Cardiac output in normal subjects: negative versus positive pressure ventilation

Effetti della ventilazione non invasiva a pressione negativa e positiva sulla gittata cardiaca

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Summary

Spontaneous inspiration and Negative Pressure Ventilation (NPV) produce a negative pleural pressure, and this reduction in intrathoracic pressure is transmitted to the right atrium. In contrast, intermittent Positive Pressure Ventilation (PPV) produces inspiratory increases in intrathoracic pressure and therefore right atrial pressure. The comparison of the cardiopulmonary effects between NPV and PPV has been previously reported in physiologic researches carried out both in animal model and in paediatric patients. Our hypothesis was that in healthy adults the application of NPV by iron lung might result in hemodynamic advantages in comparison with PPV. The hemodynamic effects of NPV and PPV, administered through iron lung and mask-ventilation respectively, were studied in 10 normal subjects. Continuous and non-invasive blood pressure and heart rate measurements were recorded by digital oscillometric photoplethysmography both at baseline and during mechanical ventilation. Iron Lung Ventilation (ILV), using intermittent NPV/CNEEP (Continuous Negative Extrathoracic End-expiratory Pressure) in assist control mode, and mask-ventilation by Bi-Level in ST mode were administered at two different settings (NPV: -15/-4 and -20/-4 cmH_2O), (PPV: +15/+4 and +20/+4 cmH_2O) respectively. The measurements lasted three minutes per setting without interruption. The mean values of all hemodynamic variables at baseline, during each step of ventilatory treatment and during the recovery phase, showed no statistically significant difference with ILV, on the contrary, during the application of mask-ventilation there was a significant decrease of diastolic, systolic, dicrotic and mean arterial pressure ($p = 0.010$, 0.002, 0.027, and 0.002 respectively), of cardiac output ($p = 0.002$), and dP/dtmax ($p = 0.037$), whereas stroke volume, pulse rate and systemic vascular resistance did not change. Our data show that both spontaneous breathing and mechanical breathing, during ILV, have the same effect on venous return in healthy subjects. In contrast, mask-ventilation produces transient hemodynamic effects due to a reduction in venous return. These results may represent the starting point for further investigation in patients with critical patients undergoing mechanical ventilation.

Riassunto

L'inspirazione spontanea e la ventilazione a pressione negativa (Negative Pressure Ventilation, NPV) generano un aumento della pressione pleurica negativa, e quindi la riduzione della pressione intratoracica che viene trasmessa all'atrio di destra. Al contrario la ventilazione a pressione positiva (Positive Pressure Ventilation, PPV) intermittente genera un aumento della pressione intratoracica e quindi della pressione atriale destra. Il confronto degli effetti cardiopolmonari tra la NPV e la PPV è stato precedentemente riportato in studi fisiologici condotti sia su modelli animali che su pazienti pediatrici. L'ipotesi di questo studio è che l'applicazione della NPV, tramite polmone d'acciaio (Iron Lung Ventilation, ILV), in soggetti adulti possa tradursi in vantaggi emodinamici rispetto alla PPV. Gli effetti emodinamici della NPV e PPV sono stati studiati in 10 soggetti sani sottoposti a ventilazione non invasiva a pressione positiva tramite Bi-Level con maschera facciale (Mask-PPV) e durante l'applicazione di NPV tramite ILV. La misurazione continua e non invasiva della pressione arteriosa e altri parametri emodinamici sono stati registrati attraverso un metodo non invasivo oscillo-pletismografico digitale. Sia la NPV, in modalità assistita controllata intermittent NPV/CNEEP (Continuous Negative Extrathoracic End-expiratory Pressure)), sia la PPV in modalità ST sono state applicate con due differenti settaggi (NPV: -15/-4 e -20/-4 cmH_2O, PPV: +15/+4 e +20/+4 cmH_2O rispettivamente). La media di tutti i parametri emodinamici in condizioni basali, durante ogni fase di trattamento ventilatorio e la fase di recupero, non ha mostrato variazioni significative durante NPV; al contrario durante l'applicazione della PPV si è rilevata una significativa riduzione della pressione diastolica, sistolica, dicrota e arteriosa media ($p = 0,010$, 0,002, 0,027, e 0,002 rispettivamente), della gittata cardiaca ($p = 0,002$), e del dP/dtmax ($p = 0,037$), mentre lo stroke volume, la frequenza cardiaca e le resistenze vascolari periferiche non hanno mostrato alcuna variazione. I risultati dimostrano che la respirazione spontanea e la NPV generano analoghi effetti sul ritorno venoso in soggetti sani. Al contrario la PPV con maschera produce transitori effetti emodinamici dovuti ad una riduzione del ritorno venoso. Questi risultati potrebbero rappresentare il punto di partenza per ulteriori studi in pazienti critici sottoposti a ventilazione meccanica.

Key words
Cardiac-output • Positive pressure ventilation • Negative pressure ventilation • Iron lung • Noninvasive hemodynamic measurement • Mechanical ventilation

Parole chiave
Gittata cardiaca • Ventilazione a pressione positiva • Ventilazione a pressione negativa • Polmone d'acciaio • Misurazioni emodinamiche non invasive • Ventilazione meccanica

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Introduction

In order to accomplish ventilation, a pressure difference must be developed intermittently across the lungs. Such pressure, called transpulmonary pressure, represents the difference between the pressure in the alveolus (i.e. inside the lung) and the pleural cavity (i.e. outside the lung). With Positive Pressure Ventilation (PPV), the transpulmonary pressure is increased by making the alveolar pressure more positive; in contrast, with Negative Pressure Ventilation (NPV), the transpulmonary pressure is increased by making the pleural pressure more negative.

Both spontaneous and mechanical ventilation induce changes in intrapleural or intrathoracic pressure and lung volume, which can independently affect atrial filling, ventricular emptying, heart rate and myocardial contractility.

Both spontaneous and mechanical ventilation induce changes in intrapleural or intrathoracic pressure and lung volume, which can independently affect atrial filling (preload), ventricular emptying (afterload), heart rate and myocardial contractility (Cardiac Output, CO). Spontaneous inspiration produces a negative pleural pressure and this reduction in intrathoracic pressure is transmitted to the right atrium. In contrast, Intermittent PPV (IPPV) produces inspiratory increases in intrathoracic pressure and therefore right atrial pressure [1].

The effects of PPV on cardiac function, in healthy volunteers receiving "mask" PPV, [2 3] were first reported by Cournand et al. They showed that right ventricular filling was inversely related to intrathoracic pressure and, as this became more positive and the right ventricular preload fell, it produced a detectable fall in CO [2 3].

Although the hemodynamic effects of NPV have not been extensively studied, most clinicians believe that these effects are opposite to those of PPV, more physiological and more likely to maintain a normal CO [4]. The exposure of the entire body (except the airway opening) to NPV would result in the same adverse hemodynamic effects seen with PPV [5]. These effects occur because intrathoracic pressure actually is raised relative to body surface pressure, reducing the gradient for venous return. Skabursis et al. [6] and Lockhat et al. [7] have shown that this is not the case when the application of NPV is confined to the thorax and upper abdomen by using cuirass or poncho wrap. Unlike tank ventilator, these machines selectively decrease intratoracic pressure, so that the right atrial pressure becomes more negative (compared to the rest of the body), potentially enhancing the gradient for the venous return. In addition, Shekerdemian et al. [8 9] studied the effects of cuirass NPV on cardiac output in healthy children and in children after simple cardiac surgery, demonstrating that cuirass NPV led to a modest improvement in the CO of healthy children while it is able to achieve a greater improvement in post-operative patients.

It has been reported that CO can be detected using a non invasive method: the Pressure Recording Analytical Method (PRAM) [10], which can derive the arterial-pressure-blood flow relationship from the analysis of the arterial pressure profile in the time domain. It has been demonstrated that, in stable patients [10] and in hemodynamically unstable patients without atrial fibrillation [11], PRAM is a valid alternative to pulmonary artery thermodiluition and it is an accurate method for monitoring CO.

The aim of this study was to evaluate the sequences of changes in CO and haemodynamic parameters by PRAM in a group of normal subjects during non invasive mask ventilation (Mask-PPV) and during NPV with an Iron Lung Ventilation (ILV).

Material and methods

Subjects

Ten healthy volunteers from our unit staff with stable hemodynamic condition, without history of previous cardiac and respiratory diseases and free of respiratory symptoms were enrolled in the study. Three subjects were ex-smokers and all of them had gave up smoking at least three years before the starting of the study. All subjects gave their written informed consent to the procedures.

Study protocol

Methods

All subjects underwent spirometric measurements, in a sitting position and at rest from at least 30 minutes, two hours before the start of the study. Arterial blood pressure and heart rate were taken in a supine position immediately before the start of the study.

Continuous and non-invasive blood pressure and heart rate measurements were recorded. Blood pressure measurements were assessed by digital oscillometric photoplethysmography (Finapres, Ohmeda, Englewood, Colorado, USA) [12-17]. Arterial blood pressure measurements were taken at the start and at the end of the protocol with a Riva Rocci sphygmomanometer [18].

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All subjects were ventilated first by iron lung and then, after 24 hours, by mask ventilation or the other way round, according to a random assignment. Randomisation was carried out using sealed envelopes

containing random assignment codes; the codes were generated from tables of random numbers by an operator unaware of the aim of the study. The two methods of ventilation were performed at the same time in the afternoon, both with the subjects lying in supine position. Before starting their ventilatory sessions, all subjects were able to familiarise with both type of ventilators and their relative interfaces for 10 minutes. At the end of these preliminary sessions, the subjects were asked to rest in supine position for 30 minutes before starting of the active session. NPV was administered by a microprocessor based iron lung capable of thermistor triggering to perform assist-control NPV (CA 1001, Officine Coppa Biella, Italy) [19] which exposes the entire body (except the upper airways) to subatmospheric pressure (i.e. negative pressure) during inspiration. PPV was administered by a Bi-Level ventilator (Bi-Pap Vision, Respironics Inc.) connected to a face mask (Respironics) with a plateau valve (Respironics).

The ventilatory treatment was carried out over two days, applying for each subject NPV and PPV in the order assigned by the randomization process. ILV was carried out in an assist-control mode, with Intermittent Negative Pressure Ventilation/Continuous Negative Extrathoracic End-Expiratory Pressure (INPV/CNEEP), at two different settings (INPV/CNEEP -15/-4 cmH_2O; and -20/-4 cmH_2O). Each setting lasted three minutes without interruption. The time of three minutes was found to be sufficient to detect early, by PRAM, the haemodynamic profile of patients with orthostatic intolerance [16]. The phases of measurement were: $T1_N$ (basal condition), $T2_N$ (-15/-4 cmH_2O), $T3_N$ (-20/-4 cmH_2O) and $T4_N$ (recovery phase). The low level of EPAP/CNEEP employed due to the fact that the Bilevel vision used had a default of 4 cmH_2O as the lowest level of pressure which can be set. Therefore in order to make comparable the experimental condition we applied the same level of continuous negative end expiratory pressure on ILV. Furthermore, the addition of CPNE to NPV was due also to improve the synchrony between the subject and the ventilator as we previously reported [19].

Positive pressure ventilation was carried out by Bi-Level in S/T mode at two different settings (IPAP/EPAP +15/+4 cmH_2O, FiO_2 21%; IPAP/EPAP +20/+4 cmH_2O, FiO_2 21%) each setting lasted three minutes without interruption during the experimental condition. The phases of measurements were: $T1_P$ (basal condition), $T2_P$ (+15/+4 cmH_2O), $T3_P$ (+20/+4 cmH_2O) and $T4_P$ (recovery phase).

Systemic arterial blood pressure, pulse rate and CO during each session of ILV, Mask-PPV and during spontaneous breathing were analysed and recorded by PRAM.

PRAM method

The PRAM method [10 17] differently from other Pulse Counter Methods (PCMs), which need external calibration and/or pre-estimated parameters from other subjects [20-25], can derive cardiac flow and arterial impedance (Z(t)) directly from the analysis of the pressure wave. The Stroke Volume (SV) calculation (based upon an objective analytic description of the profile of the entire cardiac cycle, systolic, diastolic and of pressure over time) reflects the effects of physical forces which act on the whole cardiovascular system, thus determining the relationship between arterial blood pressure morphology profile and blood flow. The PRAM system uses the pressure signal obtained both by invasive (aorta, pulmonary, femoral and radial arteries) and non invasive methods [10 16]; in this last case the pressure signal is derived from the arterioles of a finger of the hand by an oscillometric-plethysmographic cuff [10].

In detecting the SV, the PRAM system takes into account both the pulsate and the continuous blood flow contribution without the need of any external calibration or pre-estimated parameters from other subjects [10 17]. The pulsate component of the flow is given by the impedance Z(t), mainly linked to the ventricular contractility and to the aorta compliance, whereas the continuous component of the flow is mainly linked to the ventricular compliance interaction with compliance resistances of the arterial system.

The basic principle of the PRAM algorithm is the ability to detect the interactions between cardiac and circulatory systems, and therefore to calculate a new parameter that describes the work expenditure of the cardiovascular system strictly correlated to SV; this is called the Cardiac Cycle Efficiency (CCE) [17 26].

In order to verify that the pressure measurements obtained by the Finapres photoplethysmograph were not influenced by the subatmospheric pressure generated inside the iron lung, we compared these measurements with those obtained with the Riva Rocci sphygmomanometer before, during and at the end of each session.

Data processing

Analog noninvasive pressure signals acquired at a sample rate of 1,000 Hz were digitized with an analogic-digital multifunction card (DAQ Card-700, National Instruments Corp., Austin, TX) working on the tension signals with 12 bit from -2.5 to 2.5 volt. All the signals were recorded on a personal computer (Acer, TravelMate 6,000). Data from pressure signals were evaluated beat to beat in real time (Figure 1).

From the pressure signal, the following parameters were measured and estimated by computerized PRAM algorithm:

1. Pulse Rate, PR (bpm);
2. systolic, diastolic, dicrotic and mean arterial pressure (mmHg);
3. Stroke Volume, SV (mL);
4. Cardiac Output, CO (L/min);
5. dP/dt_{max} (mmHg/msec);
6. Systemic Vascular Resistance, SVR (dines*sec/cm^5).

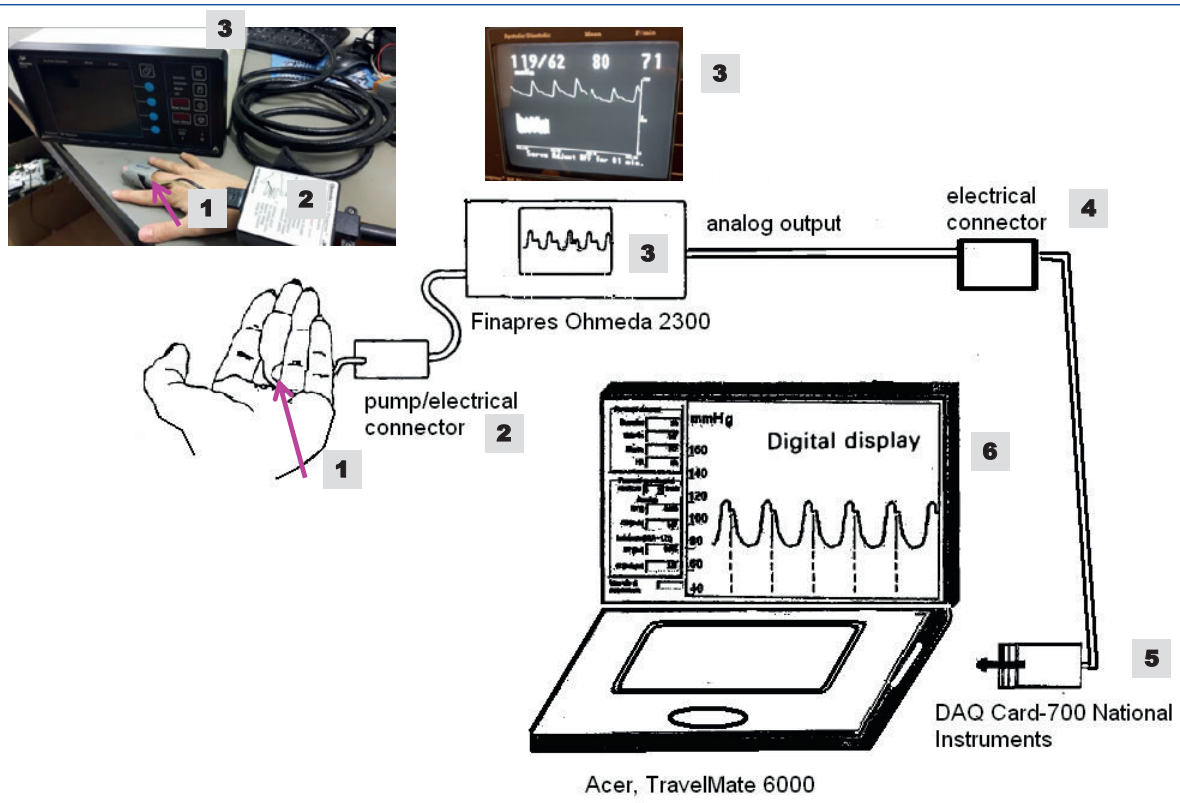

Figure 1. Schematic representation of PRAM (Pressure Recording Analytical Method).
This technology is based on the analysis of the peripheral arterial waveform by finger photoplethysmography (1. finger cuff; 2. electrical connector; 3. monitor Finapres Ohmeda 2300) without any form of external calibration and/or pre-loaded data. The system presents a module for non-invasive accurate measurement of blood pressure, Stroke Volume (SV) and Cardiac Output (CO) values. It can be connected (4. electrical connector) to the analog output of the monitoring system for the arterial pressure waves and the subsequent computation of SV and CO. The pressure signals are acquired at 1,000 Hz by means of an analogic-digital multifunction card (5. DAQ Card-700National Instruments Corp.). The pressure signals are recorded on a laptop (6. Acer-TravelMate 600) and analyzed by computerized PRAM algorithm to estimate beat to beat hemodynamic parameters.

Statistical analysis

The normal data distribution was assessed by means of Kolmogorov-Smirnov one-sample test. Data were expressed as means ± SD and comparisons were performed by Student's t-test for paired data (negative vs. positive pressures sessions) and by analysis of variance (ANOVA) and post-test (Bonferroni) (within each experimental session) using PASW statistical package 17.0 (IBM-SPSS, Chicago, IL-USA). $p < 0.05$ was considered to be statistically significant.

Results

Anthropometric, spirometric and cardiac data are reported in Table I. Six subjects were males and four females with a mean age of 45 ± 3 years (range from 36 to 45). Three subjects had a history of smoking, and all had stopped at least 3 years before the enrolment in the study. In Table II are reported the mean values (± SD) of the hemodynamic variables at basal conditions during spontaneous breathing (T1) and during each phase of the ventilatory treatment (T2, T3) with ILV and Mask-PPV.

During ILV there was no statistical significant difference in all the hemodynamic variables studied from $T1_N$, trough the steps $T2_N$, $T3_N$ and $T4_N$ (recovery from the end of the session).

During ILV there was no statistical significant difference in all the hemodynamic variables studied.

Opposite to basal condition ($T1_P$), during the application of Mask-PPV ($T2_P$, $T3_P$) and recovery phase ($T4_P$) there was a significant decrease of diastolic, systolic, dicrotic, mean arterial pressure ($p = 0.010$, 0.002, 0.027, 0.002), CO ($p = 0.002$) and dP/dtmax ($p = 0.037$), whereas no modification was found for SV, PR ($p = 0.728$) and only a slight decrease was detected for SVR ($p = 0.06$).

No statistical differences were detected in all variables when the positive pressure was increased from 15 to 20 cmH_2O. The beat to beat analysis of pressure wave morphology detected by PRAM system was not influenced by the subatmospheric pressures generated in the IL, as showed in Figure 2.

Table I. Anthropometric, spirometric and cardiac data.

Variable	Mean (SD)
• Gender, M/F	6/4
• Age, years	45 (3)
• Height, (cm)	173 (8)
• Weight, (kg)	73 (12)
• FEV_1, L; % pred	3.16 (0.39); 103 (11.8)
• FVC, L; % pred	3.82 (0.33); 107 (12.4)
• FEV_1/VC %	82.5 (4.79)
• BSA, m^2	1.86 (0.19)
• BP SYS, mmHg	121 (13)
• BP DIA, mmHg	61(10)
• HR b/min	72 (2.5)

Abbreviation. SD: Standard Deviation; FEV_1: Forced Expiratory Volume in the 1st second; FVC: Forced Vital Capacity; FEV_1/VC: Forced Expiratory Volume in the 1st second/Vital Capacity; BSA: Body Surface Area; BP: Blood Pressure; SYS: Systolic; DIA: Diastolic; HR: Heart Rate

During ILV, blood pressure values resulted similar to those obtained before and after each session. On the contrary, during Mask-PPV all variables except PR showed a progressive decline during the test; this trend remained stable during the recovery session.

In order to evaluate the differences between the mean values of the T2 sessions ($T2_N$ vs $T2_P$) and the T3 sessions ($T3_N$ vs $T3_P$) during ILV and Mask-PPV, the Bonferroni post hoc test was used. As reported in Table II, only PR did not show a significant between the values obtained using ILV and Mask-PPV in both T2 and T3 phases. During the T2 sessions diastolic, systolic, dicrotic, mean arterial pressure, SV, CO and dP/dtmax showed lower values when the subjects underwent Mask-PPV compared to those obtained with ILV (p = 0.003; 0.001; 0.010; 0.001, 0.001, 0.001, and

Table II. Hemodynamic variables during each phase of the ventilatory treatment.

	Diastolic Pressure mmHg			Systolic Pressure mmHg			Dicrotic Pressure mmHg		
	NPV	PPV		NPV	PPV		NPV	PPV	
	Mean (SD)		p*	Mean (SD)		p*	Mean (SD)		p*
T1	61.4 (10.8)	62.3 (9.4)	0.369	120.1 (13.7)	121.0 (12.1)	0.642	76.8 (12.2)	76.2 (10.5)	0.378
T2	63.8 (7.9)	50.5 (8.4)	0.003	124.5 (11.8)	102.2 (11.6)	0.001	79.4 (11.0)	66.5 (7.6)	0.010
T3	63.4 (8.2)	49.9 (9.1)	0.010	121.0 (13.3)	100.9 (10.9)	0.001	78.7 (11.1)	65.5 (8.0)	0.023
T4	60.4 (7.0)	54.4 (7.5)	0.025	114.8 (12.1)	105.0 (11.4)	0.004	75.9 (8.5)	69.1 (6.2)	0.025
T1-T4 p	0.782	0.010		0.319	0.002		0.787	0.027	

	Stroke Volume ml			Cardiac Output l/min			Pulse Rate beats/min		
	NPV	PPV		NPV	PPV		NPV	PPV	
	Mean (SD)		p*	Mean (SD)		p*	Mean (SD)		p*
T1	78.7 (15.2)	80.5 (14.4)	0.162	5.7 (0.49)	5.6 (0.42)	0.194	72.9 (10.5)	73.5 (10.1)	0.200
T2	82.2 (18.2)	73.3 (18.0)	0.001	5.8 (0.69)	4.9 (0.66)	0.001	72.2 (11.1)	68.8 (11.6)	0.174
T3	82.3 (17.9)	77.3 (18.4)	0.063	5.7 (0.63)	5.2 (0.65)	0.001	71.5 (11.0)	68.7 (11.9)	0.226
T4	83.2 (11.4)	79.6 (15.1)	0.980	5.4 (0.62)	5.4 (0.55)	0.655	70.1 (8.2)	70.0 (8.2)	0.713
T1-T4 p	0.956	0.769		0.617	0.002		0.903	0.728	

	Mean Arterial Pressure mmHg			dP/dt_{max} mmHg/msec			Systemic Vascular Resistance dines*sec/cm^5		
	NPV	PPV		NPV	PPV		NPV	PPV	
	Mean (SD)		p*	Mean (SD)		p*	Mean (SD)		p*
T1	81.2 (11.1)	82.0 (10.0)	0.532	0.95 (0.14)	0.93 (0.09)	0.291	1079 (158)	1073 (133)	0.665
T2	84.0 (8.3)	67.6 (7.9)	0.001	0.99 (0.14)	0.77 (0.20)	0.002	1095 (137)	1030 (148)	0.281
T3	82.7 (9.3)	66.9 (8.6)	0.003	0.93 (0.17)	0.79 (0.18)	0.030	1082 (138)	954 (128)	0.056
T4	78.3 (7.7)	71.2 (8.1)	0.009	0.86 (0.15)	0.78 (0.15)	0.035	1074 (108)	976 (109)	0.021
T1-T4 p	0.545	0.002		0.351	0.037		0.998	0.060	

The differences of the mean from T1 to T4 for both NPV and PPV were evaluated by ANOVA, One Way Analysis of Variance. T1 = Baseline; T2 = -15 cmH_2O for NPV, +15 cmH_2O for PPV; T3 = -20 cmH_2O for NPV, + 20 cmH_2O for PPV; T4 = recovery from the end of the session for both NPV and PPV. * The comparison of the mean values between the T2 ($T2_N$ vs $T2_P$) and T3 ($T3_N$ vs $T3_P$) sessions during NPV/PPV was analyzed by the t Student test for paired data. The comparison of the means T2-T3 by the Bonferroni post test analysis resulted not significant (p > 0.05) for all variables considered. SD: Standard Deviation

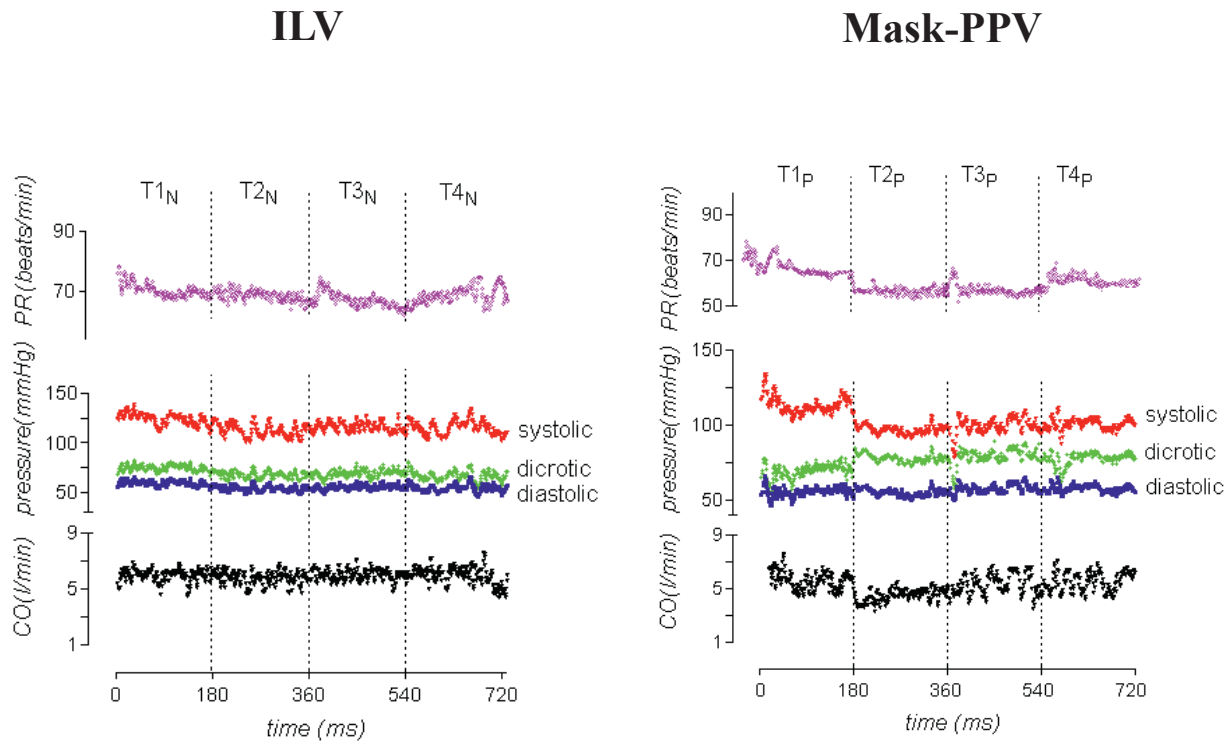

Figure 2. Analysis of pressure wave morphology detected by PRAM system.
CO: Cardiac Output; ILV: Iron Lung Ventilation; Mask-PPV: Mask-Positive Pressure Ventilation; PR: Pulse Rate; PRAM (Pressure Recording Analytical Method).
Experimental condition during ILV: $T1_N$ (basal condition), $T2_N$ (-15/-4 cmH_2O), $T3_N$ (-20/-4 cmH_2O) and $T4_N$ (recovery phase).
Experimental condition during Mask-PPV: $T1_P$ (basal condition), $T2_P$ (+15/+4 cmH_2O), $T3_P$ (+20/+4 cmH_2O) and $T4_P$ (recovery phase).

0.002 respectively), whereas no modification was detected for PR and SVR.

During the application of Mask-PPV and recovery phase there was a significant decrease of diastolic, systolic, dicrotic, mean arterial pressure, CO and dP/dtmax, whereas no modification was found for SV, PR and only a slight decrease was detected for SVR.

During T3 sessions, the values of diastolic, systolic, dicrotic, mean arterial pressure, CO and dP/dtmax were lower when the subjects underwent Mask-PPV in comparison with those obtained with ILV (p = 0.010; 0.001; 0.023; 0.003, 0.001, and 0.030 respectively), whereas no modification was detected for SV, PR, and SVR (p = 0.056).

Discussion

The results of our study show that in healthy subjects there was a different hemodynamic response to the application of a positive pressure, administered at the airway opening trough a facial mask, or to an equivalent negative pressure generated inside a body ventilator by an iron lung. Given that the hemodynamic variables obtained in our study were derived by the analysis of arterial pressure wave, we took particular attention in constantly comparing the values generated by the Finapres photoplethysmograph system with those measured by the Riva Rocci sphygmomanometer.

In healthy subjects there was a different hemodynamic response to the application of a positive pressure or to an equivalent negative pressure generated inside a body ventilator by an iron lung.

No significant variations of arterial blood pressure were detected during ILV both in phase $T2_N$ (-15 cmH_2O) and $T3_N$ (-20 cmH_2O) in comparison with basal values, whereas a statistically significant decrease of arterial pressure was found during Mask-PPV both in phase $T2_P$ (+15 cmH_2O) and $T3_P$ (+20 cmH_2O) in comparison with baseline values. Furthermore, after the application of PPV, we found that the subjects were not able to return to their basal hemodynamic values of five minutes after the interruption of the ventilatory session. This was not the case when ILV was applied. What does it mean from an hemodynamic point of view?

Cournand et al. [3] showed that in normal subjects the increase in intrathoracic pressure produced by the application of facial mask delivering Intermittent Positive Pressure Breathing (IPPB), produced a decrease in right ventricular filling and therefore in cardiac output. The decrease in cardiac output (14.5% and 16.5%) was proportionally correlated to the increase in mean/peak mask pressures (7/14 and 10.6/16.7 mmHg respectively) applied in two separate experimental condition. In a subset of subjects who underwent a 70-minute period of continuous IPPB, the decrease in cardiac output was greater during the first 10-minute period (23%) as compared to a 17% decrease present after the 40 and 70-minute periods of IPPB. In our normal subjects the application of a pressure of 15 and 20 cmH_2O resulted in a decrease in cardiac output of 14.3% and 9% from baseline values. This trend is partially in agreement with the results reported by Cournand [3]. Differently by Cournand we found a decrease in the diastolic, systolic and mean arterial pressure measurements during the application of Mask Ventilation. This may be due to a different duration of the ventilatory sessions, 10 minutes in the Cournand protocol versus 3 minutes in our protocol. However, using a shorter period of ventilation we were able to detect the initial perturbation effect on the vascular tone which can be explained by the decrease in diastolic pressure. On the contrary, the lack of significant changes in blood pressure in Cournand study [3] could be justified by the longer duration of the ventilator session, which does not allow the observation of the transient effect of cardiovascular perturbation which appears during the first few minutes. In fact, what the Authors detected could have been not the transient effect on vascular tone, but a new compensated equilibrium of the vascular system.

In our study, the observed decrease in dicrotic pressure during Mask-PPV may mean that in healthy subjects the adaptation of the cardiovascular system to the decreased venous return consists in a variation of both the time of closure and the form of wave pressure of the aortic valve. This influences the CO without any significant change in PR and, consequently, in SV whereas dP/dtmax decreased significantly ($p = 0.037$), indicating a potential mechanical stress due to PPV on the venous return.

During ILV no significant changes of the studied variables were observed at the two different setting. These results may be explained by the fact that exposing the whole body, with the exception of the head, to subatmospheric pressure inside the iron lung, the intrathoracic pressure actually generated is raised relative to the body surface pressure, thus reducing the gradient for venous return and the correlated variables. Lockhat et al. [7] showed that the cardiac output of normal dogs receiving thoracoabdominal negative pressure ventilation was significantly improved by augmentation of the systemic venous return, but this phenomenon was not present during the whole body negative pressure ventilation.

In our study, we intentionally applied negative and positive pressure for 3 minutes [16] and we thereafter increased the pressure without interruption, in order to verify the response of the physiologic system to the variation of transthoracic pressure and the type of compensation adopted by the cardiovascular system. Our data clearly show that only with the application of PPV the maximal response, in terms of reduction of cardiovascular variables (diastolic, systolic, dicrotic, mean arterial pressure, SV, CO, PR, dP/dtmax, SVR), was obtained in the first three minutes of ventilation, and that increasing the level of pressure there was no further modification of the variables detected. This may be linked to the compensatory mechanism that is put in place in healthy subjects.

Only with the application of PPV the maximal response, in terms of reduction of cardiovascular variables was obtained in the first three minutes of ventilation.

This is the first study which reports a formal comparison on the hemodynamic effects of the application of non invasive PPV and NPV in healthy subjects. Our data confirm the previous physiologic researches carried out both in animal model [7], on the comparison of PPV and NPV, and in healthy subjects [3] during PPV. Our data show that both spontaneous breathing and mechanical breathing during ILV induce parallel changes in intrapleural or intrathoracic pressure which are transmitted to the right atrium with the same effect on venous return. In contrast, Mask-PPV produces an inspiratory increase in intrathoracic pressure with important transient hemodynamic effects due to a reduction in venous return. These data however must be considered keeping in mind the following limitations of the study: the shorter duration of the application of positive pressures, and particularly the lack of a recovery time between their phases of administration, did not allow us to fully replicate the findings of Cournand. The application of the PRAM system instead of the thermodiluition technique, which represent the gold standard for hemodynamic evaluation; however, the PRAM system has been proven to be comparable with the thermodilution technique in animal models [27], in stable patients [8], septic patients [17] and also in hemodynamically unstable patients without atrial fibrillation [11].

Conclusions

Our data show that both spontaneous breathing and mechanical breathing, during ILV, have the same effect on venous return in healthy subjects. In contrast, mask-ventilation produces transient hemodynamic effects due to a reduction in venous return.

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These results may represent the starting point for further investigation in critical patients undergoing mechanical ventilation.

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Gli Autori dichiarano di non avere alcun conflitto di interesse con l'argomento trattato nell'articolo.

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