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Left ventricular function during weaning of patients with chronic obstructive pulmonary disease

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Abstract. *Objective:* Determine the evolution of left ventricular ejection fraction during weaning.
Design: Prospective study.
Setting: Intensive care unit of a university teaching hospital.
Patients and participants: 12 consecutive mechanically ventilated patients, without documented coronary artery disease, suffering from acute exacerbation of chronic obstructive pulmonary disease and able to be weaned.
Measurements and results: Left ventricular ejection fraction was determined during mechanical ventilation, inspiratory pressure support (10 cmH_2O) and spontaneous ventilation with constant inspiratory oxygen fraction using technetium ^{99m} radionuclide angiography. Spontaneous ventilation induced a significant decrease in left ventricular ejection fraction from 54.5±12.4 to 47.0±13% ($p<0.01$). Inspiratory pressure support induced a slight but non-significant decrease in left ventricular ejection fraction from 55.0±12.1 to 50.3±12.4%. Left ventricular ejection fraction was homogeneously reduced by spontaneous ventilation without patent regional wall motion abnormalities of the left ventricle. Myocardial ^{201}thallium imaging performed 15 min after weaning showed a normal perfusion in the left ventricle anterior and posterior free wall.
Conclusion: Weaning of patients suffering from chronic obstructive pulmonary disease without coronary artery disease induced a significant reduction in left ventricular ejection fraction. The non significant decrease in left ventricular ejection fraction observed with inspiratory pressure support suggested that our results might be explained by a weaning induced increase in afterload.

Key words: Left ventricular function – Weaning – Inspiratory pressure support – Chronic obstructive pulmonary disease – Coronary artery disease

Left ventricular ejection fraction (LVEF) is a global index of the extent of left ventricle fiber shortening and is considered to provide a useful measurement of left ventricular pump function [1]. Alterations in myocardial contractility and/or in afterload are the major determinants of the variations in LVEF [2]. Acute left ventricular dysfunction assessed by the onset of acute pulmonary oedema has been reported previously in difficult to wean patients suffering from chronic obstructive pulmonary disease (COPD) associated with pre-existing left ventricle dysfunction secondary to coronary artery disease (CAD) [3]. In these patients the onset of myocardial ischemia during weaning was suggested by the concomitant presence of acute left ventricle dysfunction and angioscintigraphic left ventricle regional wall motion abnormalities [3]. However the well known hemodynamic effects of positive pressure ventilation [4, 5] – i.e. left ventricular afterload reduction-particularly in chronic obstructive pulmonary disease by suppressing negative swings in intrathoracic pressure [6] suggest that, at the opposite, weaning might increase afterload and thus decrease LVEF independently of a direct effect on myocardial contractility. To address this concern we compared the evolution of Technetium ^{99m} radionuclide LVEF from mechanical ventilation (MV) to spontaneous ventilation (SV) and from MV to inspiratory pressure support (IPS) in patients suffering from COPD and free of documented CAD. The choice of the exclusion of patients with known CAD was justified by our request to focus on increase in left ventricle afterload as the sole explanation of a potential fall in LVEF since myocardial ischemia appears to be the most important cause of reduced contractility during weaning. In the same way we simultaneously compared the results obtained during weaning with those obtained with inspiratory pressure support that can reduce negative ventilatory swings and thus is hypothesized to induce a slighter increase in left ventricular afterload. [7].

Patients and methods

Patients

Twelve patients with previously well documented COPD were studied. The diagnosis of COPD was reached after clinical investigation revealed

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a history of chronic bronchitis and/or emphysema with simultaneous chest X-ray abnormalities. Severe airway obstruction was documented by standard pulmonary function tests i.e. decrease in FEV1, FVC and FEV1/FVC and/or arterial gas abnormalities suggesting alveolar hypoventilation while patients breathing room air. All patients were submitted to MV for acute respiratory failure. No patient had an history of hypertension and/or of valvulopathy and/or ventricular arrhythmias. No chest pain history evocative of acute or chronic myocardial ischemic events was previously documented. Complete physical examination did not reveal clinical signs of left ventricle dysfunction and of extracardiac diseases. No evidence of previous myocardial infarction was seen on the ECG and echocardiographic examination did not reveal global or local abnormalities in left ventricular antero-lateral free wall and inferior wall dynamics. Echocardiographic examination did not exhibit valvular apparatus abnormalities or left ventricle parietal hypertrophy. When the patients were selected for the weaning study, acute exacerbation of lung disease had been resolved for at least three days. Their ventilatory capacities exceeded standard criteria for successful weaning [8] and each patient tolerated weaning for over thirty minutes on at least two trials. None of these twelve COPD patients received any drugs, particularly vasoactive agents, except for antibiotics if necessary.

Methods and protocol

Patients who had given their informed consent were submitted to the following protocol previously accepted by the ethical committee of our hospital. As an integral part of patient care any patient underwent controlled MV with a Siemens 900 C ventilator with inspiratory oxygen fraction (FIO_2) 0.21–0.3 at a rate of 16–18 breaths/min and with a tidal volume of 6–10 ml/kg without positive end expiratory pressure. When weaning was obtained for over 30 min at least twice, LVEF was assessed with radionuclide angiocardiography. Radionuclide angiocardiography was carried out by in vivo red cell labelling using stannous pyrophosphate with ^{99m}Technetium (Tc) [9]. ECG gated ^{99m}Tc angiocardiography was performed using an equilibrium blood pool technique with a gamma camera (Sopha Medical) with a high resolution parallel colimator. After the injection of the 740 MBq of ^{99m}Tc the best left anterior oblique position patient to visualize the left ventricle was required. Then, the data were acquired 5 times with an initial adaptation period of 10 min: mechanical ventilation (MV1), SV, mechanical ventilation (MV2), IPS, mechanical ventilation (MV3). The total acquisition time lasted about 1 h. For each acquisition 16 frames with 350000 counts were recorded on a 64×64 matrix. The data were collected in a SIMIS II computer. Data computation leads to the calculation of global and sectorial LVEF after dividing the left ventricle in nine sectors. For this computer, the inferior normal limit for LVEF was 50% [10]. To determine the left ventricle end diastolic volume (LVED) the concept of a fully automated processing which allows the determination of the region of interest of the left ventricle during the diastolic phase was used [10].

During all measurements the patient was maintained in a quite stable position to prevent technical error in LVEF assessment. The same level of FIO_2 was administered whatever the ventilation modalities throughout the study. Continuous measurements of arterial saturation were performed throughout the study to insure that arterial saturation remains ≥ 90% during the procedure and particularly after weaning. IPS used was 10 cmH_2O in each patient. SV was maintained through the endotracheal tube connected to a T-piece. Heart rate was simultaneously measured over the 5 ventilation periods and systolic blood pressure (SBP) during MV1 and SV.

At 24 h later the assessment of myocardial perfusion was obtained by myocardial Thallium 201 single photon emission computed tomography imaging (myocardial ^{201}Tl SPECT imaging). The aim of this investigation was to detect the onset of myocardial ischemia during weaning. Myocardial ^{201}Tl SPECT imaging was performed 15 min after disconnection from the ventilator, a moment which was considered as the time of maximal stress following weaning, while the patient was breathing spontaneously with the same FIO_2 as during MV measurements. 111 MBq of ^{201}Tl chloride were then infused intravenously. 32 frames on 180° were acquired, with an acquisition time of 30 s per view. Data were collected on a 64×64 matrix. LV transaxial, coronal, and sagittal slices, 1 pixel thick-ie 6 mm- were reconstructed by filtered back projection using a hanning filter. Redistribution imaging was performed three hours later with the same protocol, without reinjection of the radionuclide while the patient was again submitted to MV.

Dipyridamole myocardial ^{201}Tl SPECT imaging was performed as previously described [11] 7 days later when the COPD patients were definitively weaned and stable. The acquisition protocol was the same as above. The aim of this investigation was to ensure the absence of an occult myocardial ischemia in this group of patients without any clinical or ECG signs of CAD. Our results were analyzed visually by two independent observers unaware of the patient status and the ventilatory modes.

Statistical analysis

The statistical analysis was performed as follows. The comparison between the five ventilatory modalities used a one factor variance analysis with repeated measures complemented, if significant, by an intergroup comparison using Scheffe test. The alpha risk chosen for all the analysis was 0.05.

Results

The main characteristics of the 12 severe COPD patients (10 males) enrolled in the study are listed in Table 1. Mean age was 68±9.5 years. At rest PaO_2 was 58±7 mmHg and $PaCO_2$: 52±6 mmHg and HCO_3^-: 35±3.8 mmol/l. FEV_1 was 1.0±0.2 l/s, FVC: 2.0±0.6 l and FEV_1/FVC: 52±7%. SBP was 121±10 mmHg and diastolic blood pressure 72±8 mmHg. Out of our 12 patients 10 were discharged from the intensive care unit (Table 1).

Individual and mean values of LVEF, LVEDV and heart rate are presented in Table 2 and Fig. 1. There was no significant change in LVEF during the three basal values obtained with the patients under MV (MV1, MV2, MV3) and it remained stable at about 55%. The extremes values during these basal controls were 41 and 83% for MV1, 43 and 84% for MV2 and 43 and 84 for MV3. Thus despite the lack of obvious left ventricular dysfunction 6 patients had a basal LVEF equal or inferior to 50% which indicates a probable slight occult left ventricular dysfunction. SV with stable FIO_2 was associated with a significant decrease in LVEF from 54.5±12.4 (MV1) to 47.0±13.0% (SV) ($p < 0.01$). This decrease was observed in all but one patient (Fig. 1). With IPS a slight but non significant decrease was observed from 55.0±12.1 to 50.3±12.4%. Individual analysis of ^{99m}Tc angiocardiography indicates that LVEF was homogeneously reduced without any abnormality of regional LVEF suggestive of myocardial ischemia. No significant change in LVEDV was observed during weaning. Finally, in our patients weaning was associated with a significant increase in HR ($p < 0.05$) (Table 2) without significant change in SBP (Fig. 2). Figure 3 illustrates the global and segmental analysis of the evolution of LVEF during weaning in one COPD patient exhibiting no abnormality of regional LVEF suggestive of myocardial ischemia.

Myocardial ^{201}Tl imaging showed that 15 min after weaning the perfusion appeared to be homogenous in the

Table 1. Demographic characteristics – COPD patients ($n = 12$)

Patients no.	Age (years)	Sex	FEV_1 (l/s)	FVC (l)	FEV_1/FVC (%)	SBP (mmHg)	PaO_2 (mmHg)	$PaCO_2$ (mmHg)	pH	HCO_3^- (mmol/l)	Outcome
1	75	F	0.8	1.4	56	120	56	54	7.38	36	A
2	68	M	0.9	1.4	64	120	56	44	7.38	32	D
3	76	M	0.8	1.9	52	130	64	55	7.35	37	A
4	82	M	0.9	1.5	60	120	67	48	7.37	35	A
5	65	F	1.1	2.0	55	110	60	43	7.36	31	A
6	54	M	1.3	3.6	54	130	55	59	7.37	36	A
7	68	M	1.0	2.0	50	120	65	44	7.39	31	A
8	74	M	1.0	2.1	47	140	40	59	7.38	37	D
9	68	M	0.9	2.2	42	100	56	50	7.36	44	A
10	65	M	1.1	2.0	55	120	57	60	7.37	38	A
11	67	M	0.8	1.9	42	120	58	50	7.35	31	A
12	53	M	1.2	2.3	53	130	60	53	7.38	34	A
Mean	68		1.0	2.0	52	121	58	52	7.37	35	
SD	9.5		0.2	0.6	7	10	7	6	0.01	3.8	

SBP, Systolic blood pressure; A, alive; D, deceased

left ventricle anterior and posterior free wall. In each patient there was a Tl defect of the septum with a vertical aspect. There was no redistribution phenomenon in this myocardial perfusion defect of the interventricular septum three hours later with the patient submitted to MV. Similar results were observed with myocardial ^{201}Tl dipyridamole SPECT imaging performed eight days later after definitive weaning of the patients.

Discussion

Our study clearly indicates that weaning was associated with a significant decrease in LVEF in COPD patients without known CAD. Since there is no significant change in LVEDV (Table 2) -ie preload, -two hypothesis may be discussed to explain the decrease in LVEF: decrease in myocardial contractility and/or increase in left ventricle afterload. Myocardial ischemia is potentially the most important cause of reduced contractility during weaning [12]. Thus, myocardial ischemia might occur as a consequence either of a reduction in myocardial oxygen supply or of an increase in myocardial oxygen demand or both [12]. A reduced myocardial oxygen supply may result from weaning induced hypoxemia and tachycardia. Hypoxemia may be due to the worsening of ventilation perfusion ratio mismatching [13]. Tachycardia resulting from catecholamines release, as previously evidenced [3], may limit coronary blood flow by reducing the diastolic perfusion time [12]. An increase in myocardial oxygen demand may be related to the catecholamine release and to the increased work of breathing that elevates global oxygen needs, and hence cardiac work [12].

Since our study was conducted to evidence the possibility of a reduction in LVEF which was not related to the onset of myocardial ischemia we decided to exclude COPD patients with documented CAD. The absence of documented CAD in our patients was judged by the absence of specific clinical, electrocardiographic and echocardiographic abnormalities and by myocardial ^{201}Tl dipyridamole SPECT imaging performed 8 days later when definitive weaning was obtained. Despite the choice of this kind of patients the detection of a myocardial ischemia during weaning was addressed accurately by the radionuclide analysis of left ventricle regional wall motion and coronary perfusion. Our results clearly indicate that the reduction in LVEF affected homogeneously the left ventricle without alteration in regional LVEF suggestive of myocardial ischemia. This latter finding was confirmed by the absence of myocardial perfusion defects during weaning with myocardial ^{201}Tl SPECT imaging. Yet, in our COPD patients ^{99m}Tc and ^{201}Tl studies did not indicate segmental myocardial ischemia. Our results differ from the data previously reported by Hurford et al. [14]. In their study, among 13 patients with abnormal patterns of initial myocardial ^{201}Tl uptake observed during MV, 4 patients demonstrated new LV regional defects

Table 2. Effects of weaning on the hemodynamical parameters in COPD patients ($n = 12$)

		MV1	SV	MV2	IPS	MV3
LVEF	%	54.5 ± 12.4	47.0 ± 13.0**	55.0 ± 12.1	50.3 ± 12.4	54.9 ± 12.9
HR	bpm	85.4 ± 15.6	91.9 ± 1.33*	88.3 ± 14.3	88.0 ± 13.0	88.9 ± 14.3
LVEDV	ml/m^2	137 ± 34.6	144 ± 27.3	146 ± 53	149 ± 37.3	145 ± 48.7

MV1, MV2, MV3, mechanical ventilation; SV, spontaneous ventilation; IPS, inspiratory pressure support; LVEF, left ventricle ejection fraction; HR, heart rate; LVEDV, left ventricle end diastolic volume; M ± sd, two ways variance analysis – Scheffe test
**$p < 0.01$ SV versus MV1, MV2, MV3; *$p < 0.05$ SV versus MV1

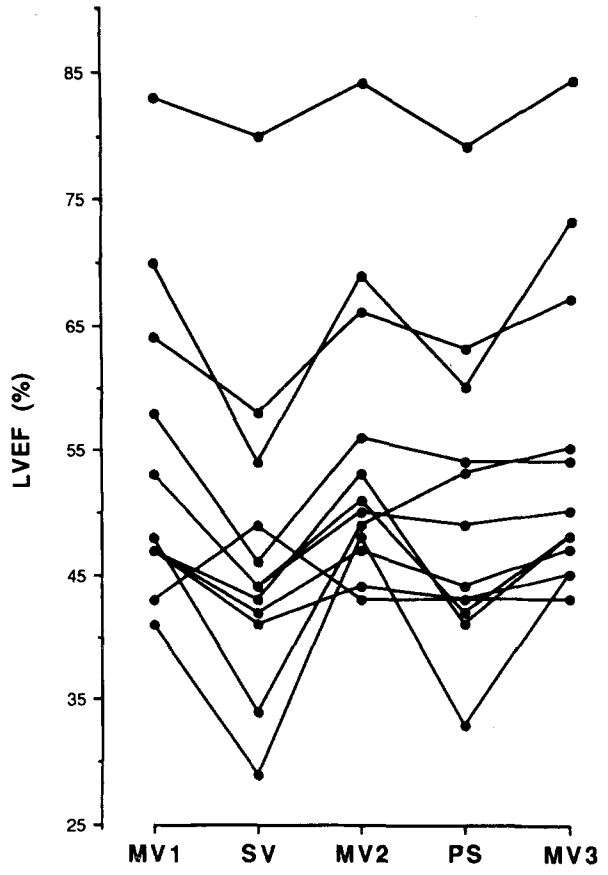


Fig. 1. Individual values of the evolution of left ventricle ejection fraction (*LVEF*) from mechanical ventilation (*MV1, MV2, MV3*) to spontaneous ventilation (*SV*) and inspiratory pressure support (*PS*) in the 12 COPD patients

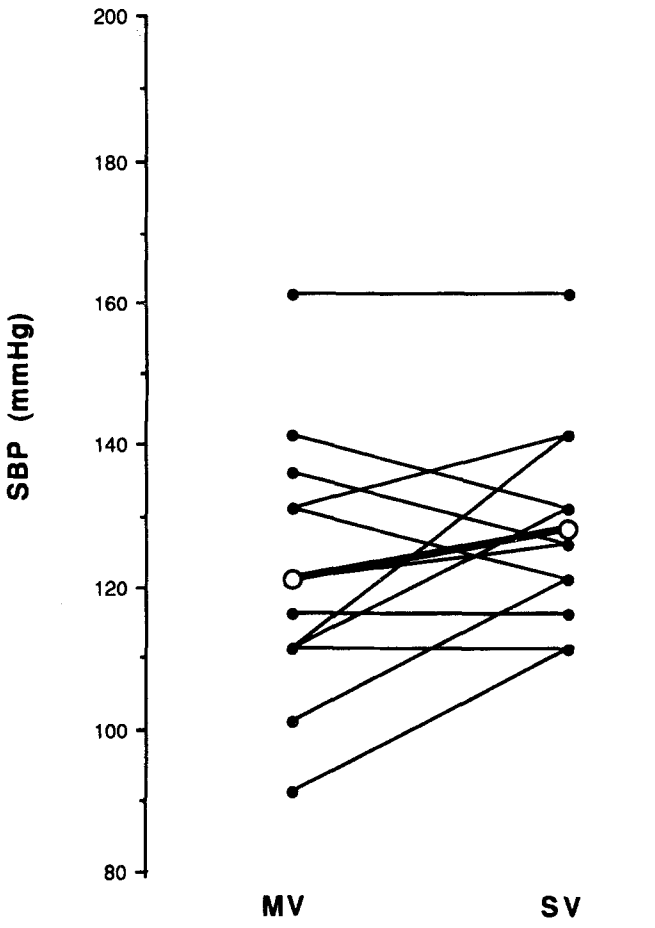


Fig. 2. Individual values of systolic blood pressure evolution (*SBP*) from mechanical ventilation (*MV*) to spontaneous ventilation (*SV*) in the 12 COPD patients

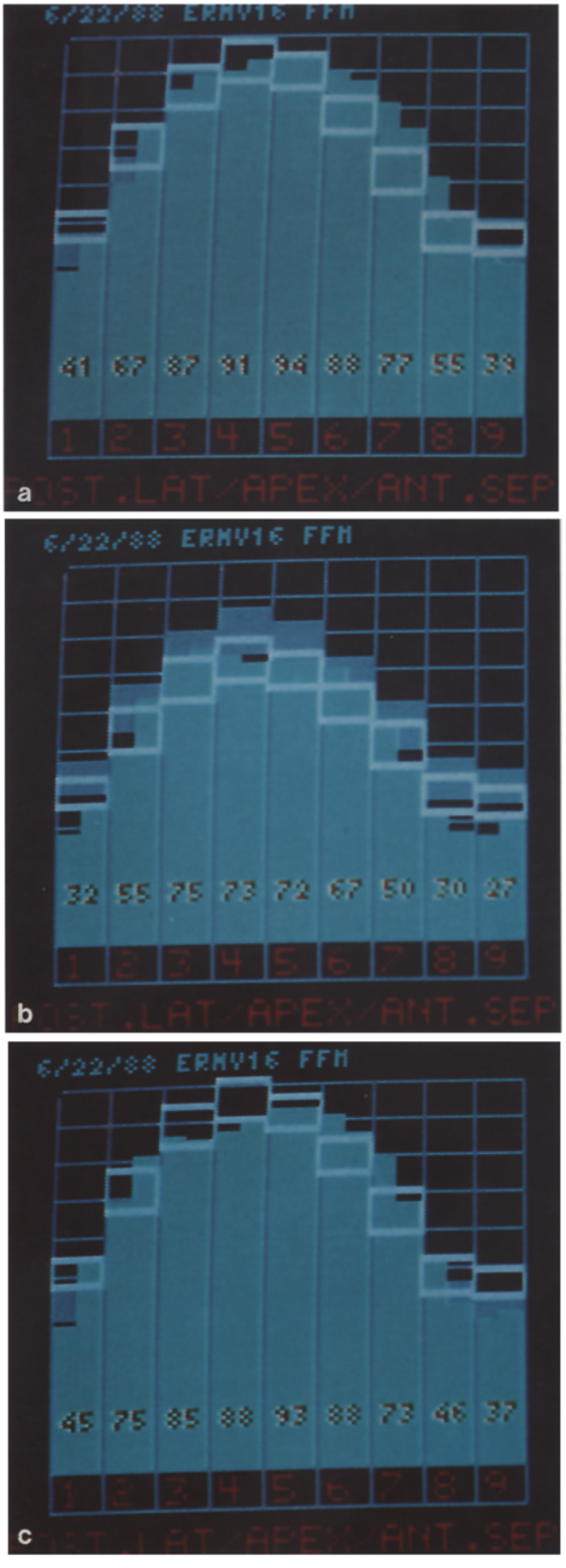
during SV with redistribution of the isotope of delayed images. Obviously the population of their study differed widely from ours in that they mainly studied patients with CAD authentified either by the clinical history (7/14) and/or by the presence of myocardial defects even during MV (13/14). In this connection, the incidence of weaning induced ischemia (4/14) could be considered as low for this particular population [14]. In the same way, Lemaire et al. found a relatively low incidence of weaning induced ischemic events to explain the onset of left ventricular dysfunction in 15 patients with COPD and preexisting heart disease [3].

In our study, it was not possible to exclude the onset of a diffuse myocardial ischemia not detected by isotopic methods. Such a diffuse myocardial ischemia could theoretically occur in the presence of equally diffuse coronary lesions.

Although we did not perform coronarography the absence of clinical history of CAD and ECG abnormality should rule out this hypothesis. On the other hand the possibility of a diffuse ischemia without coronary lesions resulting from a dramatical myocardial oxygen supply oxygen demand unbalance is quite speculative [15].

The ^{201}Tl septal defect observed in each patient during both MV and SV might suggest a biventricular interdependence phenomenon. In fact this was probably an artefact owing to the partial volume effect linked to the limited resolution of the tomographic acquisition system. This phenomenon may appear when the scintigraphic target is smaller than the spatial resolution of the system (about 15 mm) and/or when the target is far from the head of the camera, as it was the case in our study because the presence of the ventilator may prevent a correct access of the patient to the camera. Hurford et al. did not find these results probably because they used planar imaging [14].

Since the decrease in LVEF was not explained by a decreased myocardial contractility linked to myocardial ischemia the second hypothesis, i.e. increase in left ventricle afterload, may be briefly discussed. Left ventricle afterload can be defined as SBP minus intrathoracic pressure since SBP approximates intraluminal left ventricle pressure except in the presence of aortic outflow obstruction [6]. During weaning the increase in SBP and/or the sustained decrease in intrathoracic pressure may induce an increase in aortic transmural pressure and thus a fall in LVEF. Catecholamine release [3] related to emotional stress induced by disconnection from the ventilator and/or hypercapnia during SV, may elevate SBP [12]. Indeed, 5 out of the 12 studied patients exhibited an increase in SBP during weaning. However, for the whole



population SBP did not increase significantly, so that an increase in left ventricle afterload might be rather explained by a sustained decrease in intra thoracic pressure induced by weaning [16]. In fact the magnitude of the increase in left ventricle afterload during weaning should be linked to the magnitude of negative swings in intrathoracic pressure. In this way, several clinical studies reported that exaggerated negative swings in intrathoracic pressure related to spontaneous inspiration with upper airway obstruction may precipitate pulmonary oedema [17, 18]. In COPD patients exaggerated negative swings linked to airway obstruction seem likely since large negative distending pressures should be required to generate adequate tidal volume. Such a mechanism was likely during weaning of our patients although we have not measured oesophageal pressure and hence verified that the decrease in intrathoracic pressure actually occured. However the results observed during IPS might support our hypothesis. IPS is an intermediate mode of ventilation between MV und SV in terms of reduction of work of breathing [7]. Our results with IPS showing a slight but non significant decrease in LVEF were in accordance with the hypothesis of reduced negative swings and a slighter increase in left ventricle afterload with this mode.

In conclusion a decrease in LVEF during weaning was systematically observed in our COPD patients without associated CAD and was not explained by a decrease in myocardial contractility linked to myocardial ischemia. The role of increased left ventricle afterload is hypothesized and must be examined by further studies. These results also clearly indicate the need for the assessement of an occult left ventricle dysfunction before weaning of COPD patients.

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Fig. 3a–c. Global and sectorial evolution of left ventricle ejection fraction (*LVEF*) in one COPD patient during weaning. **a** Mechanical ventilation (*MV*), global LVEF: 70%. **b** Spontaneous ventilation (*SV*), global LVEF 55%. **c** MV, global LVEF 72%. LVEF was divided in 9 sectors: posterior (*post*), lateral (*lat*), apex anterior (*ant*), septal (*sep*). *Blue columns* represent COPD patient data for each sector with the value of sectorial LVEF (%). *Two tone of blue* are used: *light blue* refers to the values of sectorial left ventricle ejection fraction of this COPD patient. *Dark blue* refers to the previously reported normal mean values [10]. *White box* enclosures at the top of the figures refer to the analysis of the homogeneity of sectorial contractility [10]

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