The decrease of cardiac chamber volumes and output during positive-pressure ventilation

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Submitted 8 April 2013; accepted in final form 20 July 2013

POSITIVE-PRESSURE VENTILATION (PPV) with positive end-expiratory pressure (PEEP) is used during anesthesia and during treatment of acute critical respiratory failure including pulmonary edema (25, 28). While PPV usually improves alveolar oxygen diffusion and alleviates atelectasis and hypoxic vasoconstriction, these positive effects must be balanced against the risk of compromised cardiovascular function with a decrease in cardiac output (CO) (7, 8, 25) and often also in arterial blood pressure (18, 25). Studies on the mechanisms that lead to cardiovascular compromise with PPV have shown that PPV increases central venous and pulmonary artery pressures (4), lowers pulmonary artery capillary wedge pressure, and consequently also left ventricular (LV) filling pressure (4, 9). Echocardiographic studies suggest that LV contractility remains unchanged (2, 16, 17). It has been suggested that the reported changes in cardiac transmural pressures and the associated changes in abdominal pressure together with changes in LV afterload may result in compromised cardiac filling (25).

Filling of the cardiac chambers is not unambiguously determined from transmural pressures but can be validated with cardiac magnetic resonance imaging (CMR) that with steady-state, free-precession sequences is considered the gold standard of in vivo measurements of cardiac chamber volumes (10, 11, 21). CMR is particularly useful in evaluation of the right side of the heart, which cannot be reliably measured with echocardiography. CMR phase-contrast sequences are the gold standard for noninvasive measurements of flow in the pulmonary artery and ascending aorta. We hypothesize that PPV negatively influences the circulation mainly through impaired filling of the cardiac chambers. To test this hypothesis, we used CMR to determine cardiac chamber volumes and function during PPV in healthy subjects with pressure levels applied in the clinic (up to 20 cmH2O).

METHODS

Eighteen volunteers (18–61 yr; 7 women) without a history of cardiac, metabolic, or pulmonary disease and free of medication participated in the study after providing oral and written informed consent. The Copenhagen Ethics Committee approved the protocol (H-1-2011-073), and the study was carried out in accordance with the Helsinki Declaration. Exclusion criteria included pregnancy, claustrophobia, contraindications to CMR (pacemaker/ICD-unit and cerebral clips), and inability to undergo the positive-pressure ventilation procedure.

The protocol consisted of three consecutive periods each lasting ~30 min: one period on spontaneous breathing at atmospheric level, and two periods on noninvasive ventilation with inspiratory pressures of 12 and 22 cmH2O and expiratory pressures of 9 and 19 cmH2O, respectively. Thus patients were ventilated with 0 cmH2O (PPV0), 10 cmH2O (PPV10), and 20 cmH2O (PPV20). The pressures were chosen to match the range of pressures applied in the clinic (29, 32). At each PPV level volunteers were ventilated for 10 min before a comprehensive CMR scan was performed. Subjects underwent all pressure levels and were scanned three times. First, the subjects were scanned during spontaneous respiration (PPV0). Next, PPV10 and PPV20 where applied in random order, as a randomization system secured that an equal number of subjects started with PPV10 and PPV20, respectively.

In six subjects, systemic blood pressure was measured at the end of each scan sequence.

Positive-pressure ventilation. The subjects were noninvasively ventilated on a CMR-compatible respirator (Datex-Ohmeda Aestiva/5 MRI Anesthesia System, GE Healthcare, Madison, WI) set to press-
sure-support ventilation mode, a minimal respiratory rate of 2 min⁻¹, and a time of inspiration of 1.3 s. PPV was applied via a tight-fitting face mask used for postoperative noninvasive ventilation. In the scanner room, the ventilator was placed as close to the subject and the 300-gauss line (gauss, a measure of magnetic field strength) as possible, thereby minimizing the length of the inflexible tubes. The subjects were instructed to breath normally during PPV.

CMR protocol. Retrospectively ECG-gated CMR was performed on a 1.5-T MRI scanner with phased-array coils (Avanto, Siemens Medical Solutions, Erlangen, Germany). Following scout imaging, cine image loops of the heart were obtained with steady-state, free precession sequences with a parallel imaging acceleration factor of 2 (TRUE-FISP; echo-time 1.5 ms; repetition time 3.0 ms; flip-angle 60°; GRAPPA), a slice-thickness of 8 mm, and a temporal resolution of 24–45 ms (25 phases per cardiac cycle). First, two-, three-, and four-chamber images were obtained; second, two RV outflow tract planes perpendicular to each other were obtained; third, a cine perpendicular to aorta in the three-chamber image was obtained. From these images, a double oblique stack of the heart including both atria was obtained. Trabeculation at the level of the apex was excluded, and the papillary muscles were included in the myocardium when in continuum with the compacted myocardium (14, 31). The volumes of each short-axis slice (luminal area × slice thickness) were automatically summed to obtain ventricular and atrial volumes, respectively. The tricuspid and mitral valve planes were defined according to methods described by Prakken et al. and others (Fig. 1) (14, 27, 31). Ejection fractions were taken as the stroke volume divided by the end-diastolic volume. Image analysis was performed blinded to knowledge of the PPV level. In 10 subjects, RV and LV volumes were determined for all 25 phases of the cardiac cycle. Output from the LV and the RV, respectively, were determined with flow sequences (through-plane phase-contrast sequences; velocity encoding of 200 cm/s) with planes corresponding to the sinotubular junction and the pulmonary artery 1–2 cm distal to the pulmonary valve.

Statistics. According to published data by Grothues et al. (11) it is possible to detect changes of 10 ml in LV end-diastolic volume (LVEDV) with a power of 0.9 (α = 0.05, 2-sided) with only 10 patients. Reproducibility for RV is slightly lower than for LV (10). To allow for dropouts and slightly lower changes, we included 18 volunteers. Data were tested for normality. Changes with treatment (PPV of 0, 10, and 20 cmH₂O) were evaluated with a Student’s t-test. A two-sided P value ≤ 0.05 was considered statistically significant. Data are presented as means (±SE).

RESULTS

All subjects tolerated PPV and completed the protocol. All cardiac volumes decreased with PPV (Table 1; Figs. 1 and 2). From PPV₀ to PPV₂₀, the total cardiac volume (the sum of both atrial and both ventricular volumes) decreased from 605 (±29)
to 446 (±29) ml (26%, \( P < 0.001 \)) during ventricular diastole and from 265 (±17) to 212 (±16) ml (20%, \( P < 0.001 \)) during ventricular systole, respectively. Heart rate increased by 7 (±3) beats/min, and blood pressure was not affected by the procedure performed with average blood pressure being \([124 (±9)]/\[81 (±8)] \text{ mmHg at PPV}_0\), \([121 (±7)]/\[82 (±7)] \text{ mmHg at PPV}_{10}\), and \([122 (±9)]/\[82 (±11)] \text{ mmHg at PPV}_{20}\). We did not observe shifting of the interventricular septum in any subjects.

During PPV\(_{20}\), LVEDV, LV end-systolic volume (LVESV), and LV stroke volume (LVSV) decreased by 20, 13, and 24%, respectively (Table 1), and with little increase in HR, LVCO decreased by 16%. LVEDV decreased to the same extent with each increase in PPV (11 and 20%, respectively), while LVESV decreased 13% between rest and PPV\(_{10}\), but did not decrease between PPV\(_{10}\) and PPV\(_{20}\). As a consequence, LVSV decreased with a near-linear relation to increasing levels of PPV (Fig. 3). Right ventricular end-diastolic volume (RVEDV), end-systolic volume (RVESV), and stroke volume (RVSV) demonstrated the same absolute and relative changes as seen for the LV. Both diastolic and systolic atrial volumes decreased in relation to PPV, with atrial volumes decreasing relatively more than the ventricular. The RA volumes decreased absolutely and relatively more than the LA volumes. The RA stroke volume (RASV) and LA stroke volume (LASV) decreased by almost 50% between rest and PPV\(_{20}\).

No difference between flow in aorta and LVSV or flow in pulmonary artery and RVSV was found during any of the test settings. Flow in the aorta decreased by 33 ml/s (28%, \( P < 0.001 \)) between rest and PPV\(_{20}\), and flow in pulmonary artery decreased by 34 ml/s (29%, \( P < 0.001 \)) between rest and PPV\(_{20}\). With increasing PPV, both left and right ventricular peak-filling rates decreased, whereas the peak-emptying rates remained constant (Table 1; Fig. 4).

**DISCUSSION**

We applied magnetic resonance imaging to measured cardiac chamber volumes and right and left ventricular output during noninvasive positive-pressure ventilation to understand and quantify the influence of the latter on the heart and central circulation. We hypothesized that positive-pressure ventilation negatively affects the circulation via the Frank-Starling mechanism; i.e., that cardiac output is lowered through lowered right
and left ventricular end-diastolic volumes. We found that, in healthy subjects, increasing airway pressure to 10 and 20 cmH₂O decreases total heart volume, all four individual chamber volumes, and output of both atria and both ventricles equally and progressively. Left and right ventricle end-diastolic volumes and peak filling rates decreased progressively with an increasing positive inspiratory pressure. Heart rate increased little and consequently the decrease in ventricular stroke volumes lowered cardiac output significantly (by 8 and 16%, respectively, at 10 and 20 cmH₂O).

While PPV improves alveolar gas diffusion and reduces atelectasis and hypoxic vasoconstriction, these positive effects should be balanced against compromising cardiac function to the extent of arterial hypotension with higher PPV levels (18, 25, 28). A compromised circulation has been related to changes in intrathoracic pressure, circulating blood volume, autonomic tone, and endocrine response (25). In the acute setting mainly the influence of positive intrathoracic pressure on RV and LV pre- and afterload and diastolic interventricular interdependence have been considered important although their precise interplay has not been determined (25). With heart and lung interactions during PPV, volume displacements have been inferred from measurements of intrathoracic pressures and transmural chamber pressures, but such can be misleading estimates of chamber filling and myocyte stretch (12, 19, 25). Myocardial stretch is best reflected by chamber volumes, but RV and LV volume changes are not reliably determined with echocardiography (1). We therefore studied cardiac filling and output during PPV with CMR, the gold standard for precise and reproducible cardiac chamber volume measurements.

In this study, HR and arterial blood pressure did not change significantly and hence important adrenergic and parasympathetic influences can be ruled out. Also, we do not hold it likely that other hormone changes affect this setting significantly. During spontaneous inspiration, the intrathoracic pressure becomes subatmospheric (26), but during PPV it increases to positive values. The atria have more compressible walls than the ventricles, and the RA and LA end-diastolic volumes decreased by 31 and 39%, respectively, while the RV and LV end-diastolic volumes decreased by only 20 and 21%. In accordance with the Frank-Starling relationship, the lowered RVEDV decreases RVSV; and the reduced RVSV results in comparable changes in LSV (2, 24), especially so in the setting of increased intrathoracic pressure when the pulmonary blood volume decreases and any buffering function of the pulmonary circulation is limited (30). It has been suggested that only PPV above 10 cmH₂O lowers cardiac filling (4, 5, 22), but in our study even a PPV of 10 cmH₂O was demonstrated to lower the volume and output of all four cardiac chambers.

Even without a positive pressure applied to the airways, it is difficult to relate intracardiac pressure to central blood volume and venous return. One has to estimate transmural pressures, which is difficult as the pressure applied to airways is transferred differently to different parts of the thoracic cavity (13). If pulmonary hyperinflation compresses the LA and pulmonary veins, pulmonary venous resistance, pulmonary artery pressure, and hence RV afterload must increase (13). With respect to LV afterload, PPV decreases the transmural pressure of the LV by increasing the outside pressure on all structures of the thorax (19). Thus, if mean arterial pressure is unchanged, PPV lowers LV afterload (3, 6, 23). We found the decrease in LVEDV/SV to match the decrease in RVEDV/SV and our data are best explained by the Frank-Starling mechanism without significant influences from changes in afterload. Diastolic ventricular interdependence has been implicated for depressed cardiac function during PPV (26). In our subjects, however, RV volume was always lowered, and never increased, and hence the interventricular septum was not left shifted. Thus, in our study, ventricular interdependence does not provide an explanation for the decrease in CO (2, 15, 16, 20). Unchanged arterial pressures, end-systolic volumes, and ventricular peak-emptying rates argue against significant changes in RV and LV contractility. As shown by the analysis of changes during the cardiac cycle, the main change seen with positive-pressure

![Fig. 2. End-diastolic cardiac chamber volumes with increasing positive-pressure ventilation of 0 (PPV₀), 10 (PPV₁₀), and 20 cmH₂O (PPV₂₀) in 18 healthy subjects. †P < 0.01.](http://ajpheart.physiology.org/)

AJP-Heart Circ Physiol • doi:10.1152/ajpheart.00309.2013 • www.ajpheart.org
ventilation is a significant decrease in ventricular peak filling rate in line with the notion that changes are mainly consequences of the Frank-Starling relationship.

With cardiovascular magnetic resonance imaging, we have in healthy subjects conclusively demonstrated a negative correlation between the applied level of positive airway pressures and decreases in right and left ventricular filling and output. The influence of positive airway pressure on the cardiac function is fully explained by the Frank-Starling relationship. These changes should always be taken into consideration during treatment of patients with positive-pressure ventilation, as cardiac volumes and output are shown to diminish significantly even at a positive pressure of 10 cmH2O. At a positive-pressure level of 20 cmH2O, the cardiac volume decreases by an average of 26%.

Fig. 3. Stroke volume (SV; top) and cardiac output (CO; bottom) during positive-pressure ventilation at 0 (PPV0), 10 (PPV10), and 20 cmH2O (PPV20) for the right (broken line) and left (solid) ventricles in 18 healthy subjects. For both ventricles the same decrease in filling is seen relative to an increment in positive-pressure ventilation level. †P < 0.01, *P < 0.05 compared with previous level of PPV.

Fig. 4. Time-volume curves from mean values of the left (A) and right (B) ventricle during positive-pressure ventilation at 0 (PPV0), 10 (PPV10), and 20 cmH2O (PPV20) in 10 normal subjects. Graphs are constructed from 25 cardiac phases.

GRANTS

P. L. Madsen and K. Kyhl were both supported by the Danish Heart Foundation.

DISCLOSURES

No conflicts of interest, financial or otherwise, are declared by the author(s).

AUTHOR CONTRIBUTIONS

REFERENCES


