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Influence of Superior Vena Caval Zone Condition on Cyclic Changes in Right Ventricular Outflow during Respiratory Support

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Background: **Adequate fluid resuscitation in critically ill patients undergoing mechanical ventilation remains a difficult challenge, and diastolic and systolic right ventricular (RV) changes produced by positive airway pressure are important to consider in an individual patient with inadequate circulatory adaptation during respiratory support. We hypothesized that insufficient thoracic vena cava filling, predisposing to inspiratory collapse (zone 2 condition), may transiently affect RV outflow.**

Methods: **We measured beat-to-beat superior vena caval diameter and Doppler RV outflow during a routine transesophageal echocardiographic examination in 22 patients undergoing mechanical ventilation, all of whom required hemodynamic monitoring, and we calculated a collapsibility index for the superior vena cava as maximal expiratory diameter minus minimal inspiratory diameter, divided by maximal expiratory diameter.**

Results: **In 15 patients (group 1), the collapsibility index was low (17 ± 7%) and was associated with a moderate inspiratory decrease in RV outflow (25 ± 17%). However, in seven patients (group 2), we observed a high collapsibility index (71 ± 7%), which was associated with a major inspiratory decrease in RV outflow (69 ± 14%) combined with a reduced pulmonary artery flow period. A rapid volume expansion, only performed on group 2, markedly and significantly reduced both the collapsibility index (15 ± 12%) and the inspiratory decrease in RV outflow (31 ± 20%).**

Conclusion: **A major inspiratory decrease in RV outflow associated with a reduced pulmonary artery flow period in a patient undergoing mechanical ventilation reflected a high collapsibility index of the thoracic vena cava, suggesting a zone 2 condition, and may be corrected by blood volume expansion.**

ADVERSE hemodynamic consequences of mechanical ventilation are essentially mediated by changes in left ventricular preload produced by positive airway pressure.[1] Because pulmonary circulation, including pulmonary arteries, capillaries, veins, and the left atrium, represents the filling reserve for the left ventricle and because this reserve is supplied with blood by the right ventricle, diastolic and systolic right ventricular (RV) changes produced by positive airway pressure are important to consider in an individual patient with an inadequate circulatory adaptation to mechanical ventilation. In particular, positive airway pressure impairs venous return,[2] thus limiting RV diastolic filling, and increases RV outflow impedance,[3] thus impairing RV systolic function. The final result is a reduced RV stroke output, resulting in an incomplete filling reserve for the left ventricle.

Bedside transesophageal echocardiography is used daily in our unit as a routine hemodynamic evaluation in critically ill patients undergoing ventilation. Recently, systematic use of a multiplane transducer has given us the opportunity to record superior vena caval (SVC) dimensional changes during mechanical ventilation. We observed in several patients a partial vena caval collapse during tidal ventilation. Occurrence of this partial collapse suggested that, at this time, external pressure exerted by the thoracic cavity on the superior vena cava might be greater that the opening pressure of the vessel. In its extreme form, this situation has been defined by physiologists as a zone 2 condition.[4] The current study focused on the relation between this partial collapse and the cyclic changes in RV output observed during mechanical ventilation.

Methods

Between March and June 2000, 22 patients undergoing mechanical ventilation who required invasive radial artery monitoring because of circulatory failure were systematically examined with use of transesophageal echocardiography. The study population comprised 15 men and 7 women (mean age ± SD, 66 ± 13 yr) with septic shock associated with acute lung injury (13 patients) or acute respiratory distress syndrome (9 patients). Lung injury severity scores were 2.2 ± 0.4 and 3.1 ± 0.3, respectively.[5] At the time of the study, mechanical ventilation was used in volume-controlled mode, with a tidal volume of 6–8 ml/kg, a respiratory rate of 12–16 breaths/min, an end-inspiratory pause of 0.5 s, an inspiratory-to-expiratory ratio of 1:2, and an average positive end-expiratory pressure of 5 ± 3 cm H_2O. All patients were sedated with midazolam and sufentanil and were paralyzed with cisatracurium. In our unit, transesophageal echocardiography is a routine procedure used to assess hemodynamic status in patients undergoing mechanical ventilation. This procedure permits evaluation of left and right ventricular systolic and diastolic function. The study was accepted by the Ethics Committee of

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the Société de Réanimation de Langue Française (Paris, France), and waived informed consent was authorized.

Hemodynamic Measurements

Heart rate and systemic arterial pressure from an indwelling radial artery catheter were recorded throughout the study, together with airway pressure obtained from a side port of the tracheal tube. Central venous pressure (CVP) was measured at end-expiration and end-inspiration through an internal jugular catheter previously inserted for fluid administration. Pleural pressure (Ppl) was inferred from airway pressure using our previously published equations.[6] Transmural CVP was calculated as CVP minus Ppl. Transpulmonary pressure at end-inspiration was calculated as airway pressure minus Ppl.

Echo Doppler Measurements

Echo Doppler studies were performed with a Toshiba Corevision model SSA-350A (Toshiba France, Puteaux, France) equipped with a multiplane 5-MHz transesophageal echocardiographic transducer. Using the signal from the respirator, airway pressure was displayed on the screen of the echo Doppler device, accurately timing cardiac events during the respiratory cycle and permitting special consideration of four beats selected as follows: an end-expiratory beat defined as the last beat occurring before mechanical lung inflation (beat 1), a beat occurring during the dynamic phase of lung inflation (beat 2), an end-inspiratory beat defined as the last beat occurring during the end-inspiratory pause (beat 3), and a beat occurring at the start of exhalation (beat 4).

The superior vena cava was examined from a short- or long-axis view, using the two-dimensional view to direct the M-mode beam across the maximal diameter. From this view, we measured SVC diameter during the respiratory cycle. The collapsibility index of the superior vena cava, *i.e.*, the inspiratory decrease in SVC diameter, was determined as (maximal diameter on expiration − minimal diameter on inspiration)/maximal diameter on expiration, and was expressed as a percentage.[7]

Pulmonary artery (PA) flow velocity was recorded at the level of RV outflow tract obtained in the long axis by a transesophageal approach. From the pulsed Doppler velocity profile recorded at a high speed of 5 cm/s, we

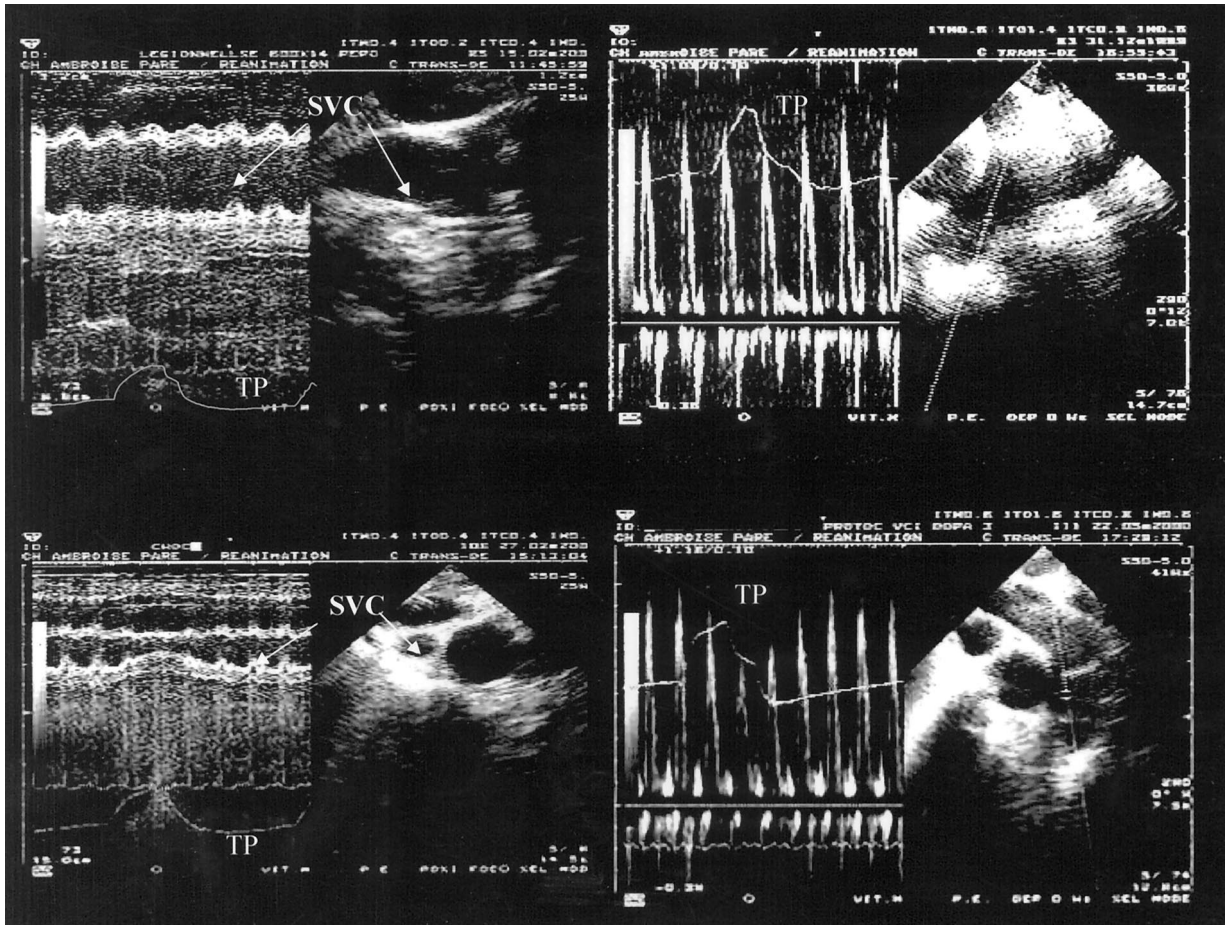

Fig. 1. Examples of group 1 (*top*) and group 2 (*bottom*) patients. On the left panel, examination of superior vena caval (SVC) diameter by combined two-dimensional and M-mode echocardiography with simultaneous recording of tracheal pressure (TP) shows minor changes during the respiratory cycle in a group 1 patient, and vena caval partial collapse in a group 2 patient. On the right panel, simultaneous recording of Doppler pulmonary artery flow velocity permits observation of beat-to-beat changes, more marked in the group 2 patient.

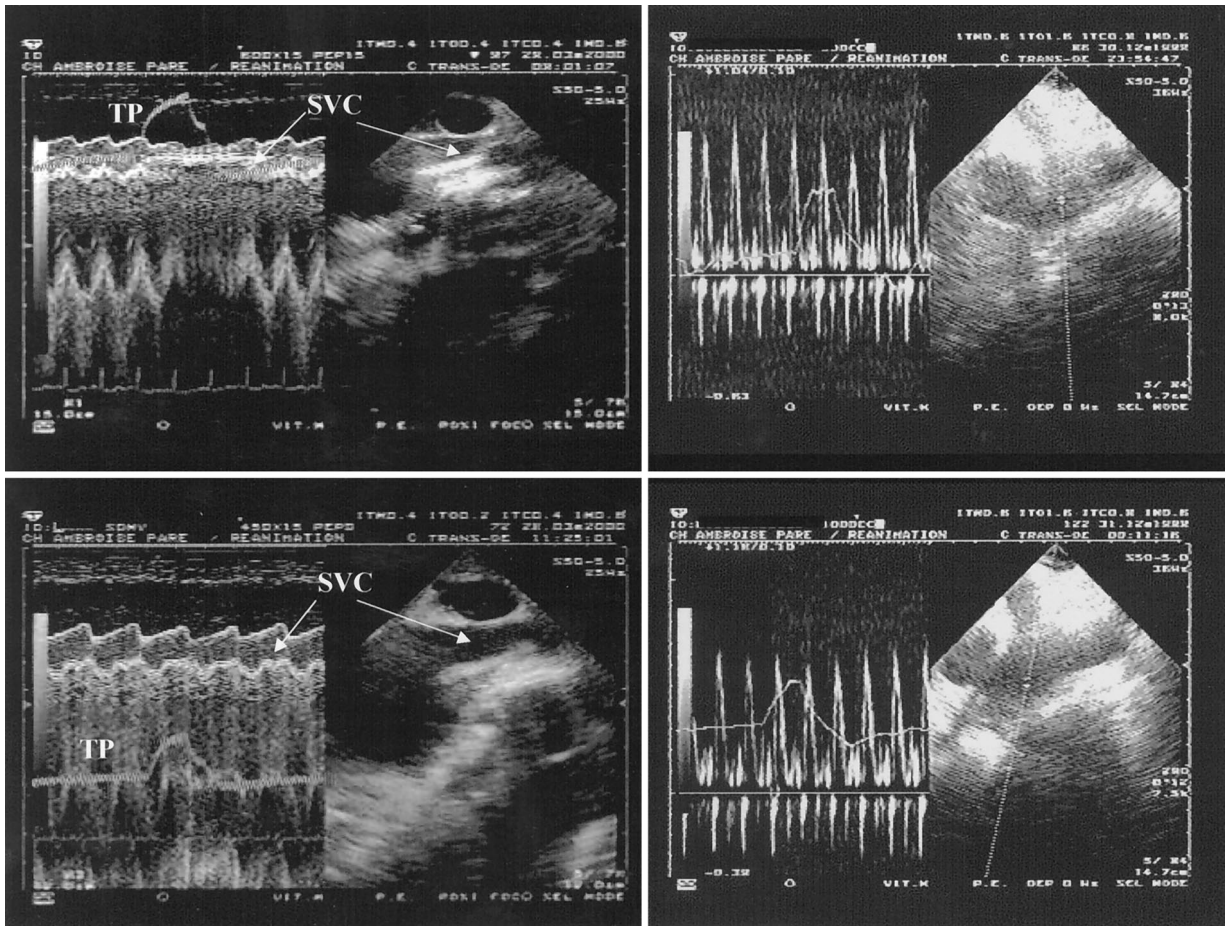

Fig. 2. Example of the effect of a rapid volume expansion on superior vena caval (SVC) size and Doppler pulmonary artery flow velocity in a group 2 patient. At baseline (*top*), combined two-dimensional and M-mode echocardiography with simultaneous recording of tracheal pressure (TP) show a vena caval partial collapse (*left*) associated with a major inspiratory decrease in pulmonary artery flow velocity (*right*; group 2A). After volume expansion (*bottom*), only slight respiratory changes in SVC diameter and in pulmonary artery flow velocity persisted (group 2B).

measured acceleration time (AcT), peak velocity (V_{MAX}), flow period (FP), and PA velocity–time integrals (PA_{VTI}). Mean acceleration was calculated as V_{MAX}/AcT. PA systolic diameter was measured on the same view, after enhanced contrast by color Doppler ultrasonography. From this diameter, we calculated the PA cross-sectional area. RV stroke output was calculated by multiplying PA_{VTI} by PA cross-sectional area[8] and was expressed as stroke index after dividing by body surface area. Cardiac index was calculated by multiplying right ventricular stroke index (RVSI), averaged by beat-to-beat measurement within three successive respiratory cycles, by heart rate. Respiratory change in RVSI was calculated as

$$(\text{beat 1 value} - \text{beat 3 value})/((\text{beat 1 value} + \text{beat 3 value})/2)$$

and was expressed as a percentage.

Patients were retrospectively divided into two groups according to their SVC collapsibility index. The collapsibility index was low (< 30%) in group 1 patients and high (> 60%) in group 2 patients. No intermediate collapsibility index (between 30 and 60%) was observed. To test the hypothesis that a high collapsibility index might reflect an inadequate blood volume, all measurements were repeated in group 2 after a rapid blood volume expansion (BVE; 7 ml/kg hetastarch, 6%, in 30 min). In group 2, measurements performed before BVE were labelled as group 2A, and measurements performed after BVE were labeled as group 2B.

Statistical Analysis

Statistical calculations were performed using the Statgraphics Plus package (Manugistics, Rockville, MD). Data are expressed as mean ± SD. Between-group comparisons regarding hemodynamic data averaged during the whole respiratory cycle (or, in the case of CVP, measured at end-expiration) were performed by means of an unpaired *t* test. The hemodynamic effect of rapid BVE on the same data in group 2 was analyzed by a paired *t* test. Changes in hemodynamic and echo Doppler parameters during the respiratory cycle were examined by analysis of variance for repeated measurements followed by the Bonferroni multiple comparison proce-

Table 1. Comparison among Hemodynamic Data at Baseline and after Volume Expansion

	Group 1	Group 2A (before BVE)	Group 2B (after BVE)
HR (beats/min)	91 ± 13	114 ± 14*	105 ± 16†
SAP (mmHg)	114 ± 23	91 ± 14*	105 ± 20†
CVP (mmHg)	12 ± 2 (9–16)	7 ± 2* (5–9)	12 ± 12† (10–15)
SI (cm^3/m^2)	24 ± 7	20 ± 6*	24 ± 8†
CI ($l \cdot min^{-1} \cdot m^{-2}$)	2.2 ± 0.6	2.3 ± 0.7	2.9 ± 0.8†
V_{MAX} (m/s)	0.66 ± 0.18	0.83 ± 18*	0.79 ± 0.19
AC_{mean} (m/s)	7.2 ± 3.1	9.2 ± 5.7	9.2 ± 3.3
FP (ms)	254 ± 46	208 ± 107*	213 ± 42
PA_{VTI} (cm)	10.5 ± 3.4	7.1 ± 3.4*	9.6 ± 3.3†

* $P < 0.05$ (group 2 before BVE *vs.* group 1). † $P < 0.05$ (group 2 after BVE *vs.* group 2 before BVE).

BVE = blood volume expansion; HR = heart rate; SAP = systemic arterial pressure (systolic value, averaged for the four beats considered in a whole respiratory cycle); CVP = central venous pressure (end-expiratory value, with maximal and minimal values in brackets); SI = stroke index; CI = cardiac index; V_{MAX} = pulmonary artery peak velocity; AC_{mean} = pulmonary artery mean acceleration; pulmonary artery FP = flow period; PA_{VTI} = pulmonary artery velocity–time integral.

dure. A *P* value of less than 0.05 was considered to be statistically significant.

Results

SVC Collapsibility Index

Among the 22 patients studied, 15 had a low SVC collapsibility index (17 ± 7%) and constituted group 1, and seven had a high SVC collapsibility index (71 ± 7%) and constituted group 2. Examples are given in figure 1. In group 2, measurements were repeated after volume expansion, a procedure which reduced SVC collapsibility index (15 ± 12%), as illustrated in figure 2. With a calculated end-expiratory Ppl (−1.2 ± 0.7 and −1.1 ± 0.7 mmHg in groups 1 and 2A, respectively) and an end-inspiratory Ppl (2.9 ± 0.9 and 3.1 ± 0.9 mmHg in groups 1 and 2A, respectively) in the same range, CVP (transmural value) was significantly lower in group 2A patients (8 ± 2 *vs.* 13 ± 2 mmHg in group 1 at end-expiration and 7 ± 2 *vs.* 12 ± 2 mmHg in group 1 at end-inspiration).

Between-group Comparison

As summarized in table 1, group 2 patients had a significantly greater heart rate, a significantly lower systemic arterial pressure (systolic value), and a significantly lower CVP. Stroke index was also significantly lower in group 2, whereas cardiac index was in the same range in both groups. Blood volume expansion, only performed in group 2 patients, produced a significant reduction in heart rate and a significant increase in systemic arterial pressure, CVP, stroke index, and cardiac index.

Cyclic Changes in Airway Pressure

Tracheal pressure changes during the whole respiratory cycle were similar in the two groups, with average plateau pressures of 23 ± 5 and 24 ± 3 cm H_2O and average positive end-expiratory pressures of 6 ± 1 and 5 ± 2 cm H_2O in groups 1 and 2, respectively. These plateau pressures resulted in calculated transpulmonary pressures at end-inspiration in the same range for both groups (18.4 ± 4 and 19.6 ± 2.3 cm H_2O in groups 1 and 2, respectively). With the respiratory rate used (12–16 breaths/min) and this external positive end-expiratory pressure, no patient had intrinsic positive end-expiratory pressure.

Cyclic Changes in RV Outflow

Cyclic changes in RVSI, evaluated by Doppler analysis of four beats selected in a respiratory cycle, are shown in figure 3. All patients had a significant reduction in RVSI at end-inspiration. However, this inspiratory decrease in RVSI was significantly more marked in group 2 patients when compared with group 1 patients (69 ± 14 *vs.* 26 ± 17%). In group 2, rapid BVE resulted in an inspiratory decrease in RVSI, which returned to the same range as in group 1 patients (31 ± 19%). An example is shown in figure 2.

Doppler Analysis of Pulmonary Artery Flow Velocity

Examples of change in Doppler velocity are shown in figures 1 and 2, and beat-to-beat analysis of Doppler measurements of pulmonary artery flow velocity are shown in figure 4. In both groups, tidal ventilation produced a significant decrease in V_{MAX} and in mean acceleration. However, FP was unchanged during the whole respiratory cycle, except in group 2 before BVE. In these patients, tidal ventilation produced a significant reduction in FP, which was corrected by BVE.

Between-group differences in Doppler velocity data averaged for the four beats considered in a whole respiratory cycle are presented in table 1. Compared with group 1, group 2 patients had a higher V_{MAX}, a reduced

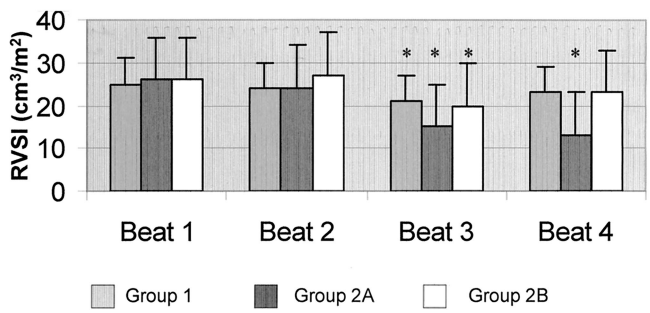

Fig. 3. Average beat-to-beat changes in right ventricular stroke index (RVSI) throughout the respiratory cycle. Four beats are individualized: (1) an end-expiratory beat defined as the last beat occurring before mechanical lung inflation, (2) a beat occurring during the dynamic phase of lung inflation, (3) an end-inspiratory beat occurring during the end-inspiratory pause and coinciding with plateau pressure, and (4) a beat occurring at the start of exhalation. Values are mean ± SD. *$P <$ 0.05 compared with the preinspiratory beat (beat 1).

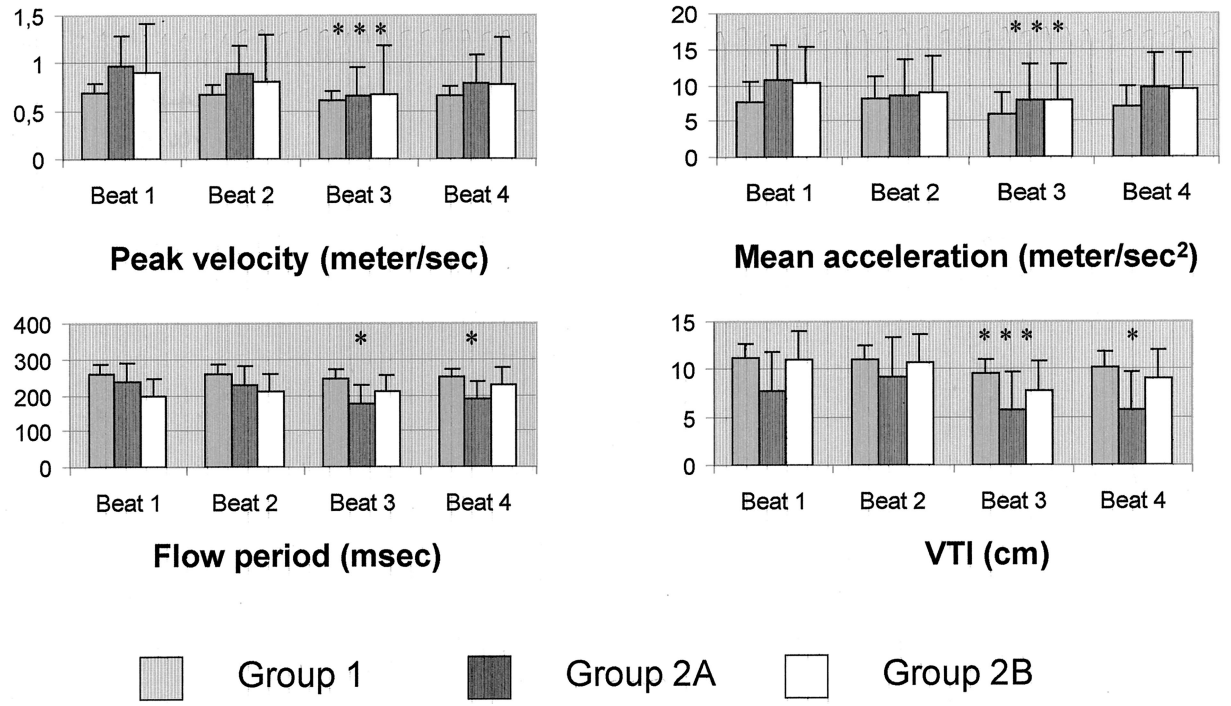

Fig. 4. The main changes in Doppler pulmonary artery flow velocity pattern observed during a full respiratory cycle in the three groups and described from analysis of four selected beats (see Methods): (1) an end-expiratory beat defined as the last beat occurring before mechanical lung inflation, (2) a beat occurring during the dynamic phase of lung inflation, (3) an end-inspiratory beat occurring during the end-inspiratory pause and coinciding with plateau pressure, (4) a beat occurring at the start of exhalation. Values are mean ± SD. *$P < 0.05$ compared with the preinspiratory beat (beat 1). VTI = velocity–time integral.

FP, and a reduced PA_{VTI}. Blood volume expansion significantly increased PA_{VTI} in group 2.

Discussion

In a clinical study performed in 1983, we confirmed that lung inflation by tidal ventilation decreased RV stroke output.[9] However, in this study, changes in RV stroke output during the respiratory cycle were evaluated by the pulse contour method, with the assumption that no major change occurred in pulmonary artery distensibility.[9] Doppler measurements performed in the current study are in accordance with this assumption, and lung inflation was actually accompanied by a decreased RV stroke output, whereas the expiratory phase was accompanied by a return to a preinspiratory value. For a long time, these changes were interpreted as resulting from a cyclic reduction in venous return by pleural pressure increase.[10] However, we have previously reported that tidal volume ventilation increased RV afterload,[11,12] and we have recently shown the major effect on RV outflow impedance of transpulmonary pressure increase during tidal ventilation.[3]

The concept of reduced venous return by pleural pressure increase was recently updated by Fessler *et al.*,[2,13] who demonstrated in an experimental study in dogs that positive airway pressure did not affect the gradient for venous return but actually lowered venous return by way of reduced venous conductance. Thus, they suggested that collapsible vessels were likely interposed between the peripheral vasculature and the right atrium.[2] It has long been known that collapsible vessels interposed throughout the circulation have a key role in flow limitation. This was first advocated by Guyton *et al.*[14] to explain the limitation of venous return improvement when pleural pressure becomes increasingly negative and was more recently reemphasized by Takata *et al.*[4] to describe abdominal vena caval zone conditions. We have localized the collapsible zone of the abdominal vena cava in its proximal part by an echographic study performed in spontaneously breathing patients during acute asthma.[15] Our current study suggested that the same concept, applied to the thoracic vena cava, was operative during mechanical ventilation (in humans, because the right atrium lies directly on the diaphragm, only the superior vena cava is intrathoracic, the intrathoracic part of inferior vena cava being purely virtual). The current two-dimensional echocardiographic study showed that in 68% of patients (group 1), pleural pressure increase during tidal ventilation was only accompanied by a slight reduction in SVC diameter, whereas in 32% (group 2) this increase produced a major reduction in SVC diameter, producing a partial collapse. One can infer that the patients in group 2 had a thoracic vena cava in zone 2 condition, a circumstance facilitating occurrence of a transmural pressure lower than the

effective opening pressure, when external pressure increases.[4] Conversely, the patients of group 1 likely had an intrathoracic vena cava in zone 3 condition, precluding inspiratory collapse.

These different zone conditions were associated in the current study with a different pattern of cyclic changes in RV outflow. Whereas the patients of group 1 (zone 3 condition) had an inspiratory decrease in RVSI close to 30%, likely explainable by an inspiratory increase in outflow impedance,[3] in the patients of group 2 (zone 2 condition), these changes were more marked, with a profound inspiratory decrease in RVSI close to 70%, despite a theoretically similar outflow impedance, as suggested by identical transpulmonary pressure at end-inspiration in both groups. This decrease was accompanied in group 2 by a significant reduction in FP, not explainable by tachycardia because it was only observed at end-inspiration. Thus, it seemed clear that a specific RV preload limitation was added to the increase in outflow impedance during inspiration in these patients. This preload limitation was corrected by a rapid BVE. After this procedure, the residual inspiratory decrease in RVSI in group 2 patients was in the same range as in group 1 patients and was explainable by the persistence of outflow impedance.

In humans, the part of venous return devoted to the SVC flow is close to 25%.[16] Thus, it is not surprising that a marked and sudden reduction in the size of this vessel might have discernible consequences for RV filling. In the current study, we observed that the partial collapse of the superior vena cava occurred when the calculated transmural pressure of the vessel was 9 mmHg or less (the highest value observed in group 2A). This finding is at variance with physiologic integrated concepts regarding venous return and right heart function: with a CVP between 6 and 12 mmHg, the right ventricle is thought to act on the flat part of its function curve,[17] a protection against an inopportune decrease in preload during respiratory support. However, these theoretical values inferred from normal physiology and related to an atmospheric external pressure may be somewhat low in patients undergoing critical ventilation. Opposed to an inspiratory increase in SVC elastance by external application of positive pleural pressure, a higher transmural value of CVP seemed to be required to keep the vessel open, and our threshold of CVP required at end-expiration to prevent SVC collapse during tidal ventilation, *i.e.*, 9 mmHg (the lowest value in group 1), was very close to the value of 10 mmHg reported by Jellinek *et al.*[18] in a recent study.

In conclusion, the current study showed that SCV partial collapse during tidal ventilation reflected insufficient venous filling and participated in the inspiratory decrease in RV outflow observed during mechanical ventilation.

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