CHANGES IN FUNCTIONAL RESIDUAL CAPACITY DURING RESPIRATORY FAILURE

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ACCURATE RESPIRATORY FAILURE is frequently characterized by an enlarged alveolar-arterial oxygen difference ($AaDo_2$) as a result of the perfusion of non-ventilated alveoli[1–3] through accumulation of secretions, inflammatory consolidation, oedema, or atelectasis. Therapy is, in part, aimed at restoring ventilation of these areas by manoeuvres such as intermittent positive pressure ventilation with large tidal volumes, chest physiotherapy, and tracheobronchial toilet.

The alveolar-arterial oxygen difference is, however, a non-linear function and is influenced by many factors other than the number of non-ventilating alveoli. A completely reliable estimate of the latter is not available, although changes in pulmonary compliance have been shown experimentally to be a sensitive test.[4,5] However, the need to pass an oesophageal balloon precludes the use of this measurement on a day-to-day basis, and consequently consideration has been given to the usefulness of lung volume measurements.[6]

This study was designed to determine the magnitude of the functional residual capacity (FRC) in patients with respiratory failure, and to define the relationship of this variable to $AaDo_2$. Further, since recumbency[7–9] and oxygen breathing may themselves cause a reduction in FRC and contribute to the results obtained, a study was designed to examine the effects of these factors in normal adults.

METHODS

The FRC was measured by a helium dilution method employing a catharometer and a spirometer.[10–13] A self-inflating bag and a suitable valving system[13] were employed in the circuit during controlled ventilation. Corrections were made for errors arising from starting at a point other than end-expiration and from the changes in the oxygen concentration used during the measurement on the catharometer reading. In intubated or tracheostomized patients a volume equal in millilitres to a third of the body weight in pounds was added to the measured FRC. The volumes were corrected to BTPS. In each instance, measurements were made in duplicate, and mean values are quoted. The mean difference between duplicate values was 110 ml (S.D. $\pm$ 73).

A gas-tight two-way tap, with a 15 ml dead space, was designed to permit easy connection of the patient to the FRC apparatus during both spontaneous and controlled ventilation. By monitoring the airway pressure it was possible to connect the patient to the spirometer at any desired pressure. This facilitated measure-

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ment of FRC during the application of the negative phase or a positive pressure hold at the end of expiration.

Arterial blood was analysed for pH, P_{CO_2} and P_{O_2} at 37° C, using an Instrumentation Laboratory pH/gas analyser. Inspired oxygen concentration was analysed on a Beckman model E2 oxygen analyser, whose accuracy had been checked with Scholandered gas mixtures.

In spontaneously breathing subjects on 100 per cent inspired oxygen, the inspired oxygen tension ($P_{I_{O_2}}$) was considered to be the same as the dry barometric pressure. During controlled ventilation, the inspired gas was sampled when the ventilator dials were set to deliver 100 per cent oxygen. The inspired oxygen tension was determined from this concentration and the dry barometric pressure. The alveolar oxygen tension was calculated assuming a gas exchange ratio of 1:1.

FRC and $A_aD_{O_2}$ *during respiratory failure*

Measurements were made in 12 patients in the supine position and were repeated at intervals during the period of respiratory failure. The initial spirometer oxygen concentration was adjusted to approximate that of the patient's inspired air immediately before the start of each measurement. A sample of arterial blood was withdrawn and the FRC was measured, first after twenty minutes of ventilation at the clinically indicated oxygen concentration (CIOC) and then at 100 per cent oxygen. The CIOC is the actual oxygen concentration which the patient had been receiving prior to the study. This is not accurately measured in patients on pressure constant ventilators[14] or when the inspired air is supplemented with oxygen during spontaneous ventilation, as when using an Edinburgh mask. In all such cases measurements at the CIOI were omitted.

In the two patients with emphysema and respiratory failure, the approximate CIOC was determined by using a mixing chamber for inspired gas. The Edinburgh mask which was used to supplement the inspired air with oxygen was positioned at the distal end of the mixing chamber. The gas was mixed in the chamber and delivered to the patient through a Hans-Rudolph valve. Determinations of FRC were made of these approximate inspired oxygen concentrations.

Measurements of FRC *in normal subjects*

The following studies were carried out in normal volunteers who did not have a history of cardio-pulmonary disease.

(*a*) Effect of changing from sitting to supine position.

(*b*) Effect of several hours of recumbency. FRC was first measured in the sitting position. Measurements were repeated immediately after assuming the recumbent position and then at hourly intervals for four hours.

(*c*) Effect of breathing air, 50 per cent oxygen, 75 per cent oxygen, and 100 per cent oxygen for twenty minutes in the supine position. The subjects were asked to sit up and take five breaths to total lung capacity (TLC) before each change in inspired gas mixture.

In order to establish a basis for comparison, each study (*a, b, c*) was preceded by having the subject take five breaths to TLC and then exhale to FRC.

Results

The results are presented in Tables I to V and Figures 1 to 3.

FRC *in normal subjects*

A large fall in FRC was observed on the subjects assuming the recumbent position (Table III). Subjects recumbent for up to four hours did not demonstrate any further fall during this period (Table IV).

Oxygen breathing caused a reduction in FRC in supine subjects (Table V). This was not usually large, and was not observed when the inspired gas mixture contained 50 per cent or 75 per cent oxygen.

TABLE I

DIAGNOSES OF PATIENTS INCLUDED IN RESPIRATORY FAILURE SERIES

No.	Age	Sex	Diagnosis
1	72	M	head injury; burr holes for subdural haematoma; G.I. bleeding; aspiration
2	39	M	bronchial asthma; pneumonia
3	68	M	myasthenia gravis; chronic bronchitis; cholecystectomy
4	51	M	crushed chest; compound fracture of tibia
5	37	M	crushed chest; contusion to kidney
6	22	F	myasthenia gravis; thymectomy
7	27	M	drug overdosage (Doridon® and Stelazine®); pulmonary oedema
8	63	M	emphysema; right heart failure
9	22	M	drug overdosage (Doridon®)
10	63	M	G.I. bleeding; ligation oesophageal varices; mediastinitis; emphysema
11	63	M	emphysema; bronchopneumonia
12	20	M	chest injury; head injury

FRC *and* $AaDo_2$ *during respiratory failure*

Except in the two patients who died, in every case the final FRC was greater than that measured on admission in respiratory failure (Fig. 1, Table II). A low FRC and a large oxygen gradient were common at the time of admission. In most cases an increase in FRC was associated with an improvement in oxygenation (Fig. 2, Table II), although this was not a constant observation.

The FRC measured at the CIOC was in most cases higher than that measured when breathing 100 per cent oxygen (Fig. 3, Table II). However, the difference in FRC as measured at the two different oxygen concentrations was usually not large.

While the data indicate the relationship between the oxygen gradient and FRC in each instance, values were not collected at sufficiently constant intervals or in sufficient numbers to permit comment on the time course of the changes observed.

Discussion

The low resting lung volumes observed in patients in respiratory failure may be due to a variety of mechanisms such as atelectasis from airway obstruction by

TABLE II

DATA OBTAINED FROM PATIENTS IN RESPIRATORY FAILURE

No.	Days from admission	Type of ventilation	$F_{I_{O_2}} = 1$				Mean FRC (ml)	$F_{I_{O_2}}$ = CIOC/100		Per cent difference in FRC
			Pa_{O_2}	Pa_{CO_2}	a_{pH}	aDO_2		CIOC (%)	mean FRC (ml)	
1*	0	c	133	34.2	7.47	533	958	77	1116	14
	2	c	308	31.7	7.50	353	1194	69	1327	10
	4	c	124	48.5	7.36	526	1005	60	1050	4
2	1	s	320	48.5	7.42	350	2250	—	—	—
	3	s	283	47.2	7.40	383	2256	—	—	—
	5	s	420	43.0	7.43	240	2617	—	—	—
	11	s	445	29.5	7.46	241	2722	air	2807	3
	18	s	438	32.4	7.48	237	2657	air	2959	10
3	0	c	205	26.4	7.50	473	1678	—	—	—
	3	c	260	31.7	7.44	383	2254	—	—	—
	5	c	370	28.0	7.50	287	2710	—	—	—
	7	c	460	34.0	7.50	198	2639	—	—	—
	10	c	340	33.0	7.50	325	2686	—	—	—
	13	s	350	33.0	7.49	325	2628	—	—	—
	35	s	425	34.2	7.46	243	2556	air	2891	11
4	1	s	62	32.0	7.51	618	1255	—	—	—
	2	c	88	26.0	7.49	588	1111	60	1324	17
	4	c	368	35.0	7.45	305	1669	30	1953	14
	10	s	410	38.5	7.46	250	1661	31	1875	11
	30	s	337	30.6	7.50	340	1514	air	1710	11
5	1	c	330	36.0	7.45	333	1269	air	1569	19
	3	c	335	34.4	7.45	335	1332	35	1610	17
	9	s	310	29.0	7.50	372	1418	—	—	—
	19	s	364	36.5	7.45	309	1517	air	1752	13
6	3	c	485	30.5	7.45	200	920	—	—	—
	4	c	468	33.8	7.44	205	978	—	—	—
	17	s	440	30.5	7.53	235	1110	air	1280	13

TABLE II (*concluded*)

No.	Days from admission	Type of ventilation	$F_{I_{O_2}} = 1$				Mean FRC (ml)	$F_{I_{O_2}}$ = CIOC/100		Per cent difference in FRC
			Pa_{O_2}	Pa_{CO_2}	a_{pH}	$AaDo_2$		CIOC (%)	mean FRC (ml)	
7	0	c	265	38.5	7.51	406	891	—	—	—
	2	c	320	31.0	7.59	344	1046	70	1258	16
	4	c	287	28.6	7.51	385	1224	—	—	—
	6	c	170	33.0	7.49	487	853	71	945	9
	24	s	489	36.1	7.44	189	1583	air	1752	9
8	0	s						25	3119	
	1	s						39	4032	
	4	s						30	4310	
	14	s						air	4381	
9	0	c	545	29.0	7.52	126	1152	air	1314	12
	1	s	540	36.0	7.44	134	1126	—	—	—
	4	s	425	36.0	7.46	231	1333	air	1487	10
10*	0	c	91	36.0	7.43	570	1074	76	1204	10
	1	c	61	37.0	7.41	602	1094	—	—	—
	4	c	105	35.6	7.50	568	1072	80	1266	15
11	3	s						31	2797	—
	6	s						31	2763	—
	27	s						air	3272	
12	1	s	278	34.8	7.47	402				
	2	s	330	35.4	7.46	353	944			
	15	s	380	32.4	7.43	301	1186	air	1348	12

*Patients expired.

TABLE III

EFFECT OF RECUMBENCY ON FRC IN NORMAL SUBJECTS

	Age	Surface area (m^2)	FRC sitting		FRC recumbent		Fall in FRC	
			ml	ml/m^2	ml	ml/m^2	ml	ml/m^2
Males								
1	26	1.71	2252	1492	2177	1293	375	219
2	32	1.74	3261	1874	2102	1208	1159	666
3	36	1.91	3270	1712	2224	1164	1049	548
4	28	1.75	2304	1317	1060	606	1244	711
5	25	1.74	2647	1521	1631	937	1016	584
6	43	1.94	2241	1155	1569	809	672	346
7	40	1.96	3336	1702	2618	1336	718	366
8	43	2.0	3130	1565	2317	1159	813	417
9	33	1.88	3289	1749	2112	1124	1177	626
10	44	1.95	3225	1654	2025	1038	1200	615
11	57	1.85	2522	1363	1940	1048	582	315
12	23	1.80	2135	1185	1416	786	719	399
13	37	2.02	3509	1595	2522	1146	987	449
14	49	1.62	2186	1349	1270	784	916	565
Mean	36.9	1.85	2807.6	1516.6	1927	1031.3	901.7	487.6
S.D.	9.8	.12	521.0	217.4	469.8	216.4	262.7	148.6
Females								
1	23	1.69	2532	1499	2035	1204	497	294
2	25	1.58	2123	1344	1486	941	637	403
3	23	1.60	1860	1663	1548	968	312	195
4	33	1.62	2685	1657	1552	958	1133	699
5	25	1.72	2394	1391	1196	695	1198	697
6	30	1.34	1821	1359	1298	969	523	390
7	36	1.58	2731	1728	1407	891	1324	838
8	23	1.57	2502	1594	1439	917	1063	677
9	50	1.81	2721	1503	1546	854	1175	649
10	57	1.46	2294	1571	1104	756	1190	815
Mean	32.5	1.58	2366.3	1480.9	1461.1	915.3	905.2	565.7
S.D.	12.06	.13	337.0	168.83	254	137.3	369.4	225.9

secretions or compression of lung tissue, pneumonic consolidation, pulmonary contusion, and pulmonary oedema. In addition to acute pulmonary disease, extrapulmonary factors may also contribute to low initial resting lung volumes. These include pleural effusion, abdominal distention, obesity, instability of the chest wall, and muscle weakness. Thus, the improvement of resting lung volume in response to appropriate therapy may be quite rapid when the aetiological factor is corrected quickly, as in cases of acute pulmonary oedema or pleural effusion, and slower in cases of lesions corrected more slowly, such as chest injuries (Table II).

The improvement in the oxygen gradient, coincident with an increase in lung volume, suggests that the increase in FRC was probably due to the opening up of previously non-ventilated alveoli.

Since many of the values of FRC observed in patients with respiratory failure were unusually low, normal values under similar circumstances of posture and inspired oxygen mixture were examined. The fall in FRC observed when these subjects assume the supine position is comparable to that reported previously.[7-9] This fall has been attributed to an elevation of the diaphragm and an increase in the pulmonary blood volume.

TABLE IV

EFFECT OF FOUR HOURS OF RECUMBENCY ON FRC IN NORMAL SUBJECTS

No.	Sex	Age	Sitting (ml)	Supine (ml)	Supine (ml) 1 hour	2 hours	3 hours	4 hours
1	M	40	3255	2318	2594	2449	2227	2374
2	M	32	2554	1468	2152	2093	2147	2108
3	M	23	2135	1185	1585	1515	1322	1401
4	M	37	3509	1595	2774	2451	2533	2593
5	M	49	2186	1349	1250	1137	1103	1255
6	M	26	2847	2113	2025	2049	2018	2008
Mean difference			+1076.33	−392.0	+114.33	+57.33	−64.83	
S.D.			426.99	487.77	117.17	125.35	78.682	
p			.01	.1	.05	.3	.05	

TABLE V

EFFECT OF CHANGE IN INSPIRED OXYGEN CONCENTRATION ON FRC IN NORMAL SUBJECTS

No.	Age	Sex	Air (ml)	50% $F_{I_{O_2}}$ (ml)	75% $F_{I_{O_2}}$ (ml)	100% $F_{I_{O_2}}$ (ml)
1	23	M	1422	1363	1403	1277
2	32	M	2198	2230	2112	1800
3	26	M	2117	1995	2111	1926
4	43	M	2651	2682	2370	2301
5	23	F	1756	1693	1804	1530
6	24	F	1610	1573	1610	1457
7	35	M	2052	1901	2031	1798
8	44	M	2209	2267	2166	2097
Mean difference				+38.875	+12.125	−171.625
S.D.				75.37	153.96	90.503
p				.1	.8	.01

Changes in lung volumes secondary to oxygen breathing have been studied by several authors. Déry *et al.*[10] demonstrated that FRC did not fall when the inspired gas contained at least 50 per cent nitrogen. Dubois *et al.*[15] showed that a fall in vital capacity with oxygen breathing could be prevented if the inspired gas contained at least 5 per cent nitrogen. The fall in FRC in relation to oxygen breathing was noted in this series only when the subjects breathed 100 per cent oxygen and was not observed when 50 or 75 per cent oxygen was breathed. This fall in FRC was in most cases not very large. As most of the patients in respiratory failure were breathing inspired gas mixtures containing less than 75 per cent oxygen when the measurements were made at the CIOC, the inspired oxygen concentration by itself probably does not explain the low FRC. Further, the increase in volume observed during the course of the patient's hospital stay suggests the presence of an additional reversible component. In these cases, therapy aimed at alveolar expansion would be justified as a part of each patient's therapeutic regimen. Such therapy would depend upon the underlying disease but might include treatment of pulmonary oedema, pleural effusion and abdominal distention, intermittent positive pressure ventilation with large tidal volumes, reversal of muscle weakness in patients with myasthenia gravis, chest physiotherapy and tracheobronchial

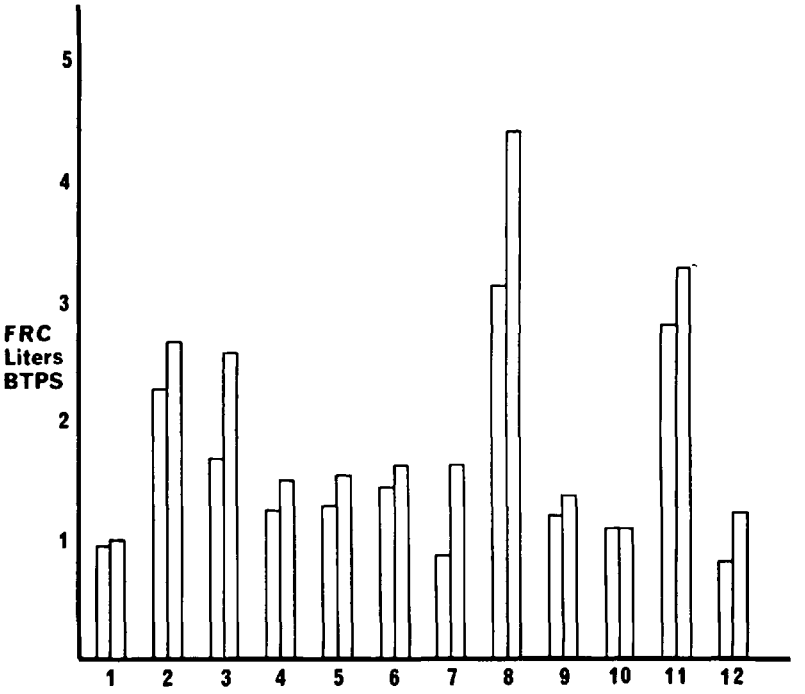

FIGURE 1. First and last values of FRC obtained in each of 12 patients studied. Initial values are to the left in each instance.

toilet, minimizing the duration of exposure to soluble gases such as 100 per cent oxygen, and the application of a positive pressure expiratory plateau.[16]

A distinction between a fall in FRC due to recumbency and denitrogenation and that due to disease is further prompted by the frequent finding that the supine position produces only a modest increase in alveolar-arterial oxygen difference in normal persons,[17–19] as opposed to the very high values seen in several of the patients presented here. Presumably, the fall in FRC associated with recumbency and denitrogenation is due to collapse of alveoli which cease to be perfused, or to factors other than alveolar collapse. Mead[20] states that the lower limits of alveolar volume are determined by the interactions of the surface tension forces and the capacity of the inspiratory muscles to develop inflating pressures. It is possible that many patients in respiratory failure demonstrate evidence of alveolar collapse because of an inability to develop inflating pressures, or because when a sufficient pressure is developed it is not transmitted to some alveoli because of airway obstruction from mucus, oedema fluid, or compression.

There is insufficient data from this series on which to base firm conclusions as to the usefulness of the FRC in the management of patients with respiratory failure. However, it is clear that resting lung volume may be extremely low, and, unless this is due to reversible atelectasis or pulmonary oedema, it may be unwise to ventilate such patients with large tidal volumes calculated on a body weight basis.

In most instances $AaDo_2$ and FRC show an inverse relationship, and knowledge

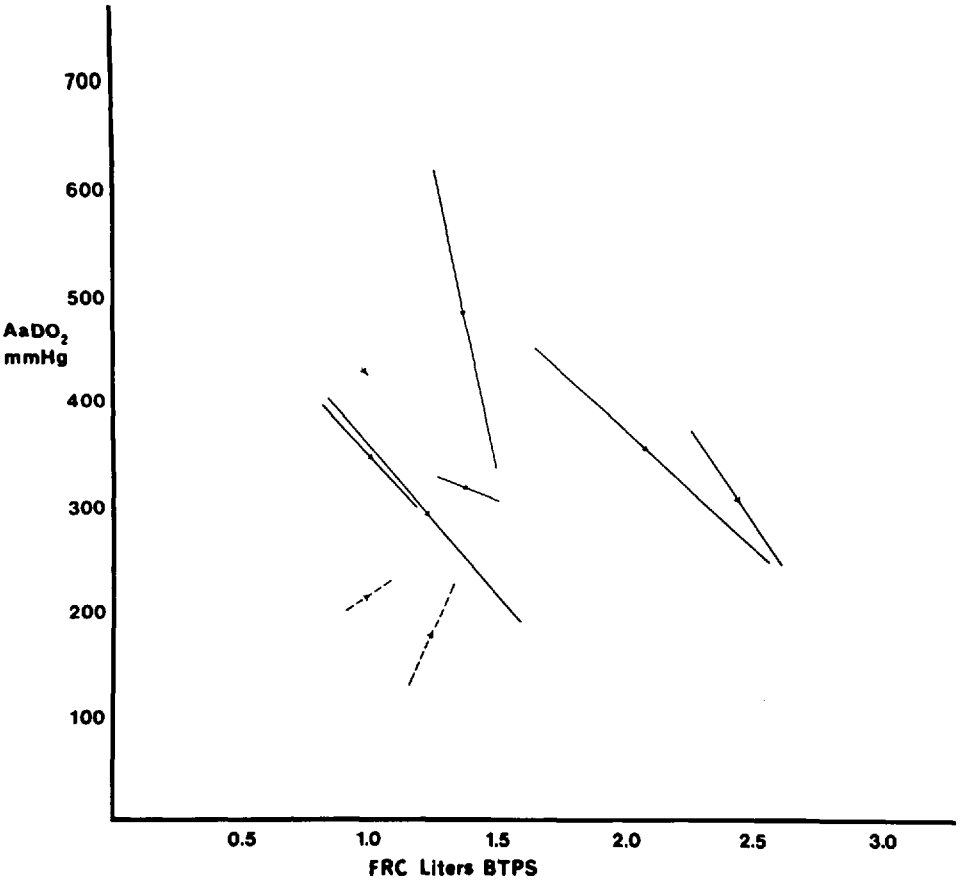

FIGURE 2. Lines joining first and last values of FRC and $AaDo_2$ obtained in patients with respiratory failure. Dotted lines are from the patients whose FRCs went up but whose oxygen gradients increased after they came off the ventilator.

of lung volume probably adds little to routine clinical management, when inspired and arterial oxygen tensions are readily available and pressure-volume relationships can be followed.

SUMMARY

Changes in functional residual capacity and their relationship to alveolar-arterial oxygen difference were observed during the course of respiratory failure in twelve patients. The influence of recumbency and oxygen breathing on FRC in normal subjects was also examined.

Low resting lung volumes and large alveolar-arterial oxygen differences were often observed at the time of admission in respiratory failure. The reduction in FRC cannot be explained on the basis that these measurements were made in recumbent patients breathing a high concentration of oxygen in the inspired gas.

An increase in FRC was often associated with an improvement in oxygenation, and it is inferred that in these patients correction of FRC is associated with the opening up of previously non-ventilated alveoli, and that therapy designed with

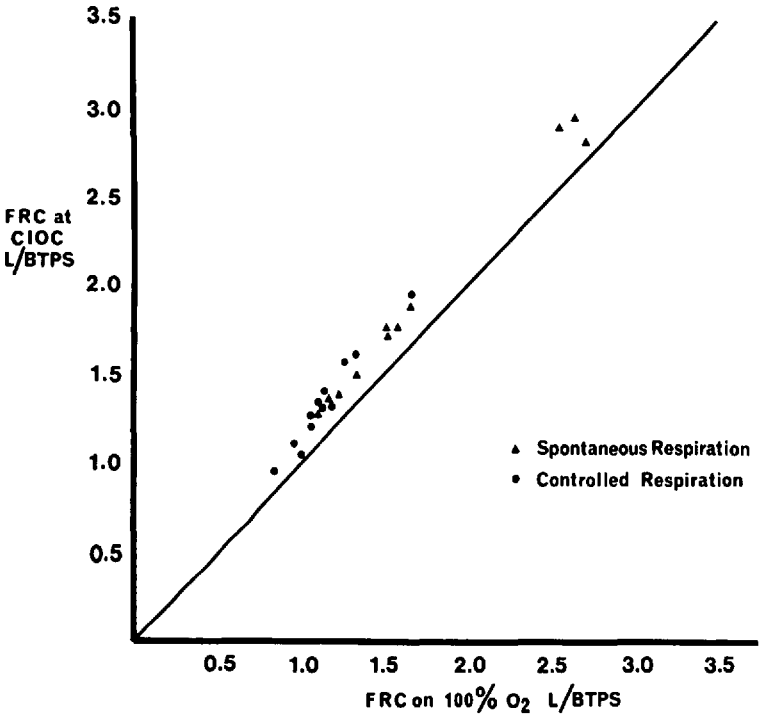

FIGURE 3. Comparison of values for FRC: breathing clinically indicated oxygen concentration and breathing 100 per cent oxygen.

this objective is therefore justified. However, when extremely low resting lung volume is due to causes not reversible mechanically, such as diffuse pneumonia, large tidal volume ventilation determined on a body weight basis may not be indicated. Measurement of FRC is not recommended for routine clinical management.

RÉSUMÉ

Au cours de l'insuffisance respiratoire survenue chez 12 malades, nous avons réussi à observer les modifications de la capacité résiduelle fonctionnelle et leur relation avec la différence en oxygène alvéolaire et artérielle. Nous avons également étudié chez des sujets normaux les effets du décubitus et de la ventilation à l'oxygène sur la capacité fonctionnelle résiduelle.

Au moment de l'admission pour insuffisance respiratoire, nous avons noté des volumes pulmonaires restreints au repos et de grandes différences en oxygène alvéolaire et artérielle. La diminution de la capacité fonctionnelle résiduelle ne s'applique pas par le fait que ces mesures ont été faites sur des malades en décubitus et respirant une atmosphère à haute concentration en oxygène.

Une augmentation de la capacité fonctionnelle résiduelle a souvent été accompagnée d'une amélioration de l'oxygénation et l'on conclut que, chez ces malades, la correction de la capacité fonctionnelle résiduelle s'accompagne de l'ouverture d'alvéoles non ventilées antérieurement et qu'ainsi, la thérapie préconisée dans ce but devient alors justifiée. Toutefois, lorsque de très petits vo-

lumes respiratoires au repos sont dus à des causes impossibles à vaincre mécaniquement, comme une pneumonie diffuse, il peut ne pas être indiqué de faire une ventilation à grand volume d'air courant calculée d'après le poids du malade. Nous ne recommandons pas le calcul de la capacité fonctionnelle résiduelle comme conduite clinique de routine.

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