

RESPIRATORY MECHANICS IN PATIENTS WITH CHAGAS DISEASE WITHOUT CARDIAC INSUFFICIENCY

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SUMMARY

Lung function was studied in the 19 patients carriers of Chagas Disease. They were symptoms free, with no cardiopulmonary manifestations and no propedeutical signs of cardiac decompensation or of pneumopathy. As a control group, 13 lung function tests were done in normal persons, with negative serological reaction for Chagas Disease. None of the 32 individuals had ever smoked. Besides the clinical examination, electrocardiograms and chest X-Rays in postero-anterior and right and left anterior oblique views were made. Finally spirometry and respiratory mechanics study were done. Lung volumes and expiratory flows were similar in both groups, being normal in relation to predict values. The nervous control of the respiratory center also had similar behaviour, which discarded central alterations. Total pulmonary resistance was normal in both groups. The lung elastic forces, studied by static compliance, were normal. The percentual relation between dynamic and static compliance was below to 70% in 7 Chagas Disease patients when respiratory frequency was increased. In none of the individuals of the control group, the relation decreased to that level. This result was understood as being due to small airways exposure.

Keywords: Chagas Disease — Pulmonary Function — Spirometry — Respiratory Mechanics.

INTRODUCTION

From the cardiological point of view, it is believed that approximately 30% of patients who had acute Chagas Disease clinically demonstrable, developed after a period of ten years, chronic cardiopathy. This long interval between the acute outbreak and the manifestation of the chronic form of the disease permitted various studies^{7,11,12,13} tending to detect precociously the eventual functional alterations of these patients even before clinical manifestations appear.

Apart from that it must be pointed out that there is a possible lung exposure to the Chagas Disease. This point of view was result of various investigations which originated certain controversies.

Thus KOEBERLE¹⁷, in autopsies on Chagas Disease patients, observed initially alterations in the respiratory system which consisted in pathological dilatation of the bronchus and reduction of the neurones of the nervous ganglions

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which are distributed along their walls. He considered this sort of bronchiectasis as typical of this entity¹⁸ suggesting that this lesion would be consequent to denervation superior to 75% of the bronchial plexus¹⁹.

On the other hand, examining Chagas patients from the functional point of view, existence of alterations in motor reactivity of the bronchus was found, evidenced by the administration of metacoline¹³. This observation lead to suppose that hypersensibility shown when this medicine is used would be consequent to parasympathetic denervation¹⁴.

In this same line of researches a reduction of forced expiratory volume during the first second was noted, in absolute values or in percentage of vital capacity²³.

ESTEVEZ et al.⁸, analysing the pulmonary mechanics of patients with Chagas miocardopathy, without cardiac insufficiency, noted a reduction of compliance verifying that alterations were more distinct in the group showing cardiac enlargement.

Summarizing, literature data evidence that respiratory manifestations are not as yet well established. Actually, studies on the subject are in conflict and do not dismiss other associated facts which could be responsible for the manifestations.

MATERIAL AND METHODS

Composed of 32 people with no clinical manifestations. The group was composed of non smokers individuals: 10 of masculine sex and 22 of feminine sex, age varying between 20 to 57 years ($36,53 \pm 9,63$). All denied cardio-pulmonary manifestations, the physical examination having shown no semiological data imputable to cardiac descompensation or any pneumopathy.

The total group was divided in two sub groups according to positiveness or negativness of immunological reaction to the Chagas Disease.

Sub-group I — Composed of 13 healthy individuals, four of masculine sex and nine of feminine sex. Their ages varied between 20 and 56 ($31,54 \pm 9,97$) years.

Sub-group II — Composed of 19 patients with positive reaction: six of masculine sex and 13 feminine, whose ages varied between 24 to 57 ($39,95 \pm 7,94$) years. None carried megaesophagus.

As a preliminary routine, they answered a questionnaire referring to smoking, existence of morbid antecedents and also presence of symptoms of cardiorespiratory exposure. They were then submitted to a severe physical examination when measurements were taken of height and weight, which also permitted to determine corporal surface.

Then, electrocardiograms and X Rays of the thorax in postero-anterior, anterior right and left oblique projections were taken on normal individuals as well as on those carriers of the Chagas Disease. By way of these procedures it was tried to evidence possible existence of cardiac exposure resulting from this disease.

After this initial phase, all individuals were submitted to spirometric proof and study of respiratory mechanics in equipment of Hewlett Packard Inc. (USA).

Spirometry was realized in the Pulmonary Function Analyzer 47402 A, the results of which are furnished through a digital system, or calculated from a graphic impressed in a xy registrator. In both cases the estimates are already corrected to BTPS.

The study of the respiratory mechanics was made on Physiograph 21526 A, using three channels. On the first, a pressure amplifier was connected. On the second a volume integrator which received signal of flow from a medium gain amplifier connected to the third channel. To measure the airways flow a heated pneumotachograph was used. This in turn, was connected to a pre-amplifier connected to a medium gain amplifier.

The spirometric study consisted in three tests, the person examined always in ortostatic position. Initially a flow volume curve was established. From this curve, values of the maximum forced expiratory flow and forced expiratory flow at 50% of vital capacity were obtained. Next a maneuver of forced vital capacity was realized establishing a volume-time curve. From this curve were obtained the forced expiratory volume during the first second, the

forced vital capacity, the percentual relation between both, and the forced expiratory flows between 25 and 75% and 75 and 85% of the forced vital capacity. Finally a maneuver was realized to determine maximum voluntary ventilation establishing the greater volume of air breathed in time unit.

For the study of respiratory mechanics the oesophagical balloon was passed by the nose, following which it was swallowed by the individual.

After putting the individual in sitting position, his nose was obstructed and the patients breathed in the pneumotacograph realizing a forced vital capacity maneuver.

The spirometric results were compared to the standards, establishing a percentage in relation to predict values.

The values of maximum voluntary ventilation were compared to those obtained through equation proposed by BATES et al.², the forced expiratory flows between 75 and 85% of vital capacity curve with those obtained through equation of MORRIS et al.²⁷, and the other results, with KNUDSON et al.¹⁶ formulas.

The pulmonary compliance and resistance were calculated from drawings obtained by the physiograph. The static compliance was determined by the variation of volume in relation to variation in esophageic pressure measured in zero flow points during inspiration.

The volume variation used was situated in limits near tidal volume, starting from functional residual capacity.

The dynamic compliance was obtained by dividing the tidal volume by the variation of the esophagus pressure obtained between the beginning and the end of respiration.

The experimental protocol was completed by registering respiration in accelerated frequency. This was controlled by metronome which allowed to maintain regular rythm of 40 respirations per minute. The individual was taught to maintain tidal volume and expiratory reserve volume. A percentual relation between dynamic and static compliance was established in the respiration frequencies studied. 70% Of predict was admitted in the present investigation as a limit value, reductions beyond this value being significant.

The relation between the variation of the esophagus pressure and the airway flow, e.g. pulmonary resistance, was analysed at the same pulmonar volume which eliminates the influence of the elastic forces under pressure. The values considered normal were established by FRANK et al.^{9,10} and MARSHALL²⁵.

The statistic treatment comprised calculation of averages and standard deviations of the functional variables previously cited.

The comparison between the variables in both groups was made by test of Wilcoxon-Mann Whitney.

The behaviour of the percentual relation between dynamic and static compliance was estimated through exact test of Fisher.

In the present investigation the level of 5% significance was adopted.

RESULTS

The averages and standard deviations of the individual characteristics are in Table I.

T A B L E I
Averages and standard deviation of age and anthropometrical data in the groups studied

Variable	Group	Average	Standard deviation
Age	Normal	31.54	9.97
(Years)	Chagas	39.95	7.94
Weight	Normal	60.22	11.39
(kg)	Chagas	62.20	9.34
Height	Normal	159.23	10.47
(cm)	Chagas	155.66	8.49
Body surface	Normal	1.613	0.168
(m ²)	Chagas	1.612	0.142

The forced expiratory volume during the first second, the forced vital capacity and the percentual relation between both are in the normal limits (> 80%) being obtained in all cases average values discreetly higher than 100%. The comparative study of the values of these variables in normal and Chagas patients did not reveal any statistically significant difference (Table II).

The same behaviour was observed in forced expiratory flows. The expiratory flows between 25 and 75% and 75 and 85% of vital capacity, as well as the instantaneous, i.e. the maximum

forced expiratory flow and flow at 50% of vital capacity are in the limits of normality. Their averages, whose values are beyond 100%, and the respective standard deviation are shown in Table III. There were no significant differences between the groups examined.

The averages of maximum voluntary ventilation the results of which are in both groups normal according to those predicted, are represented in Table II.

The ventilation per minute, as well as its relation to corporal surface are represented according to respiratory frequency analysed. The averages and standard deviations shown in Table IV demonstrated through contrasts realized, that both groups acted in a similar way. It can be noted, even raising the respiratory frequency, that the groups had the same behaviour with no statistically significant differences.

T A B L E II

Averages and standard deviation of the values obtained and of the percentage in relation to predict of the spirometric variables in both groups. Statistic values of Mann-Whitney

Variables	Group	Obtained			% Predict		
		Average	Standard deviation	U	Average	Standard deviation	U
FVC	Normal	3.97	1.11	1.44	106.46	14.00	0.71
	Chagas	3.36	0.69		102.57	16.65	
FEV ₁	Normal	3.45	0.89	1.38	112.15	11.79	0.58
	Chagas	2.94	0.62		108.84	13.26	
(FEV ₁ /FVC) 100	Normal	87.55	7.12	0.21	101.69	7.98	0.19
	Chagas	87.88	4.33		102.84	5.92	
VVM	Normal	128.77	38.35	0.98	127.15	28.61	0.69
	Chagas	120.42	34.39		134.57	14.04	

FVC — Forced Vital Capacity (l); FEV₁ — Forced Expiratory Volume during the first second of the FCV (l); (FEV₁/FVC) 100 — Forced Expiratory Volume during the first second of the FVC to Forced Vital Capacity ratio expressed as a percentage; VVM — Maximal Voluntary Ventilation (l/min)

T A B L E III

Averages and standard deviation of the values obtained and of the percentage in relation to predict of the expiratory flows in both groups. Statistic values of Mann-Whitney

Variables	Group	Obtained			% Predict		
		Average	Standard deviation	U	Average	Standard deviation	U
FEF 25-75%	Normal	4.19	0.93	0.77	104.23	19.98	0.84
	Chagas	4.04	1.11		108.26	15.65	
FEF 75-85%	Normal	1.81	0.93	1.25	144.38	60.28	0.21
	Chagas	1.40	0.70		134.36	50.11	
FEF max	Normal	7.21	1.75	0.63	103.15	15.68	0.90
	Chagas	6.96	1.88		108.15	18.00	
FEF 50%	Normal	5.25	0.98	0.77	106.31	17.59	0.17
	Chagas	5.02	1.46		106.89	21.94	

FEF 25-75% — Mean forced expiratory flow during the middle half of the FVC(1/sec); FEF 75-85% — Mean forced expiratory flow between 75 and 85% of the FVC(1/sec); FEF max — Maximal forced expiratory flow achieved during an FVC(1/sec); FEF 50% — Instantaneous forced expiratory flow after 50% of the FVC has been exhaled (1/sec)

The inspiratory and expiratory times, beside relation between inspiratory time and total time of the respiratory cycle, analysed in the same previous frequencies, showed similar statistical behaviour in the two groups referred to (Table V).

The averages and standard deviations of the pulmonary resistance are in Table VI. The values obtained were similar in both groups. In both conditions of this study the resistance is normal in all cases examined.

Both the dynamic and static compliance as well as the percentual relation between the two are reported in Table VI. Statistically there is no difference between the groups examined.

Therefore, considering that 7 Chagas patients had this relation below 70% with accelerated respiration, we observed in the exact test of Fisher (Table VII) a significant difference.

T A B L E IV

Averages and standard deviation of the values obtained during basal and accelerated respiration. Statistic values of Mann-Whitney

Variables	Group	Basal respiration			Accelerated respiration		
		Average	Standard deviation	U	Average	Standard deviation	U
f	Normal	21.31	5.41	0.82	39.77	2.68	1.86
	Chagas	19.98	6.33		40.52	4.20	
TV	Normal	0.45	0.10	0.12	0.47	0.17	0.63
	Chagas	0.44	0.10		0.48	0.12	
VE	Normal	9.45	2.90	1.29	18.81	6.34	0.77
	Chagas	8.44	2.35		19.62	4.96	
VE/BS	Normal	5.94	2.13	1.13	11.82	4.57	0.90
	Chagas	5.33	1.81		12.27	3.35	

f — Respiratory frequency per minute; TV — Tidal volume (l); VE — Expired volume per minute (l/min); VE/BS — VE to body surface ratio (l/min/m²)

T A B L E V

Averages and standard deviation of the values obtained during basal and accelerated respiration. Statistic values of Mann-Whitney

Variables	Group	Basal respiration			Accelerated respiration		
		Average	Standard deviation	U	Average	Standard deviation	U
Ti	Normal	1.31	0.27	1.13	0.73	0.07	0.79
	Chagas	1.48	0.40		0.72	0.09	
TV/Ti	Normal	0.35	0.10	1.44	0.64	0.22	1.02
	Chagas	0.32	0.10		0.68	0.19	
Ti/Ttot	Normal	0.45	0.04	0.48	0.48	0.04	0.36
	Chagas	0.45	0.06		0.49	0.04	

Ti — Inspiratory time (sec); TV/Ti — Tidal volume to inspiratory time ratio (l/sec); Ti/Ttot — Inspiratory time to total respiratory time ratio

T A B L E VI

Averages and standard deviation of the values obtained during basal and accelerated respiration. Statistic values of Mann-Whitney

	Variable	Group	Average	Standard deviation	U	
Accelerated respirat.	Cst	Normal	0.17	0.06	0.08	
		Chagas	0.18	0.08		
	RL	Normal	1.92	0.56	0.17	
		Chagas	2.11	0.98		
	Cdyn	Normal	0.17	0.05	0.38	
		Chagas	0.17	0.07		
	(Cdyn/Cst)100	Normal	103.86	16.17	0.40	
		Chagas	100.65	26.25		
	Basal respiration	RL	Normal	2.02	0.67	0.06
			Chagas	1.97	0.61	
Cdyn		Normal	0.17	0.05	0.79	
		Chagas	0.15	0.06		
(Cdyn/Cst)100		Normal	96.85	12.18	0.94	
		Chagas	87.54	26.07		

Cst — Static compliance (l/cmH₂O); Cdyn — Dynamic compliance (l/cmH₂O); RL — Total pulmonary resistance (cmH₂O/l/sec)

T A B L E V I I

Number of individuals of each group according to the percentual decrease of the dynamic to static compliance ratio

Group	Chagas	Normal	Total
Altered			
< 70%	7	0	7
≥ 70%	12	13	25
Total	19	13	32

Probability of the observed frequencies if the proportion of altered in both groups were equal = 0.014

COMMENTS

In the Chagas group 14 patients showed cardiac exposure, evidenced by electrocardiographic alterations (Table VI). Even for those whose electrocardiographic tracings were admittedly normal and therefore were in the "in-determined chronical phase"³¹ it is doubtful that there exists no cardiac lesion, since electrophysiological modifications had been shown in such patients. In both situations, however, there were no clinical evidence of functional heart alterations.

T A B L E V I I I

Electrocardiographic and radiological characteristics of the Chagas patients

Number	Electrocardiogram	Chest radiology
01	Left anterior fascicular block	Normal
02	Complete right bundle branch block with left anterior fascicular block	Normal
03	Complete AV block with pace-maker	Normal
04	Complete AV block with pace-maker	Left ventricle ↑
05	Complete right bundle branch block with left anterior fascicular block	Normal
06	Extrasystoles	Normal
07	First degree AV block	Normal
08	Normal	Normal
09	Complete right bundle branch block with left anterior fascicular block	Left ventricle ↑
10	Normal	Normal
11	Complete right bundle branch block	Normal
12	Left ventricular hypertrophy — Inative zone	Normal
13	Left anterior fascicular block — Extrasystoles	Left and right ventricle ↑
14	Extrasystoles	Normal
15	Normal	Right ventricle ↑
16	Normal	Normal
17	Normal	Normal
18	Complete right bundle branch block with left anterior fascicular block	Normal
19	Left anterior fascicular block	Normal

In this way, the results of pulmonary function tests in this groups of patients totally free from symptoms, express the real state of the respiratory function in the Chagas Disease.

The spirometry is a classical method used as a routine in studies of respiratory physiology and pathophysiology justifying its use in this research.

It was observed, under this aspect, that Chagas patients with no symptoms, just like normal individuals included in the control group, showed tests in the limit of normality. In fact analysing a population of Chagas patients with characteristics similar to our patients, MANCO²³ noted reduction of the forced expiratory

volume during the first second in absolute value as well as percentual of vital capacity. In this work, however, there is no reference to smoking, which can leave doubts on its participation on the determination of the referred alterations.

It must be emphasized that in our study the forced vital capacity and the forced expiratory volume during the first second, were normal, as well as the maximum voluntary ventilation and the forced expiratory flows. In this case, the importance of normal behaviour of flows between 75 and 85% of vital capacity and 50% of this capacity, must be emphasized since they are those which more precociously permit to recognize the functional exposure of the

small airways in the spirometric test, which fact was evidenced by MACKLEM et al.^{15,22}.

In view of the facts exposed above it is licit to believe that the "chagasic" compromising in patients exempt from cardio-respiratory symptoms, previous or present, does not alter the spirometric test. Thus, the presence of modifications of this test, in this group of patients must consequently be attributed to factors independent of the disease.

Aiming at a better evaluation of the pulmonary function, the control exercised by the respiratory center, was also examined. This has been exhaustively investigated since the classical works of HALDANE & PRIESTLEY¹⁴. It is believed that the measurement of ventilation reflects the capacity of the respiratory center to generate stimulus. BARCROFT & MARGARIE¹, and more recently CLARK & VON EULER⁴ suggested that the relation between the tidal volume and the duration of the inspiration is the better index of the nervous control of this phase. Finally, the relation between inspiratory time and total respiratory time would express the potentiality of inspiratory that is, would indicate the fraction on the respiratory cycle where the inspiratory muscles are in activity. Rigidly, however, the electric activity of the inspiratory muscles precedes in milliseconds the start of volumetrical modifications of inspiration and continues during part of expiration. These times are however clinically supposed²⁶.

During the study it was noted that the values of ventilation per minute, and particularly those referring to the relation between this and the corporal surface (which permits better comparative analysis between the results) are similar in the groups of normal and "chagasic" individuals.

In the same manner, the identity of behaviour of relations between the tidal volume and inspiratory time and between this and the total time of respiratory cycle in both groups permits to suppose that the respiratory control is normal in carriers with no symptoms of the chronic form of Chagas Disease. These observations remove any possibility of alteration of activity of the respiratory center, consequently excluding existence of alterations at the level of central nervous system.

The values of pulmonary resistance were normal. Just as it occurs in normal individuals, the carriers of Chagas Disease do not show any alteration of this variable dependent of respiratory frequency. From this observation, the absence of alteration of pulmonary function becomes evident, at least in accentuated manner.

It must be pointed out the observation of ESTEVEZ et al.⁸ who analysing functionally carriers of this disease found reduction of compliance, and alterations more pronounced in the group with cardiac enlargement. Possibly these discoveries result from increase of pulmonary elastic recoil consequent to cardiac insufficiency.

In our study, rigidly excluding patients with clinical signs of cardiac descompensation, we did not find any case of similar behaviour.

Actually, one cannot, through determinations previously cited, remove the possibility of eventual alterations in the peripheral airways. Thus, methods which permit to detect obstruction of the small airways are essential for precise diagnosis as well as to permit correct interpretation of possible alterations of the pulmonary resistance.

In fact studies of the respiratory mechanics confirmed that the conventional technics previously referred to, are not sensitive and do not usually detect this obstruction. This is due to the fact that the peripheric bronchus contribute with only 10 to 30% of the total resistance of the tracheo-bronchial tree^{5,15}. If the superior airways are included in the measurements of resistance, participation of the small airways will still be smaller³⁵. These can thus be considered in a certain way as "silent zones" in the lung.

Em 1966 MACKLEM & MEAD²¹, showed that the time constants (compliance x resistance) of the pulmonar units distal to these airways are approximately 0.01 second. Under these circumstances they concluded that a difference of 0.04 seconds between these units would be sufficient to determine reduction of dynamic compliance with increase of respiratory frequency. Consequently, the analysis of compliance in relation to frequency would be a test that would permit characterization of

obstruction in small airways^{15,21,22,33,35}. Despite elevation of respiratory frequency normal individuals maintain compliance in steady values, while accentuated decrease occur when there is the so called small airway disease^{15,21,22,35}.

In view of homogenizing the results, it was tried to interrelate the dynamic and static compliance. It was therefore possible to compare the values by way of percentual relation between both. The reduction of this relation with increases of respiratory frequency was denominated frequency dependent compliance.

In this work, it was observed that none of the normal individuals presented reduction of this relation beyond 75% and in only two this was below 80%. In view of these results the critical limit was considered 70%. This being determined, lower values permitted to describe compliance as frequency dependent.

This indicates that the regions of the lung do not show synchronism of function. At the moment of zero flow in the mouth, air is flowing in the lung from one region to another²⁹. In this way the reduction of compliance means alteration in the distribution of ventilation. In addition, the regions called "slow" will have a smaller tidal volume than the "rapid" resulting in abnormality in the distribution of inspired air²⁷.

In the present work seven patients with chronic form of Chagas Disease showed reduction in this relation, beyond the limit considered normal which permits to classify them as having frequency dependent compliance.

This data submitted to the precise test of Fisher, showed that this frequency was statistically significant when compared to that of normal individuals.

The characterization of exposure in these patients permits to suppose it is result from primary modification of the bronchial tree, or subordinated to interstitial transudation due to cardiac insufficiency⁶.

It must be observed that the primary bronchial exposure in Chagas Disease has been studied by various Authors^{8,13,17,23,32,34} but the results were controversial. It is known on the other hand, that cardiac insufficiency determines frequency dependence of compliance.

Although there are no elements to conclude in a definite form the real cause of this alteration, it must be remembered that all patients examined had no symptoms and none of them presented previous episode of cardiac decompensation.

Corroborating with this observation, a patient with normal pulmonary function, submitted to cardiac catheterism revealed normal pressure in pulmonar capillars.

These elements permit to consider that alterations in small airways are not due to pulmonary congestion, but to primary lesion of bronchi by Chagas Disease.

RESUMO

Mecânica respiratória em pacientes portadores de doença de Chagas sem insuficiência cardíaca

Os Autores estudaram a função pulmonar em 19 pacientes chagásicos. Estes eram assintomáticos, não referindo manifestações cardíopulmonares prévias ou atuais, não havendo ao exame físico dados semiológicos imputáveis a descompensação cardíaca ou qualquer pneumopatia. Comparativamente foram analisadas as provas de função pulmonar em 13 pessoas hígdas, com sorologia negativa para Doença de Chagas. Todos os componentes do estudo, isto é, os 32 indivíduos examinados negavam presentemente ou nos antecedentes o hábito de fumar. Após exame físico rigoroso, foram obtidos eletrocardiograma e radiografia de tórax nas posições póstero-anterior e oblíquas anteriores direita e esquerda, sendo a seguir submetidos a prova espirométrica e ao estudo da mecânica respiratória. Os achados obtidos revelaram, volumes pulmonares e fluxos expiratórios semelhantes nos dois grupos, encontrando-se normais em relação aos valores preditos. O controle nervoso do centro respiratório exerceu-se de forma semelhante tanto nos chagásicos quanto nos indivíduos normais, não havendo portanto, evidências de alteração a nível central. A resistência pulmonar total situou-se dentro da faixa da normalidade, em ambos os grupos. As forças elásticas dos pulmões, caracterizadas pelo estudo da complacência estática, encontraram-se normais. A relação porcentual entre as complacências dinâmica e estática foi inferior a 70% em sete pacientes chagásicos ao se au-

mentar a frequência respiratória. Em nenhum dos normais, tal relação decresceu até este nível. Este resultado foi interpretado como indicando comprometimento das vias aéreas de pequeno calibre.

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