfusion is established by a principle described as a vascular waterfall. In Zone 3, both pulmonary arterial and venous pressures exceed alveolar pressure and perfusion is determined by the arterial-venous pressure gradient. A continuous column of blood exists throughout respiration in Zone 3 and usually in Zone 2. Because the measurement of the PCW assumes a continuous column of blood from the catheter tip to the left atrium, the PCW in Zone 1 will reflect alveolar pressure not pulmonary venous pressure.

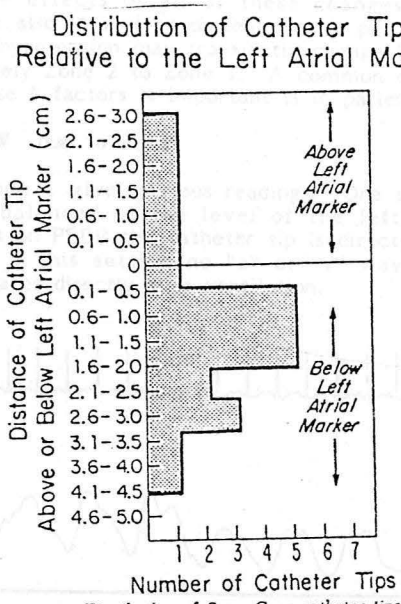
There are two additional considerations. First, the vertical gradient described by West's is anterior to posterior in supine patients. As a result, the zones are narrow and may be ill defined. Zone 1 is considered to be above the left atrium, Zone 2 at the level of the atrium and Zone 3 is below the left hilum.



Second, mechanical ventilation of patients in the supine position also alters the distribution of pulmonary blood flow. In contrast to spontaneous respiration ventilation perfusion indices are decreased at the bases adjacent to the diaphragm (116). The addition of 5 cm H_2O of PEEP generally tends to increase ventilation in more dependent lung regions while >5 cm H_2O produces hyperventilation of all zones, particularly Zone 1. Following oleic acid induced lung injury in primates, PEEP up to 15 cm H_2O improves the distribution of ventilation and blood flow in both Zone 2 and 3 (117).

The frequency with which swan ganz catheters are passed into Zone 3 has recently been reported in 30 patients in whom a catheter was inserted percutaneously without flouroscopy just prior to open heart surgery (118). During surgery a metal clip was placed on the left atrium at its junction with the right upper lobe pulmonary vein. In 12 of the 30 patients a left atrial catheter was also inserted. Postoperatively, a portable supine lateral CXR was taken to confirm

catheter location.



Distribution of Swan-Ganz catheter tips relative to left atrial marker in 30 consecutive open heart surgery patients.

Forty three percent of the catheters were within 1 cm of or above the left atrial marker but only 10% were more than 1.5 cm above the marker. Orta reported a similar catheter distribution in patients in which arteriography was used to determine the catheter location (119).

While it is commonly considered that most pulmonary blood is to the dependent part of the lung, Hughes demonstrated that regional blood flow is dependent on lung volume (120). At functional residual capacity the greatest blood flow is to mid lung which may explain the distribution of catheters to within 1 or 2 cm of the left atrium. It is frequently suggested that advancement during inspiration as lung volume is increasing may increase the chance of reaching a dependent location (Zone 3). The only reliable method to determine optimal Zone 3 catheter position is on a lateral chest film (portable, supine and slightly over penetrated to see the catheter tip) (118).

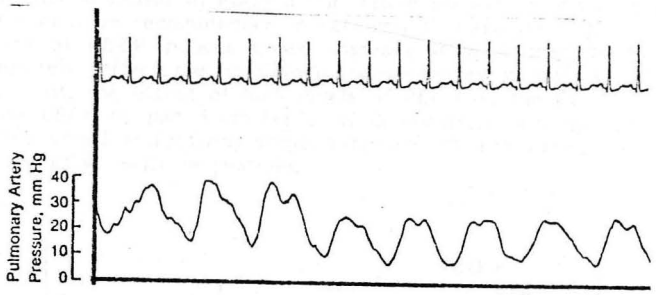
The accuracy of the PCWP measurement and the correlation between PCW and LA pressures during mechanical ventilation can be altered by:

1. The height of the pulmonary catheter tip above the left atrium.
2. Left atrial pressure (LA)
3. Pulmonary artery pressure (PA)
4. Increased alveolar pressure (PEEP)

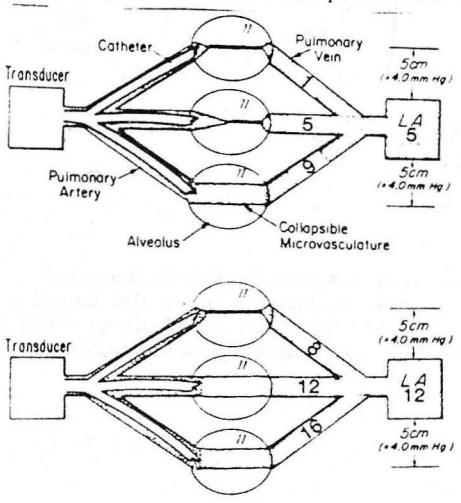
The quantitative effects of all of these changes is variable not only from patient to patient, but also in a given patient over a period of time. For example, hypovolemia and/or hypotension may transiently change Zone 3 regions of the lung to Zone 2 or more likely Zone 2 to Zone 1. A common clinical situation in which the interaction of these 4 factors is important is in patients requiring PEEP.

Alterations in the PCW due to PEEP

Catheters in Zone 1 give spurious readings. One source of error is that the transducer is usually balanced at the level of the left atrium (121), but more importantly in patients on PEEP the catheter tip is directly exposed to P_{alv}. When the balloon is inflated in this setting no "a" or "v" waves will be seen and the tracing baseline fluctuates directly with ventilation.



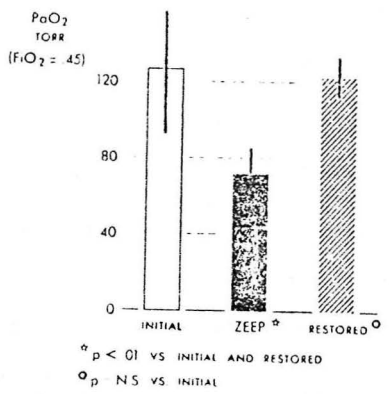
Zone 2 catheters may also give spurious readings, particularly when PEEP is >5cm H_2O. When the ballon is inflated, pressure in the vascular segment downstream decreases and vessels tend to collapse, particularly when LA pressure is low (122) or P_{alv} is very high. However, when LA pressure is close to P_{alv} accurate measurements may still be possible (118,122). Because PCW (Pv) is kept low to minimize pulmonary edema in many patients with ARDS, this consideration is clinically significant if a catheter is in Zone 2, but it may not be important in patients with cardiogenic pulmonary edema where LA pressure is high.

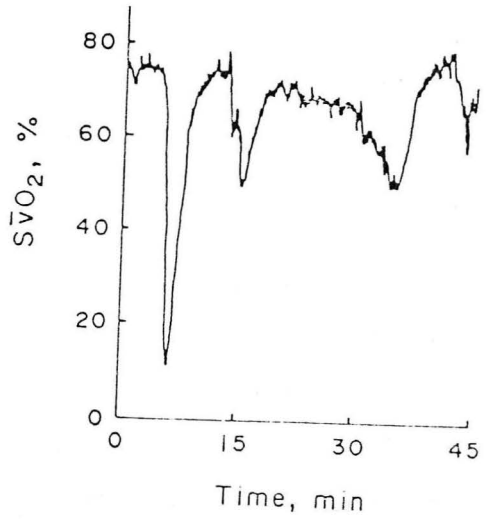


In summary, Zone 2 can be effectively converted to Zone 1 by increasing PEEP to a level where PA and Pv are exceeded or at lower levels of PEEP when PA or Pv is low due to hypovolemia and hypotension. A change from Zone 2 to Zone 1 should be suspected when any of these clinical circumstances occur, particularly if the PCW tracing changes and excessive ventilator effect is noted on the baseline.

It has recently been suggested a Zone 2 catheter may become more dependent (Zone 3) by turning a patient into the decubitus position (123). If this is done, it is necessary to readjust and recalibrate the transducers to a new atrial height. These patients will also need to be closely monitored because gas exchange may deteriorate (124), particularly if a "bad lung" is down (125).

PEEP should never be momentarily discontinued to make PCW measurements (126). Profound decreases in PaO_2 occur within seconds of discontinuing PEEP, so this practice cannot be recommended in seriously ill patients (127). Furthermore, discontinuance of PEEP induces a new unsteady state so that the PCW measured may not accurately reflect the physiologic consequences of a PCW on PEEP (128). At the very most, the effect of high levels of PEEP on the PCW can be assessed by decreasing PEEP by just 5 cm H_2O. If demonstrable changes in the PCW are noted with this small reduction, some estimate of the effect of PEEP on the accuracy of the PCW will be possible.





Good clinical and experimental studies suggest that the PCW at end expiration still reflects intraluminal left atrial pressure at levels of PEEP 10 cm H_2O and even at levels of PEEP up to 30 cm H_2O (129-132) when catheters are in Zone 3. Changes in lung compliance during respiratory failure may alter the

transmission of airway pressure to the microvasculature and thus have been reported to unpredictably change the PCW and its relationship to left atrial filling pressure (133,134). In most of the studies in which this was observed, position of the catheter tip was not checked or reported so a Zone 2 or Zone 1 effect may have occurred. In animal studies in which catheter height was carefully controlled, compliance may decrease, but this does not appear to prevent transmission of pressure to the pleural space and microvasculature or more importantly change the relationship between the PCW and left atrial pressure (129,130,135).

Human studies have similarly demonstrated that the PCW-LA relationship does not change in patients with reduced compliance after bypass surgery at levels of PEEP up to 11 cm H_2O (118). Unfortunately, the effect of high level PEEP (>15 cm H_2O) is still somewhat open to question. Jardin et al (136) directly measured pleural pressure through a chest tube or a small percutaneous catheter in 4 patients and an esophageal balloon in 6 patients with ARDS in whom a swan and left heart catheter were also inserted. PEEP was increased in 5 cm H_2O increments at 10 minute intervals up to 30 cm H_2O. Compliance was not reported but was probably very low because all 10 patients were typical of patients with ARDS (including 4 with pneumonia and 3 with gastric acid aspiration).

HEMODYNAMIC DATA AT DIFFERENT LEVELS OF PEEP

	PEEP (cm H_2O)						
	0	5	10	15	20	25	30
LVEDP (mmHg)†	9.4±1.6	9.9±2	8.6±1.4	7.5±1.4	6.3±1.3**	6.1±1.9**	6.8±1.5**
P_{pl} (mmHg)	-0.6±1.4	-0.3±1.2*	0.8±1.9**	2±2**	3.7±2.1**	4.6±1.9**	6.9±2.5**

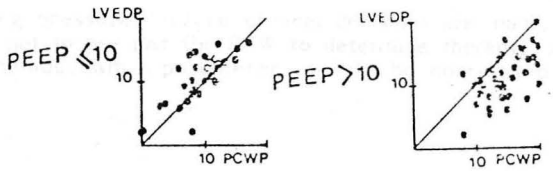
Data presented as mean±SD

LVEDP = left ventricular end-diastolic pressure, P_{pl} = pleural pressure

* $p<0.05$ for comparison with PEEP = 0 cm H_2O, ** $p<0.01$

† transmural pressure is measured pressure minus pleural pressure

Transmission of the positive end expiratory pressure to the pleural space does occur, but not significantly below 10 cm H_2O and incompletely even at 30 cm H_2O (6.9±2.5 mmHg). Correlation between PCW and LVEDP was excellent when PEEP was <10 cm H_2O, but PCW overestimated the LVEDP at levels >10 cm H_2O. Because the height of the catheter tip was not checked in these patients, it is possible that the difference between this study and almost all others is related to a Zone 2 or Zone 1 effect on the relationship between the PCW and LVEDP.



The true distending transmural pressure of a vessel or the cardiac chamber is intraluminal pressure minus the surrounding pressure. Intravascular pressures recorded in patients in the ICU are measured relative to atmospheric pressure. The confounding effect of positive pleural pressure is to overestimate actual filling pressures by the amount of pleural pressure (measured pressure - pleural pressure). For example, the measured LVEDP in Jardin's patients (136) can be estimated to have increased from approximately 10 mmHg off PEEP to 13.7 mmHg at 30 cm H_2O PEEP. In contrast, the transmural LVEDP (measured LVEDP - P_{pl}) actually fell from 9.4±1.6 mmHg to 6.8±1.5 mmHg at these same levels because pleural pressure rose to 6.9± 2.5 mmHg. If we assume as most of the literature suggests, that a true Zone 3 PCW would have increased in relationship to the LVEDP, the potential clinical errors based on using the wedge alone to assess left sided filling pressures and determine therapy in patients on PEEP are obvious.

In order to correct the PEEP induced discrepancy between the PCW measurement and true left sided filling pressures, pleural pressure must be measured (Peso) (137). However, it is possible on the basis of available data to roughly estimate a pleural pressure at different levels of PEEP.

End expiratory pleural pressure generally does not become significantly positive below 10 cm H_2O PEEP. At levels greater than 10 cm H_2O, there appears to be 2-3 cm H_2O increase in pleural pressure for every 5 cm H_2O increase in PEEP. This estimate of P_{pl} can be subtracted from measured pressures to more accurately estimate transmural filling pressures. (Remember to correct cm H_2O to mmHg before subtracting from PCW). Such estimates should be used cautiously because the compliance of the lung may variably determine more or less pleural pressure at any given level of PEEP. The best safeguard against making clinical errors is to be aware of these problems and avoid overinterpretation of absolute wedge values in patients on PEEP.

In summary, PCW measurements in patients on PEEP are unreliable if obtained from Zone 1 and usually Zone 2. Zone 3 measurements can be considered to reflect left sided filling pressures even to levels as high as 30 cm H_2O PEEP. Zone 3 can become Zone 2 as the level of PEEP increases in hypotensive or hypovolemic patients.

The relationship between PCW and LA is probably preserved at all levels of PEEP, but absolute measurements may be significantly greater than actual transmural pressures at levels >10 cm H_2O. Direct measurements (Peso) and estimates of P_{pl} can be used to correct the PCW and more accurately determine

left sided filling pressures before clinical decisions are made. At high levels of PEEP it is best not to use just the PCW to determine therapy. Instead, the PCW and all other hemodynamic parameters should be correlated with the patient's condition.

CONCLUSION

Hemodynamic monitoring involves far more than the ability to insert catheters. Physicians must know the indications for invasive monitoring as well as be able to recognize and treat potential complications. If hemodynamic monitoring is to be of value in patient management, careful attention must be paid to the methods of measurement. Physicians must be familiar with calibration and balancing of monitors and able to recognize all potential sources of error.

Quality of hemodynamic measurements is entirely dependent on the accuracy with which they are collected and reported. It is difficult enough to interpret the meaning of the many physiologic abnormalities critically ill patients may have without adding the additional uncertainty of poorly collected data. It is the responsibility of everyone involved in the care of these patients to be certain that incorrect measurements are not used to make important therapeutic decisions.

Hemodynamic monitoring should not be interpreted as perfunctory electronic surveillance. Automatic digital readouts cannot be the sole parameters used to follow a patient's clinical course. Even the best hemodynamic data is worthless if it is not correlated with changes, even very subtle changes, in the clinical condition of these patients. Availability of bedside hemodynamic monitoring has not and will never replace the nurse and physician.

Hemodynamic monitoring is useful in the management of critically ill patients. Its true impact on clinical outcome is unknown, but seems likely to be directly related to the knowledge and skill of the nurses and physicians caring for the patient.

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