Instantaneous Blood Flow Responses to Positive End-Expiratory Pressure with Spontaneous Ventilation

RICHARD A. PERSCHAU, M.D., CARL J. PEPINE, M.D., WILMER W. NICHOLS, PH.D., AND JOHN B. DOWNS, M.D.

SUMMARY Variable hemodynamic responses to positive end-expiratory pressure (PEEP) with spontaneous ventilation have been reported. To clarify these responses, 15 awake patients were studied using a catheter-tip velocity transducer to record phasic aortic root blood flow continuously before, during and after PEEP (10 cm H₂O) applied with a face mask. Central blood volume and effective ventricular filling pressures were measured. Phasic pulmonary artery blood flow was also simultaneously recorded in three of these patients.

PEEP produced an acute aortic blood flow reduction, detected within one respiratory cycle. Stroke volume decreased 12%, and since heart rate was unchanged, cardiac output also declined (p < 0.05). Inspiratory-to-expiratory aortic flow changes were less during PEEP. In contrast, inspiratory-to-expiratory pulmonary artery flow alterations were exaggerated due to a marked flow decline during expiration. Central blood volume and effective left ventricular filling pressure decreased 9% and 19%, respectively (p < 0.05 in all patients). The decrease in pulmonary artery flow was associated with a decrease in central blood volume in the three patients in whom pulmonary flow was measured. PEEP promptly reduces cardiac output during spontaneous ventilation, related to a decrease in pulmonary flow in expiration.

HEMODYNAMIC RESPONSES to positive end-expiratory pressure (PEEP) during spontaneous ventilation in awake man are not completely understood.1 Existing information has been extrapolated from animal and limited human studies. The effect of PEEP during spontaneous ventilation on cardiac output is particularly difficult to predict based on information from existing techniques to measure cardiac output.2-4

Blood flow is continuously changing during maneuvers that influence intrathoracic pressure.5-6 We do not know whether these changes are rapidly phasic or if flow and volume change proportionally so as to remain constant. Therefore, we and others6 believe that the use of the single bolus indicator technique in these settings is questionable. Cardiac output determined by indicator dilution may be erroneous, since a fundamental assumption of these techniques of measuring flow in the circulation is consistency of the blood flow.6, 7 In contrast, the catheter-mounted electromagnetic velocity probe measures blood flow continuously and permits a beat-to-beat analysis of the effects of various interventions that continuously change flow.

In this study we evaluated instantaneous blood flow responses and the relation of these responses to ventricular filling pressure changes that occur with PEEP during spontaneous ventilation.

Methods

Patients

Fifteen ambulatory men (average age 53 years, range 34–66 years) who underwent clinically indicated cardiac catheterization were studied after giving informed consent. All patients had a stable chest pain syndrome typical for angina pectoris. Each patient had coronary artery narrowing, defined as >50% diameter narrowing by coronary angiography performed after the flow studies outlined below. No patient had evidence of heart failure or other forms of heart disease. No patient had clinical evidence for pulmonary disease. Twelve patients also had spirometric studies within 3 months of these studies as part of their preoperative evaluation. Their lung volumes and flow rates were normal. The patients were not premedicated, and studies were conducted with the patient in a fasting, postabsorptive state before angiography.

Catheterization Procedures and Measurements

Cardiac catheterization was performed from a right antecubital cutdown. A #7 French Cournand catheter was positioned in the right atrium to measure pressure. Left-heart catheterization was performed with a #8 French catheter-tip blood flow velocity transducer which also contains two micromanometers (Millar Instruments Model VPC-683D). This catheter was positioned with the distal micromanometer in the left ventricular (LV) cavity and the proximal micromanometer and velocity sensor located at the upper border of the sinuses of Valsalva. This arrangement tends to stabilize the probe in the central axis of the ascending aorta, eliminates the spurious signal that appears if the probe comes to lie against the wall of the vessel, and minimizes artifacts in the recorded

From the Departments of Medicine (Division of Cardiology) and Anesthesiology, University of Florida and the Veterans Administration Medical Center, Gainesville, Florida.

Supported in part by grants from the NIH (5 RO1 HL 17717-02) and the Veterans Administration.

Address for reprints: Carl J. Pepine, M.D., Department of Medicine, Division of Cardiology, Box J-277, JMH Health Center, Gainesville, Florida 32601.

velocity wave form caused by catheter motion.\textsuperscript{10} The electromagnetic velocity sensor was energized with a Biotronex sinewave flowmeter (Model BL-613). In three patients, an additional #8 French catheter equipped with an electromagnetic flow velocity sensor (Carolina Medical Electronics) mounted near its tip was positioned in the main pulmonary artery via another vein to measure pulmonary artery blood flow.\textsuperscript{10, 11} The body of the catheter stabilizes the velocity sensor centrally in this vessel (personal observation). This velocity sensor was energized with a Carolina squarewave flowmeter (model 501D) to minimize crosstalk between the two sensors. The amplitude and contour of the electrical signals of the probes were not altered by turning off the excitation current of one or the other of the two probes.

Calibration of electromagnetic velocity catheters to measure blood flow, and their use in man, have been described in detail elsewhere.\textsuperscript{10-15} Briefly, since the velocity profiles of blood flow in the main pulmonary artery and the ascending aorta are relatively flat\textsuperscript{16, 17} the product of measured velocity and vessel cross-sectional area is volume of blood flow per unit time. Therefore, if the vessel cross-sectional area is assumed constant (i.e., rigid), the velocity signal is equivalent to a flow signal. Calibration of the velocity signals was accomplished by equating the area under the velocity curve to the average stroke volume at the beginning of each study by performing a simultaneous cardiac output determination using the indicator dilution method. Indicator dilution studies were performed with right atrial (RA) injection of indocyanine green dye and brachial artery sampling through a percutaneously introduced short #18 Teflon catheter (Longdweil).

Esophageal pressure, used as an index of intrapleural pressure,\textsuperscript{18} was measured through a fluid-filled #5 NIH catheter positioned fluoroscopically in the distal third of the esophagus.\textsuperscript{19} This catheter was constantly flushed. The patients were supine during these studies.

All pressures were referenced to the mid-chest. All fluid-filled catheters were connected to equisensitive strain gauge transducers (Statham P231a) and pressure signals were recorded simultaneously along with the flow signals on a multichannel recorder (Electronics for Medicine DR12). Standardized electrocardiographic lead II was recorded to determine heart rate and rhythm. Arterial blood gases were measured before and during PEEP to prevent hyperventilation.

**Study Procedure**

**Preparation**

Patients were brought to the laboratory before study and familiarized with the PEEP mask. An airtight, well-fitted face mask (Bird Corp, Palm Springs, California) was applied and each patient practiced breathing for several minutes. The mask was then connected in series with a one-way Rudolph valve and threshold resistance PEEP valve (Lanz Medical Products Corp, Wilmerding, Pennsylvania). This assembly allowed unrestricted inspiration at ambient pressure, but increased airway pressure to 10 cm H\textsubscript{2}O during expiratory flow. The Lanz valve was checked and calibrated to provide 10 cmH\textsubscript{2}O pressure with 1–50 l/min of air flow before each study.

With the mask in place, pressure and blood flow recordings were made and indicator studies performed. Recordings were made continuously during the addition of 10 cm H\textsubscript{2}O PEEP by connecting the PEEP valve assembly to the mask. Hemodynamic and indicator dilution recordings were made again during PEEP breathing after ventricular pressure, heart rate and aortic blood flow stabilized for 3–4 minutes. PEEP was then discontinued and the recordings were repeated.

**Data Reduction and Calculations**

Mean RA pressure was used as right ventricular (RV) filling pressure. Effective LV and RV filling pressures were calculated by subtracting esophageal pressures from LV end-diastolic and RA pressures, respectively. The esophageal pressures used in the calculation of filling pressure were measured at end-diastole. Mean pressures were obtained by electronic filtering. Mean transit time, used to estimate RA-to-brachial artery central blood volume, was determined from dye dilution curves using formulas described previously.\textsuperscript{20, 21} Stroke volume was obtained by electronic integration of the phasic blood flow signals.\textsuperscript{22} All measurements were averaged from at least 10 beats from two respiratory cycles and expressed as average values during each period. The mean ± SEM was calculated. The statistical significance of the difference between mean values for each period was determined by the \textit{t} test for paired data. \textit{P} values <0.05 were considered significant.

**Results**

**Effects of PEEP Application on Blood Flow and Volume**

Stroke volume and central blood volume data are summarized as mean values from all 15 patients in figure 1. Application of PEEP during spontaneous ventilation resulted in an average 12% decline (\textit{p} < 0.05) in stroke volume. Compared with control values, 10 cm H\textsubscript{2}O of PEEP produced a mean central blood volume decrease of 9% (\textit{p} < 0.05). Instantaneous aortic blood flow responses in all 15 patients were similar. Aortic blood flow declined significantly within two or three heart beats after application of PEEP. Aortic flow remained at a lower value throughout both phases of respiration (fig. 2). Respiratory-related variation in aortic flow decreased during PEEP breathing. Pulsatile pulmonary blood flow responses, in three patients, indicated an immediate reduction in RV stroke volume with the application of PEEP in each of these patients. This reduction occurred during the expiratory phase of the first respiratory cycle after the application of PEEP (fig. 2).

Pulmonary artery and aortic blood flow data, plotted as beat-to-beat RV and LV stroke volumes,
The reduced central blood volume was similar in magnitude to the difference between RV and LV stroke volumes observed for 20–30 beats after the application of PEEP.

**Effects of PEEP on Ventricular Filling Pressures and Heart Rate**

LV effective filling pressure declined in every patient (11 ± 2 to 8.7 ± 2 mm Hg, mean p < 0.05). The average change was a 19 ± 6% decline (p < 0.001). Esophageal pressure increased from 1.3 ± 0.3 to 5.0 ± 0.3 mm Hg (p < 0.001) with PEEP, and this increase was relatively uniform. The trend in RV effective filling pressure was an acute fall for only two to three beats immediately after application of PEEP, but within several cardiac cycles this value varied widely. Thus, the mean value over the period analyzed was not significantly changed (4 ± 1 to 3.5 ± 2 mm Hg). Effective ventricular filling pressures returned to control values after PEEP was discontinued. Heart rate was not significantly changed with the application of PEEP (77 ± 3 to 79 ± 4 beats/min) or when PEEP was discontinued (78 ± 4 beats/min).

**Discussion**

Velocity probes used in this study are similar, but not identical, to those used by others. Evaluation of electromagnetic velocity catheters in dogs showed that peak blood flow rates in the ascending aorta, measured by catheter probe, agreed closely (r = 0.98) with simultaneous measurements from a perivascular electromagnetic flow probe. Com-
comparisons of flow (catheter vs cuff), made every 10 msec, gave similar results \( (r = 0.96) \). In vitro studies using known steady blood flow rates showed that the electrical output of the catheter probe was linear \( (r = 0.998) \). Gabe et al.,\textsuperscript{12} who used an early-type velocity catheter that was introduced by Mills\textsuperscript{24} and can move laterally in the aortic root, found that cardiac output measurements showed considerable scatter about the line of identity in man. The correlation coefficient was 0.73 when compared to output determined by dye dilution. The results may be explained in many ways. For example, when the velocity sensor moves near the arterial wall, its signal is reduced, and calculated stroke volume will be low. This happens frequently with older type probes.\textsuperscript{12, 23, 24} To prevent motion, a flexible extension was added distal to the velocity sensor of newer probes.\textsuperscript{10, 11, 13-15, 22} With the extension positioned across the aortic valve, the sensor remains near the middle of the ascending aorta. Contact with the slow-moving boundary layer of blood flowing near the vessel wall is prevented.

Another problem is the estimation of vessel cross-sectional area. Vessel diameter is actually measured, and errors in this measurement are magnified when area is calculated, since area is directly related to diameter squared. During ejection, changes in area estimated by strain gauge calipers, averaged 5.5\% of the mean cross-sectional area in the ascending aorta\textsuperscript{26} and 9\% in the pulmonary artery.\textsuperscript{26} We have found that aorta diameter changes, measured at the upper border of sinuses of Valsalva, from angiograms in two projections over a wide range of stroke volume are less than those previously reported.\textsuperscript{19} We feel that the larger diameter changes reported related to open-chest measurements at the external surface of the aortic root above the pericardial reflection. When we calibrated the catheter probe, using angiographic measurements of aortic diameter...
made as described above, we found excellent agreement between velocity probe and dye-dilution measurements of cardiac output (fig. 4). In the present study, we chose to ignore the possible error associated with cross-sectional area change and calibrated the probe using stroke volume simultaneously determined by indicator dilution. In the study by Gabe et al., the velocity probe measurements were compared with those estimated from indicator-dilution recordings made either before or after, but not simultaneously.
with, the velocity record. This may also account for some of the differences.

Some limitations to the techniques in this study should be noted. The use of constant calibration factors for the aorta and pulmonary artery before and during PEEP is open to error. However, if 10 cm H\textsubscript{2}O of PEEP significantly reduces the cross-sectional area of these vessels, blood flow determined by the method used would be overestimated during PEEP. Although we found excellent agreement between the decrease in blood flow measured by the flow probe and dye dilution during PEEP, the decrease in flow may have been underestimated.

Another limitation is the interpretation of the central blood volume change. The reduction with PEEP may only reflect an alteration of the central volume. Since mean transit time is determined by the largest volume between injection and sampling sites, the reduced volume could represent a redistribution among smaller parallel volumes within the central pool, rather than an actual volume shift toward the periphery. Finally, since the supine body position increases esophageal pressure, as mediastinal structures press against the esophagus, the influence of intrathoracic pressure on ventricular filling pressure is overestimated. However, patient position was unchanged throughout the study, so the estimated change in effective filling pressure is probably a useful approximation of the influences of PEEP. Since some of the cardiac blood volume (and therefore mediastinal weight) is also measured in the central blood volume estimates, reduction in cardiac volume may account for slight changes in esophageal pressure.

Instantaneous blood flow changes associated with PEEP during spontaneous ventilation have not been previously reported in awake man. We found that stroke volume declined without change in heart rate, and therefore a small, early reduction in cardiac output occurred. Concurrently, central blood volume also declined, suggesting that blood volume may be redistributed peripherally. Instantaneous flow measurements from the pulmonary artery and the aorta were accomplished simultaneously in three patients. These data indicated that RV stroke volume declined immediately after the application of PEEP, suggesting a direct response to the sudden increase in end-expiratory airway pressure. RV stroke output was reduced throughout expiration, but returned toward control values during each inspiratory phase. Presumably, during expiration, the increase in airway pressure is transmitted through the thorax acting to decrease RV filling, promptly reducing its output. This reduced RV filling does not effect a significant decline in effective filling pressure, as would be expected from a consideration of the right ventricle's relatively flat pressure-volume relationship. During inspiration, intrathoracic pressure declined, permitting prompt restoration of RV filling and output. Thus, in the three patients with pulmonary artery flow catheters, PEEP markedly exaggerated the inspiratory-to-expiratory changes in RV output during normal breathing. Although pulmonary vascular resistance was not measured, it would be expected to increase if functional residual capacity increased, as it should have, with PEEP. An increase in pulmonary resistance may account, in part, for a reduction in RV output.

**Figure 4.** Results obtained with in vitro calibration: cardiac output, in 28 patients, calculated from the product of mean blood flow velocity (multisensor catheter) and measured vessel cross-sectional area (vertical axis) compared to output determined by dye-dilution (horizontal axis). Blood flow measurements made from the aorta (Ao) are shown in closed circles and from the pulmonary artery (PA) in open circles. The line of identity is shown.\(^\text{12}\)

**Figure 3.** (top) Disproportionate blood flow responses to positive end-expiratory pressure (PEEP). Average beat-to-beat stroke volume (vertical axis, upper panel) is shown for both right (open circles) and left ventricles (closed circles) from another patient. Addition of PEEP (vertical line, PEEP on) disproportionately changes right and left ventricular outputs, accounting for a central blood volume (CBV) reduction. After approximately 34 beats, the respective stroke volumes reach equilibration at a lower value, resulting in a reduced cardiac output (CO). E = expiration, I = inspiration. (bottom) Beat-to-beat blood flow responses to the termination of PEEP breathing (vertical line) in the same patient. Return to normal breathing immediately increases right ventricular (open circles) stroke volume during expiration. Restoration of left ventricular stroke volume (closed circles) occurs after several cardiac cycles and during inspiration. These stroke volume changes return cardiac output to the control level.
The decline in LV stroke volume was delayed and more gradual than the prompt changes observed in right-heart stroke volume. After approximately 25 cardiac cycles, right and LV stroke volumes equilibrated. In contrast to the augmented inspiratory-to-expiratory output fluctuations observed from the right heart, application of PEEP markedly reduced the respiratory-associated fluctuations in LV output (fig. 2). The differences in the rate at which the LV output declined relative to the right ventricle appears to explain the small but significant decline in central blood volume after PEEP was applied. These hemodynamic changes were restored within several cardiac cycles after the removal of PEEP breathing.

Inspiratory-to-expiratory blood flow fluctuations observed in the pulmonary artery were augmented during PEEP and could account for some of the variable cardiac output responses reported. For example, if cardiac output were measured by thermodilution, as it frequently is in the acute clinical setting, the indicator is injected into the right atrium. The average appearance time in the pulmonary artery is approximately 1–2 seconds in patients with normal cardiac output. Most of the curve is recorded within several additional seconds. Thus, if the measurement is made during the expiratory phase of respiration, when PEEP-induced reduction of RV output is maximal, a very low cardiac output would be inferred. The result of a measurement made during inspiration is apparent. These considerations may explain some of the results reported when such measurements are performed in settings where intrathoracic pressure is altered.⁴

Our results in coronary heart disease patients without heart failure demonstrate that cardiac output, determined continuously, declined during 10 cm of H₂O PEEP with spontaneous ventilation. The reduction in aortic flow was related to an immediate and disproportionate reduction in RV stroke output in three patients in whom pulmonary artery flow was also measured. These changes resulted in a decrease in central blood volume and were associated with a decline in effective LV filling pressure.

References
Instantaneous blood flow responses to positive end-expiratory pressure with spontaneous ventilation.
R A Perschau, C J Pepine, W W Nichols and J B Downs

Circulation. 1979;59:1312-1318
doi: 10.1161/01.CIR.59.6.1312

Circulation is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
Copyright © 1979 American Heart Association, Inc. All rights reserved.
Print ISSN: 0009-7322. Online ISSN: 1524-4539

The online version of this article, along with updated information and services, is located on the World Wide Web at:
http://circ.ahajournals.org/content/59/6/1312

Permissions: Requests for permissions to reproduce figures, tables, or portions of articles originally published in Circulation can be obtained via RightsLink, a service of the Copyright Clearance Center, not the Editorial Office. Once the online version of the published article for which permission is being requested is located, click Request Permissions in the middle column of the Web page under Services. Further information about this process is available in the Permissions and Rights Question and Answer document.

Reprints: Information about reprints can be found online at:
http://www.lww.com/reprints

Subscriptions: Information about subscribing to Circulation is online at:
http://circ.ahajournals.org//subscriptions/