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Isolated Ultrafiltration in Moderate Congestive Heart Failure

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Objectives. **The aim of this study was to evaluate whether ultrafiltration is beneficial in patients with moderate congestive heart failure.**

Background. **Ultrafiltration is beneficial in patients with severe congestive heart failure.**

Methods. **We studied 36 patients in New York Heart Association functional classes II and III in stable clinical condition. Eighteen patients (group A) were randomly selected and underwent a single session of ultrafiltration (venovenous bypass, mean [± SEM] ultrafiltrate 1,880 ± 174 ml, ~600 ml/h) and 18 (group B) served as control subjects.**

Results. **Two patients in group A and three in group B did not complete the 6-month follow-up study. In group A, soon after ultrafiltration there were significant reductions in right atrial pressure (from 8 ± 1 to 3.4 ± 0.7 mm Hg, pulmonary wedge pressure (from 18 ± 2.5 to 10 ± 1.9 mm Hg) and cardiac index (from 2.8 ± 0.2 to 2.3 ± 0.2 liters/min). During the follow-up period, lung function improved, extravascular lung water (X-ray score) decreased and peak oxygen consumption (ml/min per kg) increased significantly from 15.5 ± 1 (day −1) to 17.6 ± 0.9 (day 4), to 17.8 ± 0.9 (day 30), to 18.9 ± 1 (day 90) and to 19.1 ± 1 (day 180). Oxygen consumption at anaerobic threshold (ml/min per kg) also increased significantly from 11.6 ± 0.8 (day −1) to 13 ± 0.7 (day 4), to 13.7 ± 0.5 (day 30), to 15.5 ± 0.8 (day 90) and to 15.2 ± 0.8 (day 180). These changes were associated with increased ventilation, tidal volume and dead space/tidal volume ratio at peak exercise. The improvement in exercise performance was associated with a decrease in norepinephrine at rest, a downward shift of norepinephrine kinetics at submaximal exercise and an increase in norepinephrine during orthostatic tilt. None of these changes were recorded in group B.**

Conclusions. **In patients with moderate congestive heart failure, ultrafiltration reduces the severity of the syndrome.**

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In patients with advanced congestive heart failure, ultrafiltration improves the clinical condition, mitigates the neurohumoral reaction, increases urinary output and promotes absorption of excessive extravascular fluid (1–6). At the level of the lungs, this latter effect facilitates oxygen diffusion and increases arterial oxygen content, decreases pulmonary shunt and attenuates lung stiffness, respiratory muscle work, right ventricular afterload and work performed by the heart against the cardiac fossa (that is, the cavity delimited by the lungs, chest wall and diaphragm and in which the heart is nestled) (3,6–9). Excessive accumulation of fluids in the extravascular space of the lung may also be present in patients with a less advanced stage of congestive heart failure, even if they receive optimized diuretic drug therapy and do not present with peripheral edema (10). The present study was undertaken to investigate whether ultrafiltration may also be beneficial in this category of patients (New York Heart Association functional classes II and III). The effects of the procedure were assessed by repeated thoracic X-ray studies, echocardiography, pulmonary function tests and cardiopulmonary exercise tests. We also measured norepinephrine plasma levels at rest, during orthostatic tilt and exercise and before and after ultrafiltration because these measurements are indexes of the severity of heart failure (11–15) and their changes may reflect the efficacy of treatment (16–19).

Methods

Patient characteristics (Table 1). Thirty-six patients with moderate congestive heart failure, subjected to regular follow-up in our Heart Failure Clinic, participated in the study. They were in a stable clinical condition and received drug treatment (Table 1) optimized to prevent the development of peripheral edema and maintain a stable body weight (±1 kg in the previous 6 months), urinary output ≥1,500 ml/day and plasma electrolyte concentration within the normal range. Clinical condition and drug treatment in the previous 6 months were stable in all cases, and digoxin plasma levels in patients receiving digoxin were in a therapeutic range. Patients with recent myocardial infarction (<1 year), angina

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Table 1. Clinical Characteristics of the 36 Study Patients

Pt No.	Age (yr)/ Gender	DCMP	Digoxin (mg/day)	Furosemide (mg/day)	ACEinh (mg/day)	Other Medication
			Group A (with ultrafiltration)			
1	63/M	IHD	0.25	50	—	Am, Sp
2	52/M	PDC	0.20	100	C 75	—
3	67/M	IHD	0.25	75	—	Nit
4	57/M	Alc	0.25	50	E 10	—
5	69/M	IHD	0.20	125	—	Am, Nit
6	49/M	IHD	0.25	75	C 50	—
7	55/M	Alc	0.25	50	E 5	Sp
8	60/F	IHD	—	75	C 50	—
9	50/F	IHD	—	125	—	Sp
10	58/M	Alc	0.25	50	—	—
11	61/M	PDC	—	25	E 10	Nit
12	59/M	PDC	0.20	25	—	Nit
13	56/M	PDC	0.20	50	—	—
14	50/M	PDC	0.25	50	C 75	—
15	55/M	PDC	0.25	125	E 2.5	Sp
16	52/M	PDC	—	25	—	—
17	62/M	PDC	0.25	75	—	Am
18	65/M	PDC	0.25	50	—	Sp
			Group B (control group without ultrafiltration)			
1	60/M	IHD	0.20	50	—	—
2	71/F	PDC	0.25	125	E 10	Am
3	52/M	IHD	0.25	25	E 10	—
4	57/M	PDC	0.25	25	—	Nit
5	59/M	Alc	0.25	75	C 75	Nit
6	64/M	Alc	0.25	125	—	Am, Sp
7	61/M	IHD	0.20	25	—	Sp
8	66/F	PDC	0.25	25	—	—
9	74/M	IHD	0.20	50	E 10	—
10	50/M	PDC	—	25	E 20	Am
11	52/F	PDC	0.25	75	C 50	—
12	56/M	PDC	0.25	50	—	—
13	52/F	PDC	0.20	50	—	Sp
14	58/M	IHD	0.25	50	—	Nit
15	63/M	PDC	0.20	100	C 50	Am, Nit
16	66/M	PDC	0.25	25	E 10	—
17	51/M	PDC	0.25	250	C 75	Am
18	53/M	PDC	0.20	50	C 50	Nit

ACEinh = angiotensin-converting enzyme inhibitors; Alc = alcoholic; Am = amiodarone; C = captopril; DCMP = dilated cardiomyopathy etiology; E = enalapril; F = female; IHD = ischemic heart disease; M = male; Nit = nitrates; PDC = primary dilated cardiomyopathy; Pt = patient; Sp = spironolactone.

pectoris, primary valvular heart disease, intermittent claudication, fibrotic or primary vascular lung diseases, sinus or atrioventricular node dysfunction, effort-induced severe ventricular arrhythmias or an artificial pacemaker were excluded. The study protocol was approved by the local Ethics Committee. All patients gave informed written consent after receiving detailed information concerning the procedures, possible clinical benefits and investigative purposes. They were randomly divided into groups A and B, each consisting of 18 patients. Ultrafiltration was performed in group A; subjects in group B served as the control group.

Ultrafiltration. In each patient in group A, a single ultrafiltration procedure was performed during temporary admission to the intensive care unit. A 7F triple-lumen thermodilution Swan-Ganz catheter was percutaneously introduced into an antecubital or jugular vein and advanced to the pulmonary artery or wedge position when necessary. Stable hemodynamic conditions were achieved within 30 min after completion of the invasive procedures. Ultrafiltration methods have been previously described in detail (3). In brief, a D20SF Amicon diafilter, which allows subtraction of water and solutes of <50,000 daltons from blood, was inserted into a venovenous bypass circuit (double-lumen Y-shaped catheter in a femoral vein). Blood was propelled through the diafilter by a Gambro System peristaltic pump AK10 (model BMM 10-1K) regulated to generate 600 ml/h of ultrafiltrate. During ultrafiltration, we continuously monitored right atrial and pulmonary artery pressures. Ultrafiltration was contin-

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ued until right atrial pressure, measured at end-expiration, decreased by 50% of the baseline value. In group B patients, the hemodynamic evaluation, but not ultrafiltration, was performed. The day of the hemodynamic evaluation with (group A) and without (group B) ultrafiltration was considered day 0 of the study protocol.

Pulmonary and cardiac evaluations. We utilized a chest X-ray scoring approach for extravascular lung water determination (20); pulmonary function tests included a bronchodilator response evaluation (salbutamol inhalation). Maximal voluntary ventilation was assessed as the greater of that measured (60 to 70 breaths/min for 15 s) and that predicted from forced expiratory volume (1 s) × 40 (21). The prediction equation of Morris et al. (22) was used to determine forced expiratory volume. Cardiac dimensions were measured by echocardiography (model 77020/A, Hewlett-Packard). Ejection fraction was calculated by the formula of Teichholz et al. (23). The values reported are the mean of 3 consecutive beats (the mean of 10 beats was utilized when atrial fibrillation occurred). Physical performance was evaluated through cardiopulmonary exercise tests that were performed in the upright position, on a cycloergometer (Collins Pedalmate), with 30 s of unloaded pedaling, followed by 25-W increments every 3 min until the appearance of limiting dyspnea or fatigue. Expiratory gases were collected on a breath by breath basis (MMC 4400, Sensor Medics). All patients were previously trained to perform the exercise test in our laboratory. Anaerobic threshold and peak oxygen consumption were determined according to standard methods (24). Oxygen consumption at anaerobic threshold and peak exercise are expressed as oxygen consumption (ml/min per kg) during the 30 s in which an examined event occurred. Oxygen consumption values at each work load are the average of measurements obtained in the 30 s immediately preceding each increase in work load. The reported maximal ventilation, tidal volume and dead space/tidal volume ratio at peak exercise were averaged over 30 s. The dead space/tidal volume ratio was derived according to the method of Jones (25). We also utilized the prediction equation of that investigation (25) to determine maximal ventilation and dead space/tidal volume ratio at peak exercise. Oxygen pulse at peak exercise was calculated as peak oxygen consumption/peak heart rate.

Protocol. All patients were subjected to the same procedures, except that ultrafiltration was performed only in group A. Patients were hospitalized during a run-in (7-day) period and the first 4 days of the follow-up evaluation. The run-in period was utilized to confirm that the patient was in a stable clinical condition. Patients were followed-up for 6 months and the drug regimen was kept constant during this period. Cardiopulmonary exercise tests were performed at 10 AM on days −1, 4, 30, 90 and 180. Chest X-ray films, pulmonary function tests and echocardiograms were obtained at the same periods. Results for each patient were analyzed at the end of the follow-up period during the same session by three independent experts who had no knowledge of the study protocol (26).

Plasma norepinephrine evaluations. Circulating norepinephrine was measured by high performance liquid chromatography (27). Baseline determinations were made on blood samples obtained 30 min after introduction of a catheter (18G) into an antecubital or forearm vein with the patient in the supine position. We also evaluated norepinephrine kinetics during exercise and orthostatic tilt. Blood was withdrawn at rest (with the patient upright after a mouthpiece had been in position for ≥3 min), immediately before each work load increment and at peak exercise. During the orthostatic tilt test, blood samples were obtained after 20 min of rest with the patient supine and after a 10-min 60° head-up tilt. The orthostatic tilt test was performed in both groups at days −1, 4 and 90.

Statistical analysis. Data are reported as mean values ± SEM. Data were analyzed by two-way analysis of variance and differences from measurements done at day −1 versus days 4, 30, 90 and 180 were evaluated by paired Student *t* test, applying the Bonferroni method because multiple comparisons were made (28). Norepinephrine responses to orthostatic tilt were assessed as a percent, using supine measurements as the baseline values. The immediate effects of ultrafiltration on hemodynamic variables were analyzed by paired *t* test. We utilized the SPSS/PC+ Advanced Statistics V2.0 program.

Results

According to the criteria of the New York Heart Association, 5 and 13 patients in group A and 6 and 12 in group B were in functional classes II and III, respectively. According to the heart failure severity ranking proposed by Weber et al. (29), among patients in group A, 3 were in functional class A (maximal oxygen consumption >20 ml/min per kg), 4 in class B (>16 to 20 ml/min per kg), 10 in class C (10 to 16 ml/min per kg) and 1 in class D (<10 ml/min per kg); among those in group B, 4, 4 and 10 were in class A, B and C, respectively. There were six cases (two in group A and four in group B) of chronic atrial fibrillation. Left ventricular ejection fraction averaged 23.8 ± 2.1% in group A and 24.1 ± 1.8% in group B at day −1 (Table 2). The two groups were also homogeneous regarding baseline cardiac index and right atrial and pulmonary wedge pressure. The volume of ultrafiltrate averaged 1,884 ± 174 ml (duration of ultrafiltration 188 ± 8 min). No side effects or symptoms were reported during the procedure. At the end of the procedure, rest mean right atrial pressure, mean pulmonary wedge pressure and cardiac index were reduced from 8 ± 1 to 3.4 ± 0.7 mm Hg ($p < 0.001$), from 18 ± 2.5 to 10 ± 1.9 mm Hg ($p < 0.001$) and from 2.8 ± 0.2 to 2.3 ± 0.2 liters/min per m^2 ($p < 0.01$), respectively; mean blood pressure was unchanged (from 85.5 ± 2.5 to 83.5 ± 3.1 mm Hg) and total peripheral resistance increased (from 1,221 ± 45 to 1,632 ± 119 dynes·s·cm^{-5}, $p < 0.01$). In group B, right atrial pres-

Table 2. X-ray and Ultrasound Measurements

	Day −1	Day 4	Day 30	Day 90	Day 180
Group A					
EVLW	15.2 ± 2.2	8.1 ± 1.0*	8.3 ± 1.1*	8.5 ± 1.3*	9.0 ± 1.4*
LVDD (mm)	74.0 ± 1.4	72.4 ± 1.1†	72.3 ± 1.6†	73.1 ± 1.6	73.5 ± 1.7
EF (%)	23.8 ± 2.1	24.0 ± 1.4	25.6 ± 1.4	24.2 ± 1.2	25.0 ± 1.5
Group B					
EVLW	14.8 ± 2.4	15.1 ± 2.3	15.5 ± 2.1	14.9 ± 2.0	15.4 ± 2.1
LVDD (mm)	73.4 ± 2.0	75.0 ± 1.9	74.1 ± 2.6	74.6 ± 2.2	74.8 ± 2.2
EF (%)	24.1 ± 1.8	23.9 ± 2.1	23.6 ± 2.1	23.9 ± 2.3	24.0 ± 2.5

*$p < 0.01$, †$p < 0.02$ versus day −1. Data are reported as mean value ± SEM. EF = ejection fraction; EVLW = extravascular lung water determined by chest X-ray score; Groups A and B as in Table 1; LVDD = left ventricular diastolic diameter.

sure, mean pulmonary wedge pressure and cardiac index at rest were 7.7 ± 1.1 mm Hg, 18.1 ± 2.8 mm Hg and 2.9 ± 0.3 liters/min per m^2, respectively (p = NS vs. group A). Two patients in group A (one in class D and one in class C) and three in group B (two in class B and one in class C) did not complete the 6-month follow-up study. In these patients, symptoms of heart failure worsened within 1 to 3 months after the run-in period; one patient in group B was lost to follow-up evaluation.

Effects on lungs, heart and physical performance (Table 3). In group A, X-ray signs related to extravascular lung water accumulation (20) were diminished at day 4 and remained so during the next 6 months. No response to bronchodilators was documented in any patient; an improvement in lung function was invariably observed, both at baseline study and after bronchodilator inhalation in patients subjected to ultrafiltration. In the same group, a small but significant reduction in left ventricular diastolic diameter occurred after the procedure, persisted during the subsequent 30 days and was not associated with significant changes in ejection fraction (Table 2). In both groups, rest and peak exercise systemic blood pressure was unchanged during the follow-up period (Table 4). There was an improvement in exercise performance, as suggested by the increase in exercise tolerance, time to anaerobic threshold, peak oxygen consumption, oxygen consumption at anaerobic threshold, maximal ventilation and tidal volume and reduced peak exercise dead space/tidal volume ratio; oxygen pulse was unchanged (Fig. 1). These changes were present on day 4 and persisted for 6 months in 16 of the 18 patients. In the two patients whose clinical condition deteriorated during the follow-up period, oxygen consumption from day −1 to day 4 increased from 7.3 to 9.9 ml/min per kg and from 14.4 to 17.3 ml/min per kg, respectively. In the group B control patients, none of the changes just reported in group A patients occurred during the 6-month follow-up period.

Influences on plasma norepinephrine. Ultrafiltration reduced norepinephrine at rest and shifted the relation of norepinephrine to oxygen consumption during exercise downward (Table 4, Fig. 2). Peak exercise norepinephrine plasma levels were similar and within the normal range (13) during all tests; however, peak oxygen consumption was increased after ultrafiltration. In patients in group B, norepinephrine at rest was unchanged and increased during exercise to a similar extent each time (Table 4, Fig. 2). Norepinephrine response to orthostatic tilt was attenuated in all

Table 3. Pulmonary Function Test Results

	VC (liters)		MVV (liters/min)		FEV_1 (% predicted)	
	Baseline	Salbutamol	Baseline	Salbutamol	Baseline	Salbutamol
Group A						
Day −1	3.5 ± 0.1	3.6 ± 0.1	110 ± 4	111 ± 4	83 ± 6	85 ± 7
Day 4	3.9 ± 0.1*	3.9 ± 0.1*	127 ± 7*	133 ± 6*	92 ± 6*	94 ± 6*
Day 30	3.8 ± 0.1*	3.9 ± 0.1*	130 ± 6*	131 ± 5*	93 ± 5*	95 ± 6*
Day 90	3.9 ± 0.2*	4.0 ± 0.2*	128 ± 8*	130 ± 6*	95 ± 5*	96 ± 5*
Day 180	3.9 ± 0.1*	3.9 ± 0.2*	128 ± 9*	129 ± 7*	95 ± 7*	97 ± 7*
Group B						
Day −1	3.5 ± 0.1	3.6 ± 0.1	111 ± 4	113 ± 6	85 ± 7	87 ± 9
Day 4	3.4 ± 0.1	3.6 ± 0.1	112 ± 5	113 ± 6	83 ± 6	86 ± 8
Day 30	3.5 ± 0.1	3.5 ± 0.1	113 ± 6	115 ± 7	83 ± 7	85 ± 6
Day 90	3.5 ± 0.1	3.5 ± 0.1	111 ± 5	116 ± 7	84 ± 7	86 ± 8
Day 180	3.4 ± 0.1	3.5 ± 0.2	112 ± 5	116 ± 8	83 ± 5	84 ± 9

*$p < 0.01$ versus day −1. Differences between measurements obtained at baseline and after salbutamol inhalation were never significant. Data are reported as mean value ± SEM. FEV_1 = forced expiratory volume (1 s); Groups A and B as in Table 1; MVV = maximal voluntary ventilation; VC = vital capacity.

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Table 4. Norepinephrine Plasma Levels and Mean Blood Pressure Data

	Norepinephrine	Mean Blood Pressure	
	Supine (pg/ml)	Rest (mm Hg)	Peak Exercise (mm Hg)
Group A			
Day −1	680 ± 170	97 ± 3	111 ± 2
Day 4	562 ± 103*	93 ± 3	111 ± 3
Day 30	474 ± 85*	91 ± 2	109 ± 3
Day 90	421 ± 99*	92 ± 2	112 ± 4
Day 180	528 ± 97*	91 ± 2	103 ± 3
Group B			
Day −1	660 ± 155	98 ± 3	111 ± 4
Day 4	640 ± 178	96 ± 3	112 ± 5
Day 30	658 ± 179	97 ± 2	113 ± 6
Day 90	702 ± 180	95 ± 3	111 ± 5
Day 180	713 ± 176	98 ± 2	112 ± 5

*$p < 0.01$ versus day −1. Data are reported as mean value ± SEM. Groups A and B as defined in Table 1.

patients and became greater on days 4 and 90 only in patients subjected to ultrafiltration (Fig. 3); in fact, the percent increase during orthostatic tilt at days −1, 4 and 90 was 26.3 ± 2.9%, 37.4 ± 4.7% ($p < 0.01$ vs. day −1) and 45.8 ± 4.5% ($p < 0.01$ vs. day −1) in group A and 25.3 ± 3.1%, 27.2 ± 3.1% and 24 ± 3.3% (p = NS vs. day −1) in group B.

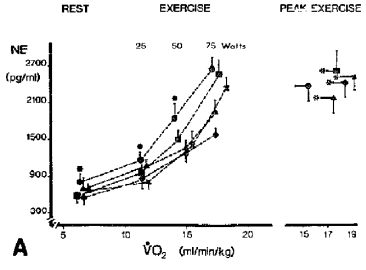
Figure 1. Cardiopulmonary exercise test results. *$p < 0.001$ versus day −1. Data are reported as mean value± SEM. A, Peak VO2 = oxygen consumption at peak exercise; Time A.T. = time to anaerobic threshold; Tolerance Time = exercise tolerance time; VO2 A.T. = oxygen consumption at anaerobic threshold; ● = group A; ■ = group B. B, O2 Pulse = oxygen pulse at peak exercise; VD/VT = dead space/tidal volume ratio at peak exercise (percent of predicted value); VE max = maximal ventilation (percent of predicted value); VT max = maximal tidal volume.

Discussion

This study shows that subtraction of approximately 600 ml/h of water from plasma to obtain a 50% decrease in right atrial pressure in patients with moderate congestive heart failure persistently reduces extravascular lung fluid, improves lung function and exercise performance and modifies norepinephrine plasma levels at rest and norepinephrine kinetics in a way consistent with a diminished severity of the syndrome.

Hemodynamic effects of ultrafiltration. Ultrafiltration lowered cardiac output and ventricular filling pressures, possibly as a consequence of reduced intravascular volume. Hypovolemia, however, was presumably counteracted by extravascular fluid reabsorption through oncotic mechanisms (30) and, at the level of the lung, by a reduction in right atrial and pulmonary venous pressure (31–34). It is documented that right atrial pressure influences both lung lymph flow (31) and bronchial vein flow (32,33) and pulmonary venous pressure affects the bronchial drainage into the pulmonary circulation (34). The significant decrease in lung congestion after ultrafiltration and the increase in vital capacity (Table 3), which is another indicator of the intrathoracic fluid content (35), are consistent with these interpretations.

Effects of ultrafiltration on pulmonary function. Pulmonary function is likely to become altered in congestive heart failure (36) and the lack of response to bronchodilator inhalation suggests that the functional level is stable. The relation between left atrial pressure and small airway resistance has been interpreted as caused by the influence of atrial pressure on the water content of the lung (37,38). Therefore, the improved pulmonary function after ultrafiltration seems to be attributable to a reduction in the excessive lung water, allowing decompression of the small airways (38). The ameliorated respiratory function after



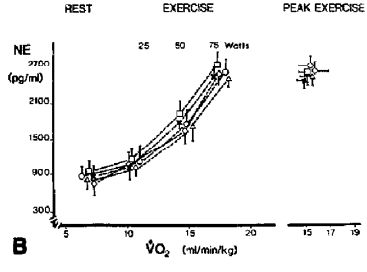


Figure 2. Norepinephrine (NE) plasma levels at rest (upright position, mouthpiece positioned for ≥3 min) and during peak exercise. Norepinephrine values during exercise are plotted versus oxygen consumption ($\dot{V}O_2$). Data are reported as mean value ± SEM. In group A (A) but not in group B (B), all norepinephrine values at rest (upright position) and submaximal exercise (25 and 50 W) were lower at day 4, 30, 90 and 180 vs. day −1 (* $p < 0.01$). *$p < 0.001$ versus day −1. A, Group A: ● = day −1, ▲ = day 4, ■ = day 30, ◆ = day 90, x = day 180. B, Group B: ○ = day −1, △ = day 4, □ = day 30, ◇ = day 90, x = day 180.

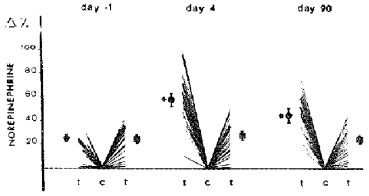


Figure 3. Percent change (Δ%) in norepinephrine during 10 min of orthostatic tilt (t) in group A (left of supine control [c]) and group B (right of supine control). ● and ◆ are mean values ± SEM in group A and B, respectively. *$p < 0.01$ versus day −1.

ultrafiltration might be particularly important during exercise when heart-lung interdependence is increased (39).

Effects of ultrafiltration on exercise performance. For an appropriate assessment with cardiopulmonary exercise testing (24,25,40) of the physical performance of patients with congestive heart failure, familiarization with the test is mandatory (41) and the effects of training should be taken into account. In our study, the majority of patients had multiple previous experiences with the cardiopulmonary exercise test, the drug regimen was kept constant and all tests were performed at 10 AM, so that the temporal relation between exercise and drug administration was uniform. In addition, a training effect was not observed in the control patients. It is also unlikely that motivation to perform exercise had an influence on our results because oxygen consumption at peak exercise and the anaerobic threshold varied similarly, even though only peak exercise measurements may be affected by the patient's motivation. The clinical condition of two subjects in group A who showed severely compromised exercise capacity at day −1 (one in class D and one in class C) worsened during the follow-up period. The improved performance observed at day 4 may suggest that these patients possibly needed repeated ultrafiltration as do patients with more advanced congestive heart failure (42). In the remaining 16 subjects, the procedure persistently augmented oxygen consumption at peak exercise and the anaerobic threshold, prolonged exercise tolerance time and time to anaerobic threshold, increased maximal ventilation and tidal volume and reduced peak exercise dead space/tidal volume ratio (Fig. 1 and 2). All these observations are consistent with improved exercise performance and suggest that at peak exercise, more lung parenchyma participated in gas exchange.

Possible mechanisms of beneficial effects of ultrafiltration. Ultrafiltration did not modify the pump function of the heart, as reflected by the left ventricular ejection fraction at rest (Table 2) and peak exercise oxygen pulse obtained after the procedure (Fig. 1). Changes in thoracic X-ray findings, pulmonary function tests, maximal ventilation and tidal volume and tidal volume/dead space ratio during peak exercise at day 4 suggest that one of the mechanisms through which subtraction of body fluid by ultrafiltration improves physical performance might be an influence on the structures around the heart, such as the cardiac fossa, lung and pulmonary vasculature (8,39). The long duration of benefits from ultrafiltration on physical performance, lung water and pulmonary function was unexpected. For various reasons, we were only able to repeat the measurement of catheter-derived variables in a limited number of patients, so that it is uncertain whether the reduction in right atrial and pulmonary wedge pressures was persistently associated with the described amelioration. Ultrafiltration might also have lowered the impedance to skeletal muscle flow (43) and improved perfusion (44) through a reduction in the water

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content of the muscles and vessel walls. However, in our patients, this seems an unlikely effect because no patient had peripheral edema and blood pressure at rest and during peak exercise did not change during the follow-up period. The interpretation that the lung was kept dry by diminished pressure in the right atrium and pulmonary veins after the procedure (allowing effective lung fluid drainage) appears more reasonable (31–34).

An analysis of daily physical activity of the subjects during the 6-month study period was not performed in the present study, but no patient was involved in a training program. However, the tendency toward a progressive increase in exercise capacity after ultrafiltration (group A) might be related to a training effect made possible by the improved physical performance observed shortly after the procedure. Ultrafiltration seems to have reversed a condition characterized by elevated right atrial and pulmonary venous pressures and increased lung water and stiffness, which in turn augmented respiratory muscle work, right ventricular afterload and the work of the heart against the cardiac fossa. Diuretic drugs in doses that prevented fluid retention were apparently unable to produce the same effects.

Effects of ultrafiltration on norepinephrine levels. In patients with congestive heart failure, circulating norepinephrine at rest is generally increased (11,12), its increase during orthostatic tilt is blunted (14,15) and, during exercise, for a given oxygen consumption, it reaches levels higher than those in normal subjects (13). Plasma levels at rest, during orthostatic tilt and at submaximal exercise are viewed as indexes of the severity of the disease (11–15). Ultrafiltration reduced norepinephrine at rest and during submaximal work loads and shifted the response to orthostatic tilt toward a more favorable pattern. Changes like these have been considered to reflect an ameliorated clinical condition (16–19) and in our study were associated with increased exercise performance.

Conclusions. Subtraction of body fluid by ultrafiltration persistently ameliorates the clinical condition of patients with moderate congestive heart failure. This effect seems to be mainly related to changes taking place within the chest.

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