Impact of Positive End-Expiratory Pressure on Thermodilution-Derived Right Ventricular Parameters in Mechanically Ventilated Critically Ill Patients

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Objectives: **To examine the effect of positive end-expiratory pressure (PEEP) on right ventricular stroke volume variation (SVV), with possible implications for the number and timing of pulmonary artery catheter thermodilution measurements.**

Design: **Prospective, clinical pilot study.**

Setting: **Academic medical center.**

Participants: **Patients who underwent volume-controlled mechanical ventilation and had a pulmonary artery catheter.**

Intervention: **PEEP was increased from 5-to-10 cmH_2O and from 10-to-15 cmH_2O with 10-minute intervals, with similar decreases in PEEP, from 15-to-10 cmH_2O and 10-to-5 cmH_2O.**

Measurements and Main Results: **In 15 patients, right ventricular parameters were measured using thermodilution at 10% intervals of the ventilatory cycle at each PEEP level with a rapid-response thermistor. Mean right ventricular stroke volume and end-diastolic volume declined during incremental PEEP and normalized on return to 5 cmH_2O PEEP ($p = 0.01$ and $p = 0.001$, respectively). Right ventricular SVV remained unaltered by changes in PEEP ($p = 0.26$), regardless of incremental PEEP ($p = 0.15$) or decreased PEEP ($p = 0.12$). The coefficients of variation in the ventilatory cycle of all other thermodilution-derived right ventricular parameters also were unaffected by changes in PEEP.**

Conclusions: **This study showed that increases in PEEP did not affect right ventricular SVV in critically ill patients undergoing mechanical ventilation despite reductions in mean right ventricular stroke volume and end-diastolic volume. This could be explained by cyclic counteracting changes in right ventricular preloading and afterloading during the ventilatory cycle, independent of PEEP. Changes in PEEP did not affect the number and timing of pulmonary artery catheter thermodilution measurements.**

KEY WORDS: ***positive end-expiratory pressure, right ventricle, stroke volume variation, thermodilution, pulmonary artery catheter, cardiac output***

LEFT VENTRICULAR STROKE volume variation (SVV) induced by mechanical ventilation has been demonstrated to be more helpful than static filling pressures in predicting fluid responsiveness, defined as an increase in stroke volume or cardiac output on fluid loading.[1,2] A decrease in left ventricular preload during an increase in positive end-expiratory pressure (PEEP), resulting in an increase in left ventricular SVV, is mediated largely through a decrease in right ventricular preload. Thus, PEEP presumably can induce an increase in right ventricular SVV as well, which has not been investigated specifically before in mechanically ventilated critically ill patients. Moreover, PEEP also may induce a rise in right ventricular SVV through increased cyclic right ventricular afterloading.[3,4] A PEEP-induced increase in right ventricular SVV can be of clinical importance because it would affect the precision of pulmonary artery catheter thermodilution measurements over the ventilatory cycle. Thermodilution still is considered the gold standard for cardiac output measurement, with the pulmonary artery catheter mostly used in patients undergoing cardiothoracic surgery.[5] The authors of this study and others have demonstrated that multiple measurements in the ventilatory cycle, preferably equally spaced or frequently performed at random intervals in the cycle, are necessary to reliably assess right ventricular stroke volume index (SVI) and cardiac output during mechanical ventilation because of cyclic changes in right ventricular loading.[6,7]

The authors measured multiple right-sided thermodilution-derived parameters equally spread in the ventilator cycle to derive right ventricular SVV at various levels of incremental and decremental PEEP in mechanically ventilated critically ill patients. The authors hypothesized that PEEP increases right ventricular SVV during mechanical ventilation, necessitating adaptation of the number and timing of pulmonary artery catheter thermodilution measurements in the respiratory cycle.

METHODS

After approval of the study protocol by the local hospital Medical Ethics Committee of the VU University Medical Center, Amsterdam, The Netherlands (Chairperson A.C. van Loenen) and after obtaining informed consent by patients' next-of-kin, the authors performed a single-center, prospective, pilot study in the Department of Intensive Care Medicine of the VU University Medical Center. The study included consecutive patients on continuous volume-controlled positive-pressure ventilation (Servo 900 B; Siemens, Stockholm, Sweden) when hemodynamic monitoring with a pulmonary artery catheter was deemed necessary for clinical management at the discretion of the attending physician. All patients in the study started off with 5 cmH_2O of PEEP, as previously described.[7] An inspiratory time of 25% was set with an end-inspiratory hold of 10%; thus, the remaining 65% of the ventilatory cycle was set as the expiratory time. Sedation was provided via unchanged intravenous infusion of midazolam and fentanyl.

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Patients were hemodynamically stable, in sinus rhythm, and without known cardiac valvular stenosis or regurgitation.

An arterial catheter (Marquette Electronics, Milwaukee, WI) for arterial blood pressure measurements was positioned in the radial artery, and arterial blood gas analysis was performed at baseline, allowing for calculation of PaO_2:F_IO_2 ratios. A rapid-response thermistor with a response time of 50 ms was inserted (93A-431H 7.5F; Edwards Life Sciences, Irvine, CA) with intracardiac electrodes via the jugular or subclavian vein and advanced until wedging of the inflated balloon occurred, and the proximal injection port, located 21 cm from the tip, recorded right ventricular pressures. The catheter then was withdrawn slowly until right ventricular pressure waveforms disappeared to place the injection port above the tricuspid valve, after which the absence of V waves was recorded to rule out hemodynamically significant tricuspid regurgitation. The injectate temperature was measured distally from the injection site using an in-line temperature probe (CO-set+ [model 93600]; Edwards Life Sciences, Irvine, CA). The analog electrocardiographic signal, rapid-response thermistor, and injectate temperature probe were applied according to built-in algorithms of an REF-1 Edwards Life Sciences computer,[8,9] yielding accurate, reproducible measurements while enabling the calculation of ventricular volumes.[10–12] This computer standard detects the R-waves and uses the downslope of the thermodilution curve to calculate the residual fraction from the relationship between successive temperature plateaus. From the residual fraction, right ventricular ejection fraction (EF), end-diastolic volume index (EDVI), and end-systolic volume index (ESVI) were derived, whereas cardiac output was measured by integrating the temperature change of the blood.[7] Right ventricular SVV was calculated for each patient and at each PEEP level as follows: $SVV\ (\%) = 100 \times (SVI_{max} - SVI_{min}) / (SVI_{max} + SVI_{min}) / 2)$, in which SVI_{max} and SVI_{min} refer to maximal and minimal stroke volume index in the ventilatory cycle, respectively.

Baseline characteristics were recorded, including the Simplified Acute Physiology II score. Ventilatory settings were assessed for each patient to determine the presence of acute respiratory distress syndrome (ARDS), assessed according to the Berlin criteria.[13] Dynamic pulmonary compliance was estimated by tidal volume / (peak pressure – PEEP). This, together with the number of quadrants with alveolar consolidations, PEEP, and PaO_2:F_IO_2 ratios, allowed for calculation of the lung injury score, which ranged from 0 (no acute lung injury) to 4 (severe acute lung injury).[14] Central venous pressure, pulmonary artery occlusion pressure (PAOP), mean pulmonary arterial pressure (PAP), and mean arterial pressure were obtained after calibration at the mid-chest level with the patient in the supine position during end-expiration at every PEEP level. Pulmonary vascular resistance index (PVRI) was calculated as PAP – PAOP / cardiac index (CI).

A phase controller regulated the moment of injection of 5 mL of 5% dextrose at room temperature, depending on the phase in the ventilatory cycle derived from the mechanical ventilator. The first bolus injection was administered precisely at the start of inflation (ie, 0% of the ventilatory cycle), with the right-sided thermodilution-derived parameters obtained after a transit time of roughly 3 heart beats, reflecting right ventricular function at the time of injection. Approximately 30 seconds later, a second injection was performed at 10% of the ventilatory cycle, and this sequence was repeated until a total of 11 equally spaced measurements were performed, covering the entire ventilatory cycle. Next, incremental PEEP levels were applied from 5-to-10 and from 10-to-15 cmH_2O with 10-minute intervals while the thermodilution measurements were repeated. Finally, decremental PEEP from 15-to-10 and from 10-to-5 cmH_2O was assessed, again with all other ventilatory settings and drug doses unaltered. A diagram of the study design of the thermodilution measurements is depicted in Figure 1.

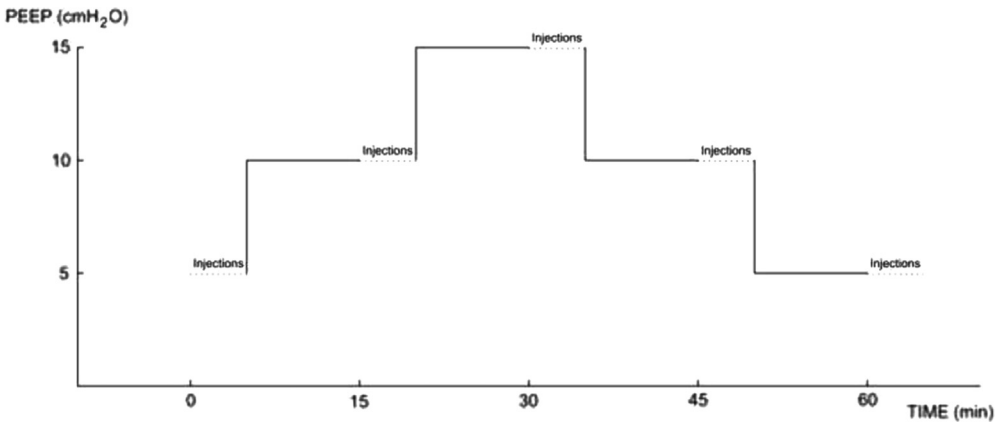

Fig 1. Diagram of the study design of the thermodilution measurements. The experiments started at 5 cmH_2O positive end-expiratory pressure (PEEP) with volume-controlled mechanical ventilation with an inspiratory time of 25%, end-inspiratory hold of 10%, and 65% of expiratory time. A phase controller timed the first injection of 5 mL of 5% dextrose precisely at the start of inflation (ie, 0% of the ventilatory cycle). The right-sided thermodilution-derived parameters were obtained after a transit time to reach the thermistor of approximately 3 heart beats. Approximately 30 seconds later after this first measurement (●) was obtained, the second bolus injection was administered at 10% of the ventilatory cycle, and this sequence was repeated until a total of 11 equally spaced measurements were obtained, covering the entire ventilatory cycle. Then, PEEP was set from 5 to 10, from 10 to 15, from 15 back to 10, and from 10 back to 5 cmH_2O with 10-minute intervals of stabilization after which the thermodilution measurements were repeated. In each patient, a total of 55 measurements were obtained in approximately 1 hour using 275 mL of 5% dextrose.