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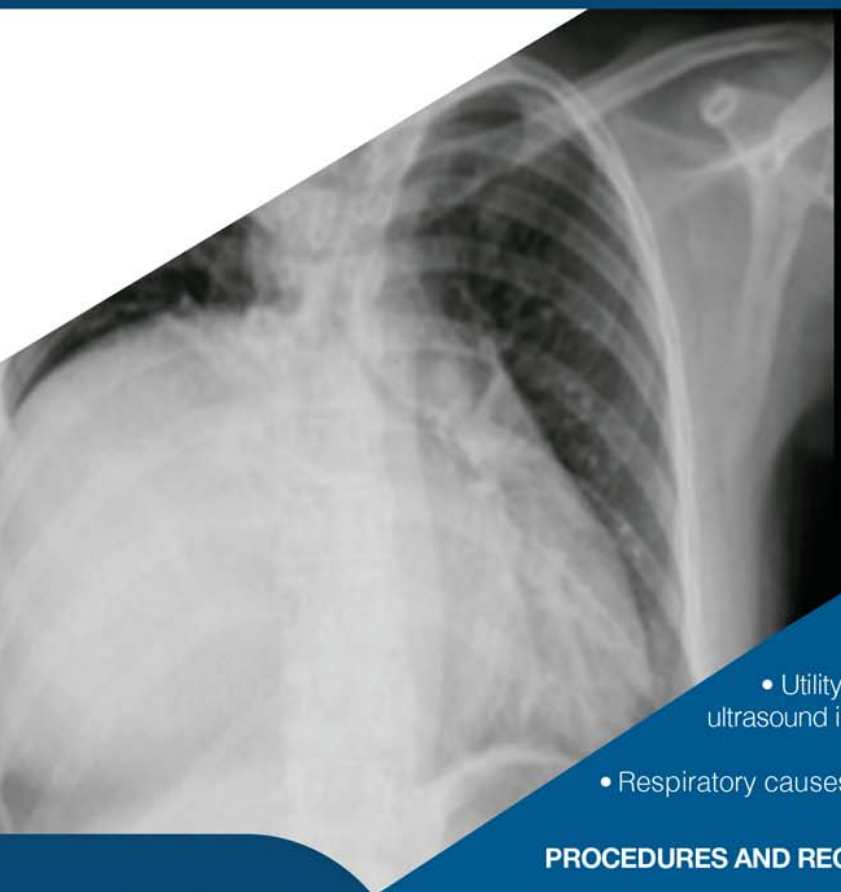

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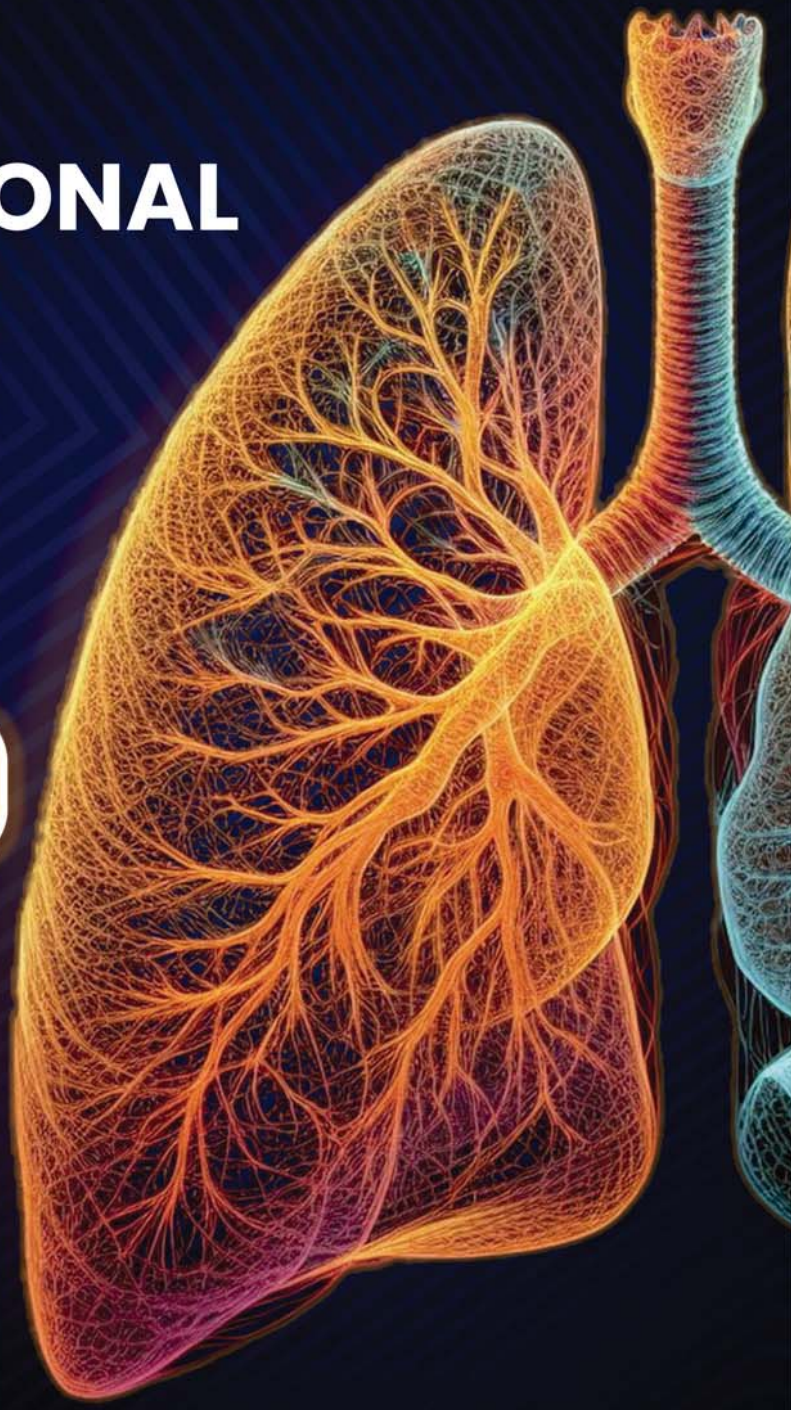

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Editorial
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Pulmonary rehabilitation: a mandatory intervention in diffuse interstitial lung diseases

Rehabilitación pulmonar: una intervención obligada en enfermedades pulmonares intersticiales difusas

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There is an urgent need to improve preventive, diagnostic and therapeutic measures in respiratory patients, including those suffering from diffuse interstitial lung diseases (DILD), perhaps even more. The health personnel who intervene every day in the complex approach to these pathologies and patients must efficiently offer interventions that expand the therapeutic options that could result in the reduction of disability and premature mortality; with this, it will be possible to meet the United Nations' Sustainable Development Goal, which is a one-third reduction in premature mortality from non-communicable diseases, including chronic respiratory diseases (CRD), by 2030. Based on estimates made globally from 1990 to 2019, CRD were the third leading cause of death responsible for 4.0 million deaths with a prevalence of 454.6 million cases worldwide. While total deaths and prevalence of CRD have increased 28.5 and 39.8%, age-standardized rates have decreased for chronic obstructive pulmonary disease (COPD) and asthma, but not for interstitial diseases.[1]

Pulmonary rehabilitation (PR) is recognized as a central component of this process. The change of health behavior is vital for the optimization and maintenance of the benefits of any intervention in chronic care, PR has taken the lead in the implementation of strategies to achieve this objective[2] and are a fundamental part of the treatment of pulmonary diseases, especially chronic, such as DILD, contributing comprehensively in the improvement of symptoms, effort tolerance, quality of life and reintegration into work, social and family activities that allow an improvement in the general and psychological health status of patients, in addition to reducing costs and the use of health services, which is a beacon of hope for the respiratory and exercise limitations they present,[2] as demonstrated in their Colombian study Betancurt PJ et al.

The pulmonary rehabilitation departments consolidated in hospitals that have research areas and ethics committees have the opportunity to enrich the scientific evidence through their studies and research protocols in the different respiratory pathologies. There is little scientific evidence published globally for the benefits of long-term pulmonary rehabilitation programes (PRP) for patients with DILD, as demonstrated in two Cochrane reviews.

2013 ATS/ERS statement on pulmonary rehabilitation defines it as «a comprehensive intervention based on a thorough patient assessment followed by patient-adapted therapies including, but not limited to, exercise training, education, and behavior change, designed to improve the physical and psychological condition of people with chronic respiratory diseases and promote long-term adherence to health-enhancing behaviors.»[2] It is a conceptual definition and therefore does not identify the specific structure, environment, and supports that are required for PRPs to be successful.[3]

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New models of PR, such as telerehabilitation, and web-based PR have demonstrated in some trials, driven by non-inferiority and using robust methods, results similar to those of traditional PR in a hospital setting, which expand access to and increase participation in PR. The expected outcomes are improvements in breathlessness, quality of life and exercise tolerance and a reduction in hospital admissions.[3]

The future of PR is geared towards engaging more patients in personalized programs. To that end, programs should be widely publicized and health professionals should be trained to deal with the individual needs and preferences of the cases. The exercise program should be viewed as an individualized program at the limit of the patient's abilities to provide as powerful a training stimulus as possible. Towards the end of the program, subjects need to develop self-management skills that allow them to live with their disease, maintain the benefits of the program, and translate them into better quality and quantity of physical activity.[4,5]

Successful implementation will be judged only if the essential components of the pulmonary rehabilitation program (PRP) are delivered, changes are measured, and if the expected results are achieved, a rigorous approach to quality.[3]

There remains a real challenge in investigating the long-term benefits of PR and its maintenance programs. It is naive to believe that the effects of a few weeks program would last forever, when followed by a maintenance program they are likely to translate into significant long-term health benefits through improved cardiovascular fitness, metabolic, or muscular.[4] In several diseases such as interstitial[6] diseases, asthma,[2] in pretransplant patients[7] with pulmonary hypertension,[8] in patients with COVID-19,[9] among other CRD.

We must remember that you should not enter a PRP or any of its components (e.g. pulmonary physiotherapy) without having a specialist doctor who is treating and monitoring a patient with CRD or acute. Ideally, the specialist doctor should give indications of the scope of each component of the PRP.[2,10,11]

Patients who suffer from DILD and go through the complex journey of diagnosis, treatment and clinical evolution from the moment they detect that the cough and dyspnea they perceive is not normal, to the moment they experience the adverse effects of the different treatments proposed to them, deserve to have the benefit of a PRP. It is up to the health system to form multidisciplinary groups in PR to provide personalized care to these patients and that they have the opportunity to access the benefits that PR can offer them.

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Effect of a physical exercise and education program in patients with diffuse interstitial lung diseases

Efecto de un programa de ejercicio físico y educación en pacientes con enfermedades pulmonares intersticiales difusas

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ABSTRACT. Introduction: diffuse interstitial lung diseases (DILD) are a group of diseases that compromise the alveolar and capillary basement membranes, that is, the anatomical interstitium. Exercise and education are recommended intervention strategies for patients regardless of the cause of DILD. **Objective:** to establish the effects of a physical exercise and education program in patients with idiopathic pulmonary fibrosis and other DILD on dyspnea, functional aerobic capacity, anxiety/depression and health-related quality of life. **Material and methods:** quasi-experimental study, all patients were linked for convenience and signed the informed consent. They were divided into two groups: patients with idiopathic pulmonary fibrosis and other DILD, evaluated before and after the exercise and education program in clinical variables, functional capacity, anxiety/depression and quality of life. **Results:** 68 patients were linked, 30 with idiopathic pulmonary fibrosis and 36 with other DILD. Both groups presented improvements in the distance traveled in the 6-minute walk test, dyspnea and quality of life p-value ≤ 0.05. The idiopathic pulmonary fibrosis group presented improvements in anxiety and depression and the other DILD group in anxiety. **Conclusion:** all patients present significant improvements in functional capacity, dyspnea, anxiety and quality of life, the group of idiopathic pulmonary fibrosis additionally improves in depression, being the variable with significant changes between the groups.

Keywords: lung diseases interstitial, dyspnea, quality of life, exercise tolerance, idiopathic pulmonary fibrosis.

RESUMEN. Introducción: las enfermedades pulmonares intersticiales difusas son un grupo de enfermedades que comprometen las membranas basales alveolares y capilares, es decir, el intersticio anatómico. El ejercicio y la educación son estrategias de intervención recomendadas para los pacientes sin importar la causa de las enfermedades pulmonares intersticiales difusas. **Objetivo:** establecer los efectos de un programa de ejercicio físico y educación en pacientes con fibrosis pulmonar idiopática y otras enfermedades pulmonares intersticiales difusas en la disnea, capacidad aeróbica funcional, ansiedad/depresión y calidad de vida relacionada con la salud. **Material y métodos:** estudio cuasiexperimental, todos los pacientes se vincularon por conveniencia y firmaron el consentimiento informado. Se dividieron en dos grupos: pacientes con fibrosis pulmonar idiopática y casos con otras enfermedades pulmonares intersticiales difusas, evaluados antes y después del programa de ejercicio y educación en variables clínicas, capacidad funcional, ansiedad/depresión y calidad de vida. **Resultados:** se vincularon 68 pacientes, 30 con fibrosis pulmonar idiopática y 36 con otras enfermedades pulmonares intersticiales difusas. Ambos grupos presentaron mejorías en la distancia recorrida en la prueba de marcha de los seis minutos, la disnea y la calidad de vida $p \leq 0.05$. El grupo de fibrosis pulmonar idiopática presentó mejorías en la ansiedad y depresión, y el grupo de otras enfermedades pulmonares idiopáticas en la ansiedad. **Conclusión:** todos los pacientes presentaron mejorías significativas en la capacidad funcional, disnea, ansiedad y calidad de vida. El grupo de fibrosis pulmonar idiopática adicionalmente mejoró en la depresión, siendo la variable con cambios significativos entre los grupos.

Palabras clave: enfermedades pulmonares intersticiales, disnea, calidad de vida, tolerancia al ejercicio, fibrosis pulmonar idiopática.

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INTRODUCTION

Diffuse interstitial lung disease (DILD) represents a set of conditions that involve the alveolar and capillary basement membranes, i.e., the anatomical interstitium;[1] more than 150 different types of DILD are currently known, however, it is only possible to establish the etiological diagnosis in approximately 30-40% of cases.[1]

These diseases have been classified as having similar clinical features (dyspnea as the predominant symptom), radiological (diffuse pulmonary infiltrates), physiological (preferential alteration of gas exchange), and anatomopathological (preferential alteration of lung support tissues).[2] However, the most commonly reported type of DILD is idiopathic pulmonary fibrosis (IPF).[1]

In terms of incidence and prevalence, it differs substantially given the methodology used to diagnose it, in turn, changes in the classification and appearance of new entities make it difficult to collect epidemiological data; these diseases occupy one of the first places of morbidity and mortality in the world. In the United Kingdom the prevalence is 1.5 to 1.8 per 10,000 inhabitants, while in Spain there was an incidence of 7.6 per 100,000 inhabitants.[3]

There are environmental or exogenous factors that are involved in the pathogenesis of the disease, not to mention also endogenous factors such as gastroesophageal reflux and autoimmunity,[3] among the sociodemographic risk factors found in the appearance of DILD are considered male, be over 40 years of age and have been an active smoker for more than 30 packs in the year.[4]

As for the diagnosis of DILD, the clinical evaluation includes factors such as exercise intolerance, limitation in ventilation, gas exchange, diffusion and circulation, which deteriorate the individual early, in addition to functional capacity and health-related quality of life.[3] Some diagnostic aids, such as chest radiography , allow observing alterations of interstitial predominance with patterns: reticulonodular, ground glass and honeycomb.[5] In addition to this diagnostic aid, currently high-resolution computed axial tomography (CAT) has shown sensitivity in terms of the diagnosis of DILD.[5] Restrictive alteration is generally evident in spirometry, with a decreased forced vital capacity (FVC) in relation to the forced expired volume in the first second/normal forced vital capacity (FEV1/FVC) and the reduction of the diffusion capacity of carbon monoxide (DLCO) turns out to be a frequent finding.[1] Functional tests, such as the six-minute walk test (6MWT), turn out to be a predictor of mortality and help to individually assess patients.[6]

Exercise intolerance is one of the most frequent conditions in patients with DILD, it is usually related to the sensation of dyspnea during exertion and progressive increase in fatigue, which causes a worse quality of life.[7] Changes in respiratory pattern and decreased tidal volume further functionally limit patients with DILD, so pulmonary rehabilitation is widely recommended since clinical improvements have been documented in 6MWT, dyspnea and health-related quality of life (HRQoL).[8]

However, there are few studies in our context that report interventions related to pulmonary rehabilitation (PR) in subgroups of patients with DILD, since the behavior may not be the same. For this reason, the objective of this study was to establish the effects of PR in patients with IPF and other DILD on dyspnea, functional capacity, anxiety/depression, and HRQoL.

MATERIAL AND METHODS

A quasi-experimental study in which all patients with DILD who met the inclusion criteria were linked for convenience and completed a physical exercise and education program in a clinic in the city of Cali, Colombia, during 2019.

This study took into consideration and adopted the recommendations of the declaration of Helsinki and was approved by the Ethics Committee of the participating Institution according to minutes 126.01.05.02, which classified it as research with a risk greater than the minimum according to resolution 008430 of 1993 of the Ministry of Social Protection of Colombia.

Patients who met the following inclusion criteria were linked: diagnosis of DILD through a medical history confirmed by a radiologist and pulmonologist and in those cases that merited additional examinations, they were diagnosed by a multidisciplinary medical team through chest X-rays, pulmonary function tests and CAT, for which two groups were formed (IPF and other DILD),[9,10] admission to the physical exercise and education program of the clinic for the first time, so that at the time of admission they had not received exercise recommendations and all participants were sedentary/inactive. Exclusion criteria were patients with beta-blocking or anti arrhythmic drugs, presence of pacemakers, cardiac arrhythmias, uncontrolled arterial hypertension (160/100 mmHg), saturation during 6MWT < 80% and other uncontrolled cardio metabolic diseases and presenting respiratory comorbidity such as chronic obstructive pulmonary disease (COPD) and asthma.

For the development of the study, the following variables were taken into account: age, sex, place of residence, socioeconomic status, type of DILD, post bronchodilator volume flow curve spirometry FEV1, FVC, FEV1/FVC taken from the patients' medical records. At the beginning and end of the physical exercise and education program, the variables were taken: dyspnea in the activities of daily living of the Medical Research

Council (MRC), peripheral oxygen saturation (SpO_2), weight, body mass index (BMI), for functional aerobic capacity the distance traveled in the 6MWT, anxiety/depression with the Hospital Anxiety and Depression Scale (HADS) questionnaire and HRQoL with the Saint George's Respiratory Questionnaire (SGRQ).

Measurements

In a first encounter, 6MWT was performed in the morning in a 30-meter-long corridor, in which the patient was instructed to walk as fast as possible for 6 minutes in a path delimited by two cones.[11] SpO_2 and heart rate were measured through a pulse oximeter (NONIN GO2 FINGER pulse oximeter® PN# 9570). At the end of the TC6M, the distance traveled in meters and the VO2e (estimated oxygen consumption) were obtained with the formula VO2e = 3.5 mL/kg/min + (vel m/min × 0.1).[12]

After the 6MWT, the HADS hospital anxiety and depression questionnaire was applied to each of the participants; this questionnaire takes into account the score obtained for each subscale with values of 0-3, the score range being between 0-21, it is considered normal when the anxiety or depression subscale has a score of 0-7, doubtful of 8-10 and clinical problem greater than 11.[1,13]

At the end, the SGRQ questionnaire was carried out in a self-directed manner, which includes 50 questions that are distributed in the domains symptoms, activity and impact; the score obtained varies between 0 = best performance and 100= worst performance.[1]

Physical exercise and education program

The physical exercise and education program was carried out for 24 sessions, carrying out three sessions per week for eight weeks of exercise and educational activities. The patients performed continuous exercise in recumbent bicycle and endless band for 30 minutes starting at 50% of the VO2e obtained in the 6MWT that increased to 80%, supplementary oxygen was administered to those patients who presented a desaturation in the 6MWT ≥ 4% or who during the exercise the SpO_2 was < 90%.[1,14] Muscle strengthening of the upper limbs was performed with four sets of 12 repetitions with a minute of rest at 40% of the maximum resistance (MR), which increased to 60% of the MR at four weeks; the progression of the exercise was carried out taking into account the score in the modified Borg dyspnea always maintaining the activities between 3-5/10. In education activities, patients received individual and group sessions on the following topics including: disease awareness, medication optimization, oxygen use, feeding, panic measures, relaxation techniques, and home breathing exercises.[14] Patients were also educated and encouraged to increase their levels of physical activity beyond the program on non-training days.[14]

Statistical methods

The information collected was entered in a Microsoft Office Excel® 2010 book in which a database was built that was then analyzed in the SPSS statistical package version 24; through descriptive tests the qualitative variables were presented in frequency and percentage, through the Kolmogorov-Smirnov test the parametric behavior of the quantitative variables was assumed presenting them in mean ± standard deviation; to compare the variables at the beginning and end after the physical exercise and education program in the groups, a t test was performed for paired samples; in turn, the results were compared between the IPF group and the group of other DILD at the beginning and end of the physical exercise and education program by performing the t test for independent samples. A significance of 95% and a p-value < 0.05 was considered statistically significant.

RESULTS

66 patients were initially linked to the study, 30 with IPF and 36 with other DILD; however, during the rehabilitation sessions one patient with IPF and four patients with other DILD presented exacerbation so they left the PR program *(Figure 1)*.

The majority of participants were found to be male, 55.7%; age showed a mean of 61.05 ± 16.24 years. Regarding the socioeconomic stratum, it was found that the highest percentage was classified as medium with 79.3% in IPF and 50.0% in DILD followed by classified as low and finally high. Compared to the type of interstitial

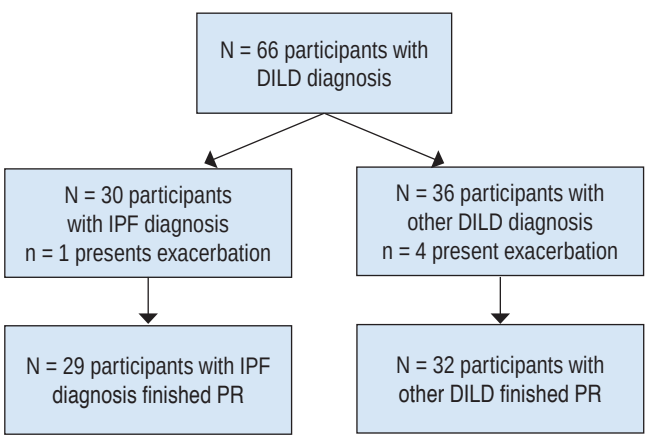

Figure 1: Admission of patients to the pulmonary rehabilitation program. DILD = diffuse interstitial lung disease. IPF = idiopathic pulmonary fibrosis. PR = pulmonary rehabilitation.

Table 1: Socio-demographic and clinical characteristics.

Variables	Total N = 61 n (%)	IPF N = 29 n (%)	DILD N = 32 n (%)	p
Sex				0.390
Male	34 (55.7)	14 (48.3)	20 (62.5)	
Female	27 (44.3)	15 (51.7)	12 (37.5)	
Age (years)*	61.05 ± 16.24	64.97 ± 16.09	57.50 ± 15.78	0.072
Socioeconomic status				0.070
Low	16 (26.2)	4 (13.8)	12 (37.5)	
Medium	39 (63.9)	23 (79.3)	16 (50.0)	
High	6 (9.8)	2 (6.9)	4 (12.5)	
Place of residence				0.272
Cali	58 (95.1)	29 (100.0)	29 (90.6)	
Outside of Cali	3 (4.9)	0 (0)	3 (9.4)	
Type of interstitial disease				NA
Idiopathic pulmonary fibrosis	29 (47.5)	29 (100.0)	0 (0)	
Lupus erythematosus	2 (3.3)	0 (0)	2 (6.3)	
Pneumoconiosis	6 (9.8)	0 (0)	6 (18.8)	
Silicosis	2 (3.3)	0 (0)	2 (6.3)	
Interstitial pneumonia	4 (6.6)	0 (0)	4 (12.5)	
Other unclassified DILDs	18 (29.5)	0 (0)	18 (56.3)	
FEV1* (% predicted)	63.72 ± 17.65	68.57 ± 18.36	59.33 ± 16.02	0.040
FVC* (% predicted)	60.06 ± 13.52	63.44 ± 13.38	56.99 ± 13.10	0.062
FEV1/FVC* (%)	90.62 ± 21.23	89.16 ± 19.51	91.94 ± 22.90	0.613

IPF = idiopathic pulmonary fibrosis. DILD = diffuse interstitial lung disease. FEV1 = forced expired volume in the first second. FVC = forced vital capacity.
* Values expressed in mean ± standard deviation.

disease, 29 patients equivalent to 100% belonged to the IPF group, followed by other unclassified DILD 56.3%; pneumoconiosis 18.8%; interstitial pneumonitis 12.5%; silicosis 6.3% and lupus 6.3% respectively; finally, lung function shows reduced forced vital capacity (FVC) in both groups *(Table 1)*.

Regarding the changes in the 6MWT pre- and post-program of exercise and education, it is found in the IPF group statistically significant improvement going from 371.79 ± 121.39 meters to 435.38 ± 109.75 and clinically with an increase of 63.59 ± 12.67 meters; the same happens in the DILD group where a statistically significant improvement is shown going from 353.0 ± 121.13 meters to 415.0 ± 107.91 meters and clinically significant of 62.00 ± 8.19 meters. The functional aerobic capacity shows that the estimated VO_2 shows a statistically significant improvement in the IPF group from 9.47 ± 2.16 mL/kg/min pre PR to 10.77 ± 1.82 mL/kg/min post PR; the same response is evident in the DILD group from 9.17 ± 2.12 mL/kg/min to 10.43 ± 1.79 mL/kg/min post PR. In addition, six patients with IPF (20.1%) and five with other DILD (15.6%) required the use of supplemental oxygen during 6MWT, a situation that required these patients to perform it during exercise sessions. Dyspnea measured with the MRC scale shows a statistically significant change when comparing pre- and post- PR data in both the IPF and DILD groups; the same is true for the HADS scale for anxiety and depression in both groups *(Tables 2 and 3)*.

The health-related quality of life, measured with the SGRQ questionnaire in the IPF group and DILD group shows statistically and clinically significant changes in the domains of symptoms, activity and impact with a pre PR total score in the IPF group of 50.14 ± 18.90 points and post PR of 34.00 ± 17.40 points with a difference of 16.14 ± 2.22 points; the same results are evidenced in the DILD group where a pre PR total score of 54.78 ± 17.58 points and post PR of 44.53 ± 19.11 points with a difference of 10.25 ± 3.04 points is presented *(Tables 2 and 3)*.

When comparing the results obtained from the means versus pre- and post-exercise tolerance PR between the two groups IPF and DILD, a statistically significant change was evident only at the end of the intervention in the HADS questionnaire for depression with a value of p = 0.047 *(Table 4)*.

DISCUSSION

The objective of this study was to establish the effects of a physical exercise and education program in patients with IPF and other DILD on dyspnea, functional aerobic capacity, anxiety/depression and health-related quality of life, for which it was important to understand that IPF and DILD comprise a great heterogeneity and individual variety due to their pathological process, where we can find different causal factors and benefits of exercise according to the type of DILD.

Taking into account the above, this study found that the male sex occurs more frequently in other DILDs, which may be due to a greater relationship with a decrease in steroid hormones such as dehydroepiandrosterone responsible for decreasing fibroblast proliferation and increasing apoptosis.[15] However, it contrasts with other authors who show prevalences in men of 72.4% in patients with IPF.[16]

With respect to age, this study shows that participants have an average age of 61.05 ± 16.24; despite understanding that IPF and DILD can have genetic compromises and be generated at any stage of life, it has been found that their symptomatology hasa greater presentation from adulthood where, being more predisposed to these diseases, some authors mention that some components of RNA telomerase promote fibrogenesis,[15] in the same way it is related to what was described by other authors in the context of rehabilitation programs.[16]

In both IPF and DILD, a decrease in the percentage of the predicted FVC was found through spirometry, evidencing a possible restrictive ventilatory pattern with greater compromise in the group of other DILDs, which was classified as moderately severe and moderate in the IPF group, which is due to the fact that in these two diseases an important restrictive compromise is generated due to their pathological process related to inflammation and attempts at tissue repair, which leads to loss of elasticity of the pulmonary parenchyma, thus decreasing pulmonary ventilation and gas exchange, producing hypoxia and subsequently dyspnea as an initial symptomatology in patients.[17]

There were no significant changes in BMI in the comparison groups; this could be due to the time of intervention in the physical exercise and education program, since they are not long enough to generate changes that contribute to the decrease of the fat component in this type of patients.[18,19] In addition, this study did not carry out a nutritional control and follow-up that will cause relevant changes related to the intervention.

Table 2: Changes in anthropometrics, functional aerobic capacity, dyspnea anxiety/depression and health-related quality of life in patients with IPF (N = 29).

Variables	IPF, mean ± SD			p
	Physical exercise and education		Mean differences ± SE	
	Initial	Final		
Weight (kg)	67.03 ± 13.24	67.41 ± 13.78	-0.37 ± 0.49	0.434
BMI (kg/m^2)	26.23 ± 4.47	26.36 ± 4.6	-0.13 ± 0.17	0.459
Distance travelled 6MWT (m)	371.79 ± 121.39	435.38 ± 109.75	-63.59 ± 12.67	0.000
SpO_2 at rest (%)	95.90 ± 2.70	95.62 ± 2.61	-0.28 ± 0.37	0.463
SpO_2 final (%)	88.86 ± 8.85	89.10 ± 5.70	0.24 ± 0.74	0.747
Desaturation percentage	7.03 ± 4.99	6.52 ± 5.03	-0.51 ± 0.68	0.452
VO_2e (mL/kg/min)	9.47 ± 2.16	10.77 ± 1.82	-1.31 ± 0.29	0.000
MRC	2.10 ± 1.01	1.10 ± 1.08	1.0 ± 0.15	0.000
HAD anxiety	6.31 ± 5.11	3.83 ± 3.37	2.48 ± 0.65	0.001
HAD depression	5.52 ± 4.09	3.83 ± 2.98	1.69 ± 0.59	0.008
SGRQ symptoms	50.90 ± 20.23	36.00 ± 17.68	14.90 ± 3.06	0.000
SGRQ activities	61.83 ± 20.99	48.41 ± 28.99	13.41 ± 4.61	0.007
SGRQ impact	40.86 ± 22.18	24.41 ± 16.77	16.45 ± 2.59	0.000
SGRQ total	50.14 ± 18.90	34.00 ± 17.40	16.14 ± 2.22	0.000

IPF = idiopathic pulmonary fibrosis. SD = standard deviation. SE = standard error. BMI = body mass index. 6MWT = 6 minute walk test. SpO_2 = partial oxygen saturation. VO_2e = estimated oxygen consumption. MRC = Medical Research Council. HAD = hospital anxiety and depression scale. SGRQ = Saint George's respiratory questionnaire.

Table 3: Changes in anthropometrics, functional aerobic capacity, dyspnea anxiety/depression and health-related quality of life in patients with other DILDs (N = 32).

Variables	Other DILDs, mean ± SD			
	Physical exercise and education		Mean differences ± SE	p
	Initial	Final		
Weight (kg)	67.84 ± 14.26	68.66 ± 13.72	-0.82 ± 0.48	0.098
BMI (kg/m^2)	31.16 ± 5.34	31.46 ± 5.32	-0.29 ± 0.17	0.102
Distance travelled 6MWT (m)	353.0 ± 121.13	415.0 ± 107.91	-62.00 ± 8.19	0.000
SpO_2 at rest (%)	95.22 ± 2.72	95.31 ± 2.73	-0.09 ± 0.69	0.893
SpO_2 final (%)	86.94 ± 6.8	86.91 ± 5.59	0.031 ± 0.88	0.972
Desaturation percentage	8.28 ± 5.93	8.38 ± 5.24	-0.09 ± 0.79	0.906
VO_2e (mL/kg/min)	9.17 ± 2.12	10.43 ± 1.79	-1.26 ± 0.23	0.000
MRC	2.38 ± 1.07	1.78 ± 1.26	0.59 ± 0.21	0.007
HAD anxiety	5.38 ± 3.79	3.81 ± 3.33	1.56 ± 0.46	0.002
HAD depression	5.25 ± 3.52	4.34 ± 4.41	0.91 ± 0.69	0.198
SGRQ symptoms	51.97 ± 18.38	38.28 ± 17.40	13.69 ± 3.12	0.000
SGRQ activities	68.31 ± 18.30	57.25 ± 22.67	11.06 ± 3.24	0.002
SGRQ impact	44.59 ± 19.79	35.84 ± 20.26	8.75 ± 3.81	0.029
SGRQ total	54.78 ± 17.58	44.53 ± 19.11	10.25 ± 3.04	0.002

DILD = diffuse interstitial lung disease. SD = standard deviation. SE = standard error. BMI = body mass index. 6MWT = 6 minute walk test. SpO_2 = partial oxygen saturation. VO_2e = estimated oxygen consumption. MRC = medical research council. HAD = hospital anxiety and depression scale. SGRQ = Saint George's respiratory questionnaire.

It was found that the IPF group travels a greater distance in the 6MWT than the DILD group, but this difference is not significant; it is evident that both groups significantly improve the distance traveled in the 6MWT due possibly to the fact that physical exercise performed in this type of patients contributes to improving oxygen transport and oxygen exchange at the tissue level, which contributes to greater fatigue resistance due to better beta-oxidation and oxidative phosphorylation at the mitochondrial level, which contributes to the generation of energy in the muscle fiber and as a result a better tolerance to exercise also expressed in better functional aerobic capacity.[16] It was found that the IPF group travels a greater distance in the 6MWT than the DILD group, but this difference is not significant; it is evident that both groups significantly improve the distance traveled in the 6MWT due possibly to the fact that physical exercise performed in this type of patients contributes to improving oxygen transport and oxygen exchange at the tissue level, which contributes to greater fatigue resistance due to better beta-oxidation and oxidative phosphorylation at the mitochondrial level, which contributes to the generation of energy in the muscle fiber and as a result a better tolerance to exercise also expressed in better functional aerobic capacity.[16]

The SpO_2 in the two groups IPF and DILD show significant desaturation during 6MWT, which is due to a decrease in alveolar ventilation and gas exchange due to the restrictive ventilation pattern generated in their pulmonary parenchyma, which does not change after the exercise and education program and even these two diseases do not show significant differences when evaluating SpO_2 after 6MWT.[7] It is important to note that this situation described above forced 11 patients of all of them to use supplemental oxygen during the exercise sessions; however, this situation showed that there were no differences between the intervention groups, so both groups had similar functional performance conditions, both in 6MWT and in the exercise sessions.[7,20]

In the dyspnea measured with the MRC scale, it was evidenced that both groups of patients presented a significant improvement; a situation that can be explained because the exercises performed in the exercise and education program allows the training of peripheral muscles causing a better tolerance to the effort evidenced in the increase of the distance traveled in the 6MWT.[16]

For both groups of patients , there was a significant improvement in anxiety after the physical exercise and education program, this could occur since the patients

presented improvements in MRC dyspnea related to effort tolerance and activities of daily living, a situation that allows patients to improve their capacity and functional independence.[21,22] Additionally, the group of patients with IPF presented significant improvements in the depression domain of the HADS questionnaire, this related to the greater increase in this group of patients in the distance traveled in the P and the lower MRC dyspnea score that allows patients to perceive greater functional independence and less care by caregivers.[23]

Changes in HRQoL show that patients with IPF and other DILDs improve clinically and significantly in the domains of symptoms, activities and impact; however, the IPF group shows greater changes in SGRQ scores compared to the group of other DILDs. These results are related to the benefits reported by other authors;[24,25] additionally, patients with IPF usually have a worse clinical prognosis, which clearly shows that they benefit more from a structured exercise program and educational sessions that allow them to better perceive their disease in relation to the environment around them.[26]

This study is relevant since interventions related to exercise and education in patients with DILD have not been well documented in Latin America. In turn, this study could be a benchmark in future studies that decide to implement similar interventions to benefit patients in variables such as functional aerobic capacity, dyspnea, anxiety/depression and HRQoL.

The main study limitations are related to the pulmonary function tests used in patients, given that plethysmography and DLCO provide more relevant information on the structural deterioration and prognosis of patients. On the other hand, being one of the first studies in our context that differentiates the effects of exercise and education according to the type of DILD, the implementation of other strategies such as respiratory muscle strengthening, intermittent and interval exercise could show additional gains to those already reported in this study. In addition, it can be considered a possible bias to consider that the exercise was only carried out in the context of the program and that the patients did not exercise in the context of the home or their social relationships. On the other hand, aspects related to pharmacological treatment with steroids, or an analysis by subgroup of patients with supplemental oxygen use during exercise sessions, were not taken into account in this study, which can clearly influence the final result of the measurements. Finally, the quasi-experimental design of this study considerably affects the external validity of the study, so randomized controlled clinical trial designs are recommended in future investigations.

Table 4: Comparison of changes in anthropometric variables, functional aerobic capacity, dyspnea anxiety/depression and health-related quality of life.

	Physical exercise and education			
Variables	Initial Mean differences ± SE	p	Final Mean differences ± SE	p
Weight (kg)	-0.81 ± 3.5	0.819	1.24 ± 3.5	0.726
BMI (kg/m^2)	4.93 ± 5.67	0.328	5.09 ± 5.7	0.351
Distance travelled 6MWT (m)	-18.79 ± 31.09	0.548	0.47 ± 27.89	0.468
SpO_2 at rest (%)	-0.68 ± 0.69	0.334	0.66 ± 0.69	0.655
SpO_2 final (%)	-1.93 ± 1.63	0.243	0.13 ± 1.45	0.134
Desaturation percentage	1.25 ± 1.41	0.381	0.16 ± 1.32	0.164
VO_2e (mL/kg/min)	-0.30 ± 0.55	0.590	-0.34 ± 0.46	0.472
MRC	0.27 ± 0.27	0.314	0.68 ± 0.30	0.424
HAD anxiety	-0.94 ± 1.14	0.417	-0.02 ± 0.86	0.648
HAD depression	-0.27 ± 0.97	0.785	0.52 ± 0.97	0.047
SGRQ symptoms	1.07 ± 4.94	0.829	2.28 ± 4.57	0.915
SGRQ activities	6.49 ± 5.03	0.206	8.84 ± 6.63	0.127
SGRQ impact	3.73 ± 5.40	0.490	11.43 ± 4.68	0.429
SGRQ total	4.64 ± 4.67	0.324	10.53 ± 4.68	0.851

SE = standard error. BMI = body mass index. SpO_2 = partial oxygen saturation. VO_2e = estimated oxygen consumption. MRC = medical research council. HAD = hospital anxiety and depression scale. SGRQ = Saint George's respiratory questionnaire.

CONCLUSIONS

Patients with IPF and other DILDs who undergo an eight-week exercise and education program at a clinic in Cali, Colombia, have a similar increase in distance traveled on the 6MWT, significant improvements in functional aerobic capacity, dyspnea in activities of daily living CRM, and anxiety in all health-related quality of life domains. Depression only showed significant improvement in the IPF group.

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Utility of Balik's formula for the quantification of pleural effusion by ultrasound in the postoperative period of cardiac surgery

Utilidad de la fórmula de Balik para la cuantificación del derrame pleural por ultrasonido en el posoperatorio de cirugía cardiaca

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ABSTRACT. Introduction: pleural effusion is caused by an imbalance between oncotic and hydrostatic pressure through the pulmonary capillaries or by increased permeability. Ultrasound at the patient's bedside allows for efficient diagnosis in various areas, due to its portability and low cost, enabling the quantification of pleural fluid, determination of its characteristics, and guidance for percutaneous drainage. Post cardiac surgery, large pleural effusions can affect the patient's recovery journey. **Material and methods:** we conducted a cross-sectional study of 26 nonconsecutive adult patients who underwent cardiac surgery in whom pleural effusion was detected by ultrasound in the postoperative period. The pleural effusion volume, quantified by Balik's formula, correlated with the amount of pleural fluid drained. In addition, the characteristics of the fluid were defined to determine any correlation with Light's criteria. **Results:** there was a strong positive correlation between the volume quantified by Balik's formula and the amount of pleural fluid drained. We also found that the characteristics of drained pleural effusion, as determined through ultrasound, had sufficient diagnostic accuracy to differentiate between transudate and exudate compared with Light's criteria. **Conclusions:** there is a strong positive correlation between the fluid volume quantified by ultrasound with Balik's formula and the volume drained in the postoperative period of cardiac surgery, in addition to high diagnostic accuracy in the identification of the fluid as transudate or exudate.

Keywords: pleural effusion, lung ultrasound, point-of-care ultrasound.

RESUMEN. Introducción: el derrame pleural es causado por un desequilibrio entre la presión oncótica e hidrostática a través de los capilares pulmonares o por un aumento de la permeabilidad. La ecografía a pie de cama del paciente permite un diagnóstico eficiente en diversas áreas, por su portabilidad y bajo costo, posibilitando la cuantificación del líquido pleural, determinación de sus características y orientación para el drenaje percutáneo. Después de una cirugía cardíaca, los derrames pleurales grandes pueden afectar el proceso de recuperación del paciente. **Material y métodos:** realizamos un estudio transversal de 26 pacientes adultos no consecutivos intervenidos de cirugía cardíaca en quienes se detectó derrame pleural mediante ecografía en el posoperatorio. El volumen del derrame pleural, cuantificado por la fórmula de Balik, se correlacionó con la cantidad de líquido pleural drenado. Además, se definieron las características del fluido para determinar cualquier correlación con los criterios de Light. **Resultados:** hubo una fuerte correlación positiva entre el volumen cuantificado por la fórmula de Balik y la cantidad de líquido pleural drenado. También encontramos que las características del derrame pleural drenado, determinadas por ultrasonido, tenían suficiente precisión diagnóstica para diferenciar entre trasudado y exudado en comparación con los criterios de Light. **Conclusiones:** existe una fuerte correlación positiva entre el volumen de líquido cuantificado por ultrasonido con la fórmula de Balik y el volumen drenado en el posoperatorio de cirugía cardíaca, además de una alta precisión diagnóstica en la identificación del líquido como trasudado o exudado.

Palabras clave: derrame pleural, ecografía pulmonar, ecografía en el punto de atención.

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INTRODUCTION

Normally there is approximately 1-10 mL of fluid in the pleural space. This fluid is constantly produced and reabsorbed, and the amount of fluid is maintained by a balance between oncotic and hydrostatic pressure of the parietal and visceral pleura. Disruption in this balance causes the fluid to accumulate in the cavity.[1]

Pleural effusion is caused by an imbalance between oncotic and hydrostatic pressure through the visceral and parietal pleura, an increased permeability, or reduced absorption. It can occur as a result of lung parenchymal disease, infection, malignancy, and inflammatory processes. There are other factors that contribute to the accumulation of pleural fluid in the critical care setting, such as volume overload, renal or hepatic failure, myocardial depression, hypoalbuminemia, infections, and malnutrition.[2] In the postoperative period of cardiac surgery, pleural effusions, especially those that require a secondary drainage procedure during recovery, are associated with significantly worse outcomes including increased mortality, longer in-hospital stay, and higher complication rates. Of patients undergoing coronary artery bypass grafting or heart valve surgery, between 41% and 89% develop pleural effusions in the first seven days after surgery and 10% develop a pleural effusion occupying more than 25% of the hemithorax in the subsequent month. Causes of pleural effusions after cardiac surgery include diaphragm dysfunction, internal mammary artery harvesting (only in internal mammary artery grafting), and other perioperative complications (e.g., sepsis, congestive heart failure, pulmonary embolism, and chylothorax).[3]

There are various imaging methods to evaluate the lung, pleura, and pleural cavity. While the presence of a pleural effusion is frequently suspected from a chest X-ray, it does not allow the detection of other fluid characteristics or its quantification. Characteristics such as localization, thickening, or fibrosis usually need characterization by axial computed tomography. Ultrasound at the patient's bedside allows for the diagnosis of pleural effusion in various hospital settings (due to its portability, low cost, absence of radiation, and short examination time), enabling the quantification of pleural fluid, determination of some characteristics of the effusion, and guidance for drainage by thoracocentesis or tube thoracostomy, thus improving the success rate of the procedures by up to 97%. Ultrasonographic diagnosis requires the identification of fluid in the pleural space with the typical anechoic (black) image between the diaphragm and the chest wall, which allows even small amounts of fluid to be identified.[4,5]

Regarding the etiology of the pleural effusion, ultrasound does not allow sufficient discrimination in the different etiologies and the compositions of the effusion. The

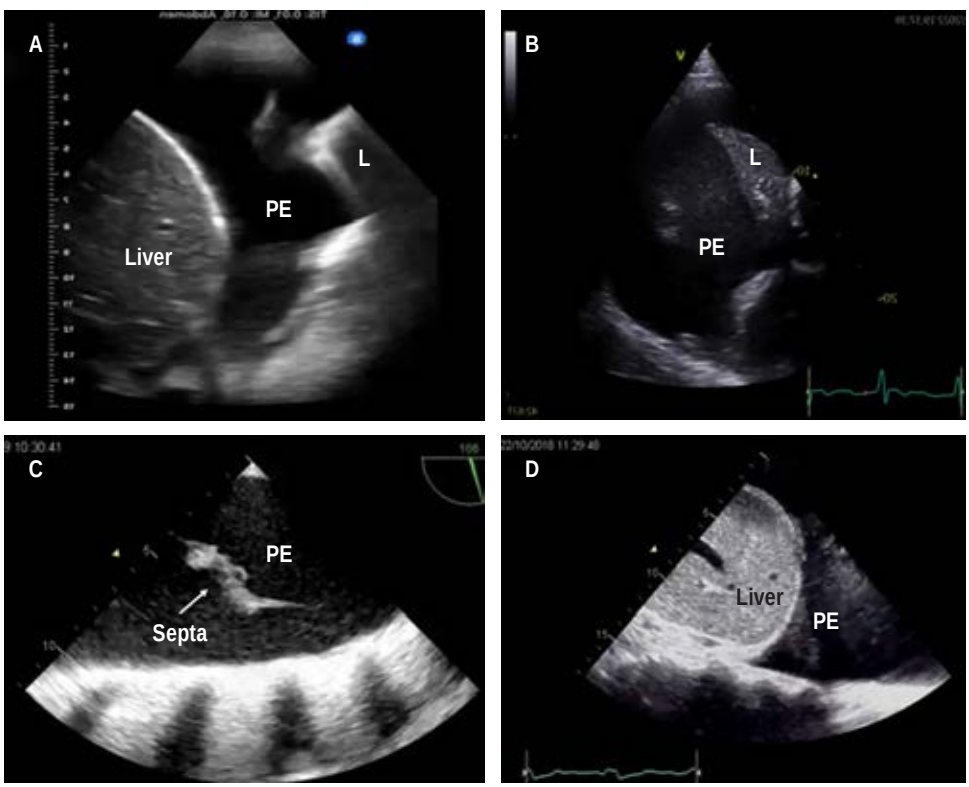

Figure 1:

A) Anechoic pleural effusion, suggesting transudate.
B) Non-septated complex pleural effusion.
C) Septated complex pleural effusion.
D) Homogeneously echogenic pleural effusion. **B-D)** Correspond to exudate.
PE = pleural effusion. L = lung (compressive atelectasis).

sonomorphological characteristics may vary depending on its nature, cause, and chronicity. The appearance of the pleural fluid can be divided into four patterns: (1) anechoic *(Figure 1A)*, (2) non-septated complex (defined by the presence of particles within the pleural fluid) *(Figure 1B)*, (3) septated complex (defined by the presence of septa and fibrin in the pleural fluid) *(Figure 1C)*, and (4) homogeneously echogenic («bright» pleural effusion) *(Figure 1D)*, the last being the most common in hemothorax and empiema.[6]

Importance

In chest X-ray, the accuracy to quantify the volume of the effusion is limited. Ultrasound allows for the detection of volume from 5 mL and volume quantification. Some formulas have been described for the quantitation of the effusion.[7,8] Balik's method found a significant positive correlation between the volume quantitation and the drained measurement. In addition to the quantitation of the effusion volume, Balik's method also allowed decision making regarding the realization of the therapeutic drainage, with success in guiding thoracentesis of 100% and no complications such as pneumothorax or bleeding reported.[9]

Investigation goals

Our primary goal was to determine the correlation between the amount of pleural fluid quantified by ultrasonography using Balik's formula and the amount of fluid drained in the postoperative period of cardiac surgery. Our secondary objective was to determine the diagnostic accuracy of the ultrasonographic characteristics of the fluid to classify it as transudate or exudate.

MATERIAL AND METHODS

This was a cross-sectional study of 26 nonconsecutive adult patients who were admitted to the critical care unit at the *Instituto Nacional de Cardiología Ignacio Chávez* in Mexico City, Mexico, from 1 May to 30 October 2021, following cardiac surgery, in whom ultrasonographic evaluation was conducted upon arrival in postoperative critical care. For the ultrasonographic evaluation, operator-obtained images were generated using a phased array sector probe at 2-3 MHz, from the patient's right or left side, with sonographic equipment including the following modes: M-mode, 2D mode, color Doppler, pulsed wave Doppler, continuous wave Doppler, and tissue Doppler. The use of sonographic equipment with advanced software technology was not necessary. With the patient in a mild torso elevation of 15°, the transducer was placed at the PLAPS point (intersection between the posterior axillary line and the 7th or 8th intercostal space, slightly above the diaphragm),[5] with the probe marker pointing toward the patient's head. The diaphragm, liver, and spleen had to be clearly visualized *(Figure 2)*. Then, the maximum distance in millimeters was measured between the parietal (from the lung inferior border) and visceral (to the inferior border of the diaphragm) pleura at maximum inspiration *(Figure 3)* using the formula: volume = 20 × separation (in millimeters).

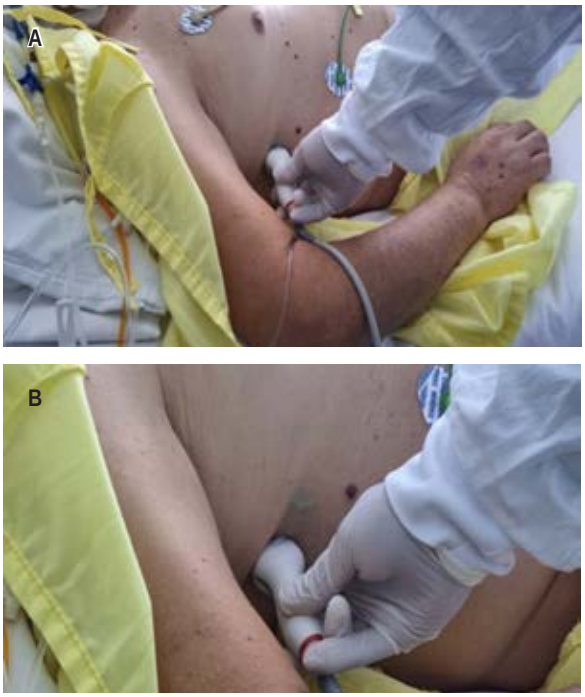

Figure 2: A) Position of the ultrasound probe at the patient's right or left side. **B)** Probe marker pointing toward the patient's head.

Then, the pleural effusion was classified by ultrasonography as:

1. Transudate (anechoic) or
2. Exudate (non-septated complex, septated complex, and homogeneously echogenic).

Images were processed and analyzed after acquisition. One physician (a critical care physician with training in critical care ultrasonography) acquired the images, and the images were then processed and measured by three different physicians (clinical cardiologists, DMS, EGC, and ELD with training in echocardiography) using imaging software. We reduced bias by blinding the person who analyzed, processed, and measured the images.

The thoracic tubes were placed by the cardiothoracic surgery service after performing the ultrasound making,

without real-time guide, using Argyle TM Thoracic Catheters of 32 Fr when the effusion was echogenic or complex, and Blake drains (usually 24 Fr), when the effusion was anechoic.

The biochemical analysis of the fluid was performed to classify the pleural effusion as exudate according to Light's criteria:[10]

1. The ratio of pleural fluid protein to serum protein is greater than 0.5.
2. The ratio of pleural fluid lactate dehydrogenase (LDH) and serum LDH is greater than 0.6.
3. Pleural fluid LDH is greater than 0.6 or 2/3 times the normal upper limit for serum.

Statistical analysis

We performed the Shapiro-Wilk test of normality for continuous variables and reported these as a median and interquartile range because all were nonparametric. Comparisons of continuous variables were made using the Kruskal-Wallis test. We report categorical variables as frequencies and percentages and used χ^2 or Fisher's exact probability tests, as appropriate, to compare expected values. We used Pearson's correlation coefficient to calculate correlation coefficients, with the following r value strength categories: 0.1-0.29 = weak, 0.3-0.49 = medium, and 0.50-1.0 = strong. We used 2 × 2 tables to calculate sensitivity, specificity, predictive values, and likelihood ratios. Statistical analyses were performed using STATA v. 14, and $p < 0.05$ was considered statistically significant.

RESULTS

Demographic and surgical characteristics

Most patients were males (65%) with a mean age of 55 years (range 45-64 years). The most frequent comorbidities were heart failure (65.4%), hypertension (34.6%), and history of myocardial infarction (23.1%). The median of the left ventricular ejection fraction was 45%. The most frequently used drugs in the preoperative period were beta-blockers, anticoagulants, statins, antiplatelet drugs, diuretics, angiotensin-converting enzyme inhibitors, and angiotensin II receptor antagonists *(Table 1)*. The most frequent surgery was aortic valve replacement in 34.6%, followed by coronary artery bypass graft surgery in 15.4% with a mean extracorporeal circulation time of 157 minutes and aortic clamping of 107 minutes *(Table 2)*.

Characteristics of pleural effusion

The median volume quantified by ultrasound was 600 mL, and the median volume drained was 550 mL. There was a strong positive correlation ($r = 0.67$, $p < 0.0001$). Of the total number of patients, pleural effusion was classified as transudate by ultrasonography in 15 patients (57.7%) and by Light's criteria in 16 patients (61.5%). The most frequent drainage method was tube thoracostomy (84.6%), being more frequent on the left side (53.8%) *(Table 3)*. When the diagnostic test evaluation for the presence of transudate vs. exudate by ultrasound was performed and compared with Light's criteria, the sensitivity and specificity were 81.25% and 80%, respectively. There was a positive predictive value

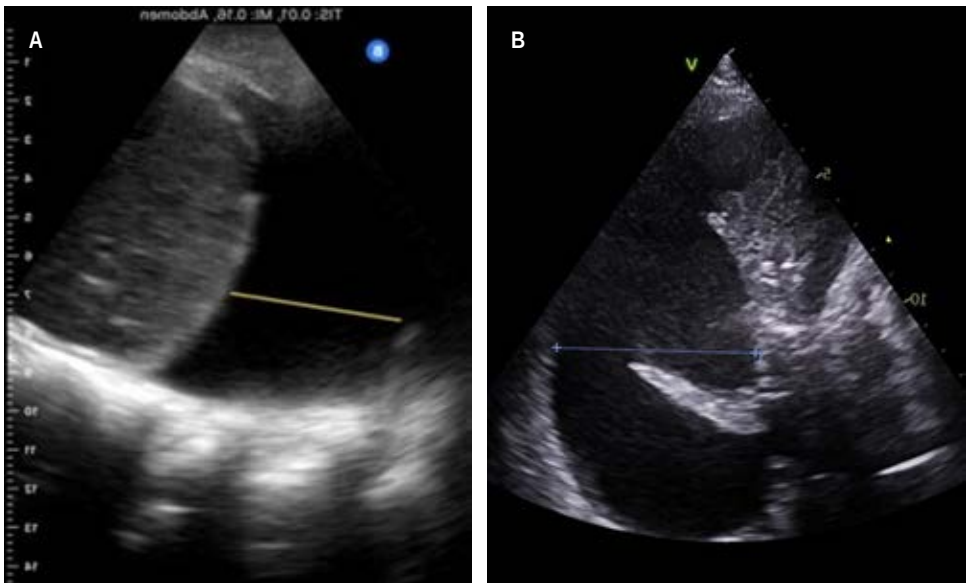

Figure 3:

The measurement is made from the lower border of the lung (parietal pleura) to the abdominal structure (visceral pleura). **A)** Anechoic pleural effusion. **B)** Non-septated complex pleural effusion.

Table 1: Baseline characteristics.

Variable	n (%)
Age (years), median [IQR]	55 [45-64]
LVEF (%), median [IQR]	45 [32-54]
Gender	
Men	17 (65.4)
Women	9 (34.6)
Body mass index	
Underweight	2 (7.7)
Normal range	10 (38.5)
Overweight	7 (26.9)
Obese class I	6 (23.1)
Obese class III	1 (3.8)
Heart failure	17 (65.4)
Hypertension	9 (34.6)
Prior myocardial infarction	6 (23.1)
Dyslipidemia	4 (15.4)
Diabetes	4 (15.4)
Stroke	3 (11.5)
Chronic obstructive pulmonary disease	1 (3.8)
Chronic renal disease	1 (3.8)
Peripheral vascular disease	1 (3.8)
Prior medication	
Beta-blockers	11 (42.3)
Anticoagulants	10 (38.5)
Statins	10 (38.5)
Diuretics	9 (34.6)
Antiplatelet drugs	8 (30.8)
Angiotensin-converting enzyme inhibitors	7 (26.9)
Angiotensin II receptor antagonists	6 (23.1)
Aldosterone antagonists	4 (15.4)
Oral hypoglycemic drugs	3 (11.5)
Calcium channel blockers	3 (11.5)
Cardiac glycoside	2 (7.7)
Amiodarone	2 (7.7)
Levothyroxine	1 (3.8)
Allopurinol	1 (3.8)

LVEF = left ventricular ejection fraction. IQR = interquartile range.

of 86.66%, a negative predictive value of 72.73%, and a positive likelihood ratio of 4 *(Table 4)*.

DISCUSSION

Pleural effusion occurs frequently in patients admitted to intensive care units and varies according to the technique used, from 8% with physical examination to 60% using imaging techniques. Early drainage of clinically significant pleural effusion is associated with improved oxygenation and diagnostic accuracy without increased complications.[11] In postoperative cardiac surgery patients, pleural effusion can cause atelectasis, increased risk of pneumonia and empyema, arrhythmias (such as atrial fibrillation), prolonged in-hospital stay, need for hemodialysis, and higher mortality.[3] Modifiable associated factors in the management of drains that may contribute to the accumulation of pleural effusion include early removal of chest drains, higher outputs, and removal during or close to mechanical ventilation.[12] Risk factors that have been identified include being female and previous conditions such as heart failure, atrial fibrillation, peripheral vascular disease, and prior use of anticoagulant or antiarrhythmic agents.[13] In addition, dedicated follow-up and treatment of postoperative effusions enhance recovery by 15% measured by improvement in the distance walked one month after cardiac surgery.[14]

Table 2: Surgical characteristics.

Variable	n (%)
Surgery	
Aortic valve replacement	9 (34.6)
Coronary artery bypass graft	4 (15.4)
Coronary artery bypass graft + aortic valve replacement	3 (11.5)
Mitral valve replacement	2 (7.7)
Mitral valve replacement + aortic valve replacement	2 (7.7)
Coronary artery bypass graft + mitroaortic valve replacement	2 (7.7)
Coronary artery bypass graft + mitral valve replacement	1 (3.8)
Extracorporeal circulation time (min), median [IQR]	157 [110-214]
Aortic clamping (min), median [IQR]	107 [89-147]

IQR = interquartile range.

Table 3: Characteristics of pleural effusion.

Variable	n (%)
Ultrasonographic classification	
Transudate	15 (57.7)
Exudate	11 (42.3)
Light's criteria classification	
Transudate	16 (61.5)
Exudate	10 (38.5)
Drainage method	
Thoracentesis	4 (15.4)
Thoracic tube	22 (84.6)
Localization	
Left lung	14 (53.8)
Right lung	12 (46.2)
Ultrasonically quantified volume (mL), median [IQR]	600 [400-800]
Drained volume (mL), median [IQR]	550 [440-800]

IQR = interquartile range.

Table 4: Diagnostic test evaluation for the diagnosis of transudate vs exudate by ultrasound.

	Light's criteria		
	Transudate n (%)	Exudate n (%)	Total n (%)
Ultrasound			
Transudate	13 (81.2)	2 (20.0)	15 (57.7)
Exudate	3 (18.7)	8 (80.0)	11 (42.3)
Total	16 (100.0)	10 (100.0)	26 (100.0)
Diagnostic test evaluation			
Sensitivity	81.25%		
Specificity	80.00%		
PPV	86.66%		
NPV	72.73%		
LR +	4.06		
LR -	0.23		
Accuracy	80.77		

PPV = positive predictive value. NPV = negative predictive value. LR = likelihood ratio.

In our study, most of the population was male, with a median age of 55 years. The majority of the patients had a history of heart failure, followed by hypertension and myocardial infarction, which suggests that these patients could have a greater probability of presenting pleural effusion in the postoperative period due to increased hydrostatic pressure.

Among the drugs administered to our patients, a higher proportion of patients were taking anticoagulants and antiplatelet drugs, which could also contribute to the development of pleural effusion. Regarding surgical variables, the median extracorporeal circulation time was 157 minutes, and the aortic clamping time was 107 minutes, which suggest that prolonged extracorporeal circulation pump and aortic clamping times (> 100 minutes) may be a risk factor for developing pleural effusion due to increased bleeding.

The median volume measured by ultrasonography was 600 mL, and one evacuate was 550 mL. When the correlation was determined between the measurement performed by ultrasound using Balik's formula and the volume of liquid drained, there was a strong positive correlation. In the only previous study evaluating the estimation of volume by ultrasound in the postoperative period of cardiac surgery, the maximal distance between mid-height of the diaphragm and visceral pleura, using the formula volume = 16 × separation (in millimeters), was used, and the authors found a significant positive correlation between the volume estimated and the volume drained. The ultrasonographic characteristics of the effusion were not described.[15]

Although there are studies that have previously compared formulas for the quantitation of pleural effusion, the equation used by us and proposed by Balik et al.[9] is validated for mechanically ventilated patients in a supine position and with a mild torso elevation of 15º. This is the position in which we usually find our patients in the intensive care unit in the immediate period after cardiac surgery, so we think it is more adequate in this population.

When the characteristics of the pleural effusion were evaluated by ultrasonography, we found that 57% corresponded to transudates and the rest to exudates, according to the echogenicity of the effusion. When the fluid was evacuated, the type of effusion was corroborated by Light's criteria. A total of 61% corresponded to transudate.

Yang et al. evaluated a cohort of 320 patients with pleural effusion, finding high sensitivity, but poor specificity of anechoic effusions for transudative effusions.[16] In a cohort of 126 patients with transudative pleural effusions, Chen et al. found that an anechoic pattern was present in 45% (57/127), while a complex non-septated pattern was seen in 55% (70/127); transudative fluid was never complex septated or homogeneously echogenic.[17] A recent evaluation of 300 pleural effusions in 285 patients demonstrated that the detection of septations or homogenous complexity was 94% specific and carried a 96% positive predictive value for exudative fluid. Furthermore, anechoic fluid did not reliably predict the presence of transudative fluid.[18] Regarding the analysis of the characteristics of the fluid by ultrasound, in our series, high sensitivity, positive predictive value, and positive likelihood ratio (81.25%, 86.66%, and 4.06, respectively) stood out. It is important to mention that this is the first time that these findings have been evaluated in postoperative cardiac surgery patients who had an increased risk of transudate due to increased hydrostatic pressure.

Regarding the exudates, when a septated complex and homogeneously echogenic pleural effusion was identified by ultrasound, it always corresponded to exudate according to Light's criteria.

Complications associated with chest tube placement are reported in the medical literature in up to 40% of cases.[19] In 22 of the patients of our study (84%), the effusion was evacuated by placing a thoracic tube without complications. The complications that occurred were: one patient with tube malposition, one patient with minor bleeding from the insertion site, one patient with insertion site infection, and one patient with re-expansion pulmonary edema.

In up to 84% of the patients, the effusion was evacuated by placing a thoracic tube without complications, even though complications associated with the placement of a chest tube are reported in 20-30% of cases. The most frequent location of pleural effusion was on the left side in up to 53% of cases, as previously reported,[19] which suggests that the anatomical relationship of the heart with the left pleura could be a factor in the patients who presented with a greater effusion on the left side.

Study limitations

This study was conducted at a single medical center and should be replicated at other centers to assess the protocol's reproducibility. In addition, study outcomes should be interpreted with caution due to the small sample size and because it was performed in a specific subpopulation (postoperative cardiac surgery patients). Thus, the findings may not generalize to all critical care patients. Finally, given that the study was conducted in a cardiovascular critical care unit, where point-of-care ultrasonography evaluation is routine, adequate training is necessary before applying these techniques.

CONCLUSION

We found a strong positive correlation between the volume of pleural effusion quantified with Balik's formula by ultrasound and the volume drained in postoperative cardiac surgery patients. We also found an adequate diagnostic accuracy of the ultrasound in the identification of the type of effusion compared with Light's criteria.

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Respiratory causes of death in Mexico 2021

Muertes de origen respiratorio en México en 2021

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ABSTRACT. Introduction: in the international classification of diseases (ICD-10), deaths of primary respiratory origin are scattered across several sections, uncommonly compiled together as often happens with neoplasias and cardiovascular deaths, leading to underestimation of the impact of respiratory diseases and the influx of resources to the patients. **Material and methods:** mortality statistics for Mexico for 2021 coded with the ICD-10 were reviewed. All causes of death, primarily respiratory, were added, both from section J, and from those distributed in other sections, and compared against those that occurred in 2015. **Results:** in 2015, 79,383 respiratory deaths (12.6% of the total) were coded, of which 54,173 were in the respiratory «J» codes and the rest (25,210) in other codes, while in 2021 there were 349,491 (31% of the total), an impressive increase due to the COVID-19 pandemic. The most common causes of death were COPD, pneumonia-influenza, malignant tumors of the chest, neonatal respiratory deaths, disorders of the pulmonary circulation, interstitial diseases, asthma, and tuberculosis. **Conclusions:** respiratory diseases are an important cause of death in Mexico with and without respiratory pandemic, so the appropriate training of personnel and granting sufficient resources to care for the sick must be supported.

Keywords: ICD-10, respiratory tract diseases, mortality.

RESUMEN. Introducción: en la clasificación internacional de enfermedades (ICD-10) las muertes de origen primario respiratorio se encuentran dispersas por varios apartados y cuando no se agrupan todas se infravalora su importancia, lo que puede reducir el impacto público de las enfermedades respiratorias y la afluencia de recursos y tratamientos para los pacientes. **Material y métodos:** se revisaron las estadísticas de mortalidad de México de 2021 codificada con la décima clasificación internacional (ICD-10). Se sumaron todas las causas de muerte primariamente respiratoria tanto del apartado J, como las distribuidas en otros apartados y se compararon contra las ocurridas en 2015. **Resultados:** se codificaron en 2015, 79,383 muertes respiratorias (12.6% del total), de las cuales 54,173 estaban en los códigos respiratorios «J» y el resto (25,210) en otros códigos mientras que en 2021 fueron 349,491 (31% del total), un incremento impresionante debido a la pandemia de COVID-19. Dejando de lado el COVID-19, las causas más comunes de muerte de origen respiratorio fueron la enfermedad pulmonar obstructiva crónica, la neumonía-influenza, los tumores malignos del tórax, las muertes respiratorias neonatales, los trastornos de la circulación pulmonar, las enfermedades intersticiales, el asma y la tuberculosis. **Conclusiones:** las enfermedades respiratorias son causa importante de muerte en México con y sin pandemia respiratoria, por lo que se debe apoyar el entrenamiento de personal capacitado y recursos suficientes para la atención de los enfermos.

Palabras clave: ICD-10, enfermedades del tracto respiratorio, mortalidad.

INTRODUCTION

Respiratory diseases are a primary cause of mortality and morbidity in the world,[1] much more remarkable once acute and chronic causes are added, as well as infectious and non-infectious ones. This fact can be intuited by observing that, worldwide, several respiratory diseases appear in the first 10 causes of disease and death, chronic obstructive pulmonary disease (COPD) is the third cause of death.[2]

In the current International Classification of Diseases (ICD-10) the main acute and chronic respiratory diseases of the entire respiratory tract and chest are in section «J»;[3] however, many others are classified in other sections.[2] The objective of this work, an update of the one carried out in 2015,[4] is to describe the main causes of respiratory death

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in Mexico in 2021 and compare them with those of 2015. This description is important, since the causes of respiratory origin are scattered throughout several chapters of the ICD-10, and at the national and international level there is an underestimation of the importance of respiratory diseases that can decrease awareness about them in general and especially about chronic diseases, this in turn can lead to a scarce budget allocation and poor patient care, in addition to a decreased influx of people interested in training in respiratory diseases at least in some countries, who maybe deficient in qualified personnel to care for them.

MATERIAL AND METHODS

For this work, the mortality statistics of Mexico in 2021, codified with the tenth edition of the International Classification of Diseases (ICD-10),[3] were analyzed. Those of 2015 were taken from the World Health Organization (WHO) website, which are the statistics that each country reports and were the reason for a previous study.[4] As ICD-10 incorporates in its latest versions thousands of diagnostic codes and procedures, we use clinical classification software (CCS) that reduces the diagnostic codes to 285 mutually exclusive *(Table 1)*[5] and additionally according to the scheme of Becker and collaborators[6] that reduces them to less than 100, in order to describe in a standardized way the main certified causes of death that include a classifiable cause. Subsequently, all causes of death of respiratory origin classified within any chapter of ICD-10[2] were grouped, including those within and outside respiratory group «J».

RESULTS

Table 1 shows the respiratory deaths coded outside group J (25,210) and those within group J (54,173), for a total of 79,383 deaths of respiratory origin in 2015, of which approximately one third were classified outside section J. In 2021, respiratory deaths totaled 349,491 (31% of the total). These grouped totals are calculated in the same way, summing scattered causes in different chapters of the classification and, therefore, have overlapping codes. For example, respiratory cancers appear in the total of respiratory deaths and in the total of cancer deaths, and pulmonary vascular diseases appear in both respiratory and cardiovascular diseases. *Table 2* describes the main causes of death in Mexico according to clinical classification software (CCS)[5] with mutually exclusive groupings.

DISCUSSION

The results described highlight the importance in Mexico of respiratory diseases, much more notable in 2021 due to the COVID-19 pandemic, a primarily respiratory disease. While recognizing that SARS-CoV-2 generates multi-system complications especially in the so-called prolonged COVID, the main cause of death is respiratory failure. In addition, the respiratory ailments, frequent and not, that caused certified deaths in Mexico are described. This information is important for planning services and training respiratory disease experts. Except for COVID-19, the distribution in 2015 and 2021 is similar with the exception of some codes that increased in 2021 substantially compared to 2015, but which may be contaminated by the COVID-19 pandemic such as influenza and pneumonia, respiratory failure, and acute respiratory distress syndrome (ARDS) *(Table 1)*.

Several groups of diseases that would need to be reinforced in assistance and training programs for adults and children draw attention. In adults are notable *cor pulmonale*, pulmonary arterial hypertension, diseases of the pulmonary vasculature and the obesity syndrome hypoventilation and sleep apnea, which already causes significant morbidity and is growing in proportion to obesity. They also highlight benign and malignant chest tumors, HIV respiratory complications, and acute and chronic respiratory failure. But without a doubt, COPD, pneumonia and influenza cause the majority of respiratory deaths.

In general, respiratory diseases, especially chronic ones, are under diagnosed and under treated, while a growing increase in their causal factors can be demonstrated: smoking, exposure to polluted air, overcrowding, survival of premature children with bronchopulmonary dysplasia, population aging and the persistence of other factors such as poverty, the use of solid fuels and limited access to health services.

The determinants of the minimization of respiratory diseases are undoubtedly several, and include the efficient management of groups interested in other diseases, which can contribute to the heterogeneous way of classifying deaths, since some codes are derived from etiology, while others are based on pathophysiological mechanisms, and others are classified by affected organ or system.

This heterogeneous way of classifying weakens the position of specialists focused on an apparatus or system, such as the respiratory system, whose causes of death are broken down into several sections of the ICD-10.[2] For example, perinatal respiratory problems and those related to pregnancy, childbirth and the puerperium are classified separately from group J, which helps to highlight the significant health risk posed by the reproductive phenomenon, especially in some regions. The same applies to respiratory complications of rheumatic diseases and those of external agents.

However, this strategy is done at the expense of diluting the relevance of the respiratory system as an organ of shock and in a health system that competes for limited and fixed resources, whether economic or human, it can

Table 1: Respiratory deaths in and out of ICD-2015 and 2021 «J» codes.

Deaths due to respiratory disorder	2015	2021
COVID-19	–	238,677
COPD, emphysema, BC (J41-44)	23,851	21,212
Influenza and pneumonia (J10-18)	18,458	54,596
Malignant tumors of the chest (C30-40)	7,825	7,678
Neonatal hypoxia, aspiration, neonatal pneumonia	6,817	4,840
Drowning	4,949	3,778
Interstitial lung disease* (J45-46)	3,181	3,962
Other respiratory diseases (J98)	2,768	1,885
Cor pulmonale, thromboembolism, PAH (I26-28)	2,108	2,464
Tb and complications (A15, A16, A19, B90.9)	1,983	2,133
Asthma (J45-46)	1,296	1,426
NS low ARI (J22)	743	405
HIV and *P. jirovecii* or with pneumonia	697	747
Pulmonary edema (J81)	657	664
Lung damage from external agents (J68-70)	645	710
Respiratory failure (J96)	550	909
Effusion, pneumothorax, and pleural diseases (J90-94)	524	779
Pulmonary or pleural suppuration (J85-86)	394	504
Acute bronchitis (J20)	376	252
Congenital respiratory malformations	294	184
Unspecified bronchitis (J40)	208	69
ARDS (J80)	164	882
Pulmonary cystic fibrosis	144	169
Superior ARI (J0-6)	136	87
Diseases of the nose, sinuses, throat, larynx (J30-39)	135	144
Acute bronchiolitis (J21)	87	35
Air or fat embolism, traumatic or for other cause	72	55
Obesity-hypoventilation syndrome (E66.2)	62	49
Poorly specified thoracic tumors (C76.1)	54	37
Sleep apnea (G47.3)	43	71
Ear and mastoid problems	38	34
Pertussis	36	19
Benign chest tumors (D14, 15, 19)	26	5
Lung aspergillosis	15	28
Congenital and acquired chest deformities	14	7
Pulmonary coccidioidomycosis	8	10

Contents

Table 1 continues: Respiratory deaths in and out of ICD-2015 and 2021 «J» codes.

Deaths due to respiratory disorder	2015	2021
Pulmonary candidiasis	8	13
Pulmonary histoplasmosis	5	12
Pneumocystosis	4	10
Pulmonary zygomycosis	0	4

ICD = International Classification of Diseases. COPD = chronic obstructive pulmonary disease. BC = chronic bronchitis. ARI = acute respiratory infection. NE = non-specific. HIV = human immunodeficiency virus. ARDS = acute respiratory distress syndrome.
Deaths in J codes are identified in the table. Total non-respiratory deaths 548,254, group respiratory deaths were 54,173 (25,210 out of group J). One reported case of non-tuberculous mycobacteriosis, pulmonary nocardiosis, cryptococcosis: pulmonary, pulmonary toxoplasmosis and pulmonary paracoccidioidomycosis and two deaths from HIV and lymphoid interstitial pneumonia and pulmonary actinomycosis.
* Includes idiopathic, by rheumatic disease and external factors, organic and inorganic powders. See annex for ICD-10 codes not specified in the table. In 2021 total coded deaths 1,116,705, 767,214 non-respiratory. One death due to non-tuberculous mycobacteriosis (A31), HIV and LIP (B22.1), pulmonary cryptococcosis B45, pulmonary or respiratory echinococcosis, pulmonary sarcoidosis D86, pulmonary toxoplasmosis B58.

Table 2: Main grouped causes of death (Mexico 2015 and 2021).

Disease	2015	2021
COVID-19 (U7-10)	–	238,781
Diabetes (E10-E14)	96,508	140,729
Myocardial ischemia (I20-I25)	85,967	176,639
Cirrhosis, hepatitis and other liver diseases (K70-K76)	34,932	41,890
Cerebrovascular diseases (I60-I69)	33,409	37,169
Chronic diseases of the lower airway (J40-J47)	25,424	22,748
Hypertensive disease (I10-I15)	22,754	31,382
Homicides (X85-Y09)	19,968	35,700
Influenza and pneumonia (J10-J18)	18,458	54,596
Traffic accidents (V00-V89)	16,148	15,066
Perinatal deaths (P00-P96)	12,844	10,331
Total deaths of the year	665,688	1’116,705

Grouping of deaths classified by ICD-10 according to LC-CODE grouping.

be disadvantageous for the adequate care of respiratory diseases, especially those that lack well-defined etiological agents, or when they are multiple, as well as for having personnel trained in these diseases. It is still contradictory from the historical point of view for the respiratory specialty that tuberculosis, the origin of pneumology, is classified outside the respiratory group and within infectious diseases, very correct by etiological agent, but excluded from the respiratory group. From a practical point of view, the classification by etiology, and not by organ or system, or by altered function, or as it originally occurred, by symptoms or syndrome, is the most recent and advanced, and allows to identify preventive measures. However, we have examples where having an etiological agent, such as smoking, with multiple consequences and damaged organs, a group based on a relatively non-specific functional alteration is maintained, such as chronic obstruction to the passage of air, which immediately calls for intervention with bronchodilators, but not with measures to stop smoking, the main cause in almost everyone.

The data shown have known limitations, since they are based on death certificates[7] and on using, in general, only one cause of death and not several described in the certificate.[8-10] When multiple causes of death are used, an even greater increase in the contribution of respiratory diseases is expected than that described in this work using only one.[10-12] But similar results are obtained from widely used estimates based on disease models and risk factors, such as those of the Global Burden of Diseases[1] information with which an analysis of the health situation in Mexico was made.[13]

CONCLUSION

In addition to mortality, it is important to consider other health indicators, such as the disease itself, disability and the use of health services that undoubtedly contribute to the burden of disease in a country. Within respiratory diseases, asthma and several diseases of the upper airway generate a considerable burden of disability and care services, but on the other hand the impact on deaths is limited, although relevant since they are considered preventable deaths *(Table 1)*.

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Clinical and immunologic characteristics of tuberculosis: comparison between children and adults

Características clínicas e inmunológicas de tuberculosis: comparación entre niños y adultos

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ABSTRACT. Pulmonary tuberculosis (PTB) remains a global public health problem, despite the efforts made in programs to eliminate it, the goals have not been attained, partially due to limitations in the time of diagnosis of the disease, which allows transmission to others. PTB is an infectious disease that infects people of all ages, when diagnosing PTB in children, it is necessary to take into account the age-specific characteristics of the disease, since although the risk of PTB is higher in younger infants, from the age of five the risk decreases, they have a functional immune response similar to that of adults and it must be taken into account that transmission in children is usually by close contact with an adult patient with PTB. The diagnosis of TB in children and adults is based on a combination of clinical, radiological, microbiological and immunological findings. In this review we identify the main clinical differences that occur in children and adults with TB and the differences between clinical guidelines and research reports, as well as immunological findings that could have an application in timely diagnosis.

Keywords: pulmonary tuberculosis, diagnosis, clinical features, immunologic features.

RESUMEN. La tuberculosis pulmonar continúa siendo un problema de salud pública a nivel global, a pesar de los esfuerzos en programas para eliminarla, las metas no se han alcanzado, en parte por las limitaciones en el tiempo del diagnóstico de la enfermedad, lo que permite la transmisión a otras personas. La tuberculosis pulmonar es una enfermedad infecciosa que infecta a las personas de todas las edades, pero en particular cuando se trata de diagnosticar tuberculosis pulmonar en niños, es necesario considerar las características específicas de la edad, ya que mientras el riesgo de tuberculosis pulmonar es mayor en los lactantes más pequeños, a partir de cinco años disminuye el riesgo, ya que poseen una respuesta inmunitaria funcional similar a la de los adultos y se debe tomar en cuenta que la transmisión en niños generalmente es por contacto estrecho con un paciente adulto con tuberculosis pulmonar. El diagnóstico de la tuberculosis en niños y adultos se basa en una combinación de hallazgos clínicos, radiológicos, microbiológicos e inmunológicos. En esta revisión identificamos las principales diferencias clínicas que se presentan en niños y adultos con tuberculosis y diferencias entre las guías clínicas y los reportes de investigación, así como los hallazgos inmunológicos que podrían tener una aplicación en el diagnóstico oportuno.

Palabras clave: tuberculosis pulmonar, diagnóstico, características clínicas, características inmunológicas.

INTRODUCTION

Tuberculosis (TB) is a disease spread through the air that can infect people of all ages. Because of the route of transmission, pulmonary tuberculosis (PTB) is the most common clinical form. The World Health Organization (WHO) estimates that 10.0 million people were infected with TB in 2019, of which 56% are adult men (≥ 15 years), 32% adult women (≥ 15 years) and 12% are children (< 15 years).[1] In an *M. tuberculosis* infection there are differences

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in bacillary load, diagnosis, disease spectrum, risk factors and clinical characteristics that vary according to the age of the infected subjects.[2,3]

Neonates (0-12 months) and infants (12-24 months) are five to 10 times more likely to progress to active TB after infection, and are also more likely to develop severe and disseminated forms of the disease. Most adults are able to contain *M. tuberculosis* without developing active disease or eliminating the microorganism and it is estimated that only 5-10% of infected people will develop active TB.[4] Age and maturation of the immune system are major promoters involved in the development and phenotype of TB infection. Changes in risk and disease development have been observed at different stages of growth *(Table 1)*.[5,6]

CLINICAL MANIFESTATIONS OF PULMONARY TB IN CHILDREN AND ADULTS

Adults and children with PTB show varied and distinct clinical manifestations. In children, clinical diagnosis is chosen over microbiological diagnosis, and although most cases have no signs or symptoms, it is estimated that a diagnosis is only achieved in 70% of cases.[7] Contact with a person with TB, contact history, is one of the most important factors in the clinical diagnosis of PBT in children.[8] In the case of adult contact with PTB, signs and symptoms may be common with other respiratory infections, making timely diagnosis and treatment of PTB difficult.[6] Children 5 to 10 years of age may have clinically silent disease while children under two years of age are more likely to have signs and symptoms of lung disease.[9-11] Some common constitutional symptoms include decreased appetite (alteration of weight percentiles in children under 15 years of age), fatigue, and fever *(Table 2)*.[11-13]

In infected adults, the signs and symptoms are clearer, among the main clinical manifestations are: fever, loss of appetite (weight loss), asthenia, profuse night sweats and general malaise. A special form of onset is tuberculous pneumonia, which may present as a radiological clinical manifestation similar to that of bacterial pneumonia *(Table 2)*.[6,8,13-16]

The WHO establishes a cough of any duration as a sign of PTB, in recent reports chronic and incessant cough that does not improve in more than three weeks, ruling out other causes, is mentioned; however, the Clinical Practice Guide mentions productive cough greater than two weeks, this being the only relevant clinical difference by time of evolution, in addition the information on signs and symptoms is scarce in children with TB who become the most affected by treatment.

DIAGNOSIS OF PULMONARY TB IN CHILDREN AND ADULTS

It is estimated that TB in all its forms affects up to a quarter of the world's population,[16] and that the disease of PTB is mostly underestimated in children, these data represent a challenge for the timely diagnosis of PTB. That is why the variety of signs and symptoms that occur, as well as the absence of these, should be evaluated and clinical data explored in the primary caregiver or the history of recent contacts.[11,17,18] The difficulty in establishing a definitive diagnosis, coupled with the frequency of extra pulmonary disease in young children, makes the public health priority lower than in adults.[19-22]

The diagnosis of PTB is based on multiple modalities, including clinical, radiological and bacteriological data. Clinically, children have forms of paucibacillary PTB (few *M. tuberculosis* bacilli) or extra pulmonary TB.[11,23,24] In neonates to school children (0-10 years) TB diagnostic tests are usually performed using invasive procedures.[25] For both adults and children we can include imaging studies such as chest radiography, which is commonly the most informative research, although there are significant differences, among which we can find according to age, high-resolution chest computed tomography (CT) that provides more accurate visualization, but its use should be limited to complicated cases.[11,18,25,26]

Microbiological diagnosis is limited by the difficulty of obtaining sputum samples in children, since they can rarely provide a sample of expectorated sputum, coupled with the fact that children produce few bacilli, makes microbiological isolation for bacilloscopy tests not very sensitive, the

Table 1: Risk of developing active tuberculosis (TB) at different stages of growth.[5,6]

	Age (%)					
	Young neonatal-infant	Older infant	Preschoolers	Schoolchildren	Adolescent	Adults
Pulmonary TB risk	30-40	10-20	5	2	10-20	5-10
Extrapulmonary TB risk	10-20	2-5	0.5	< 0.5	< 0.5	< 0.5

Young neonatal-infant: 0-12 months old. Older infant: 12-24 months old. Preschoolers: 2-5 years of age. Schoolchildren: 5-10 years of age. Adolescent: 11-19 years of age. Adults: 19 years of age and older.

Table 2: Tuberculosis (TB) clinical manifestations, signs and symptoms in children and adults.[6,8,11-16]

	Reports		Clinical Practice Guide		WHO consolidated guidelines on tuberculosis 2022. Diagnosis and treatment	
	Signs	**Symptoms**	**Signs**	**Symptoms**	**Signs**	**Symptoms**
Children	Lost of weight*	Night sweats	Lost of weight*	Weakness o fatigue	Lack of weight gain Delayed growth	Night sweats
	Fever of > 38 °C during at least two weeks, ruling out other common causes	Non-specific toxic signs	Fever	Lack of appetite	Fever	—
	Chronic and incessant cough that does not improve ≥ 3 three weeks	Signs of hypersensitivity such as erythema nodosum	Productive cough ≥ 2 weeks	—	Cough of any duration Chest pain Hemoptysis	—
	Wheezing Neonatal and infants: common Preschoolers and schoolchildren: uncommon	—	—	—	Dyspnea	—
Adults	Productive cough ≥ 2 weeks	Shivers	Productive cough ≥ 2 weeks	Night sweats	Cough of any duration	Night sweats
	Hemoptysis	Lack of appetite	Hemoptysis	Lack of appetite	Hemoptysis Chest pain Dyspnea	—
	Fever**	Fatigue	Fever	Fatigue General malaise	Fever	—
	Lost of weight	—	Lost of weight	—	Lost of weight	—

* According to the child's growth curve and percentile chart. ** Greater than 38.3 °C. Data from other Clinical Practice Guide reports.
World Health Organization (WHO) Consolidated Guidelines on Tuberculosis. Module 3: Diagnosis and treatment. Rapid diagnostic means for the detection of tuberculosis.

culture of *M. tuberculosis* only detects about 30-40% of cases in children.[7] So smear microscopy has been replaced by smear tests nucleic acid culture and amplification in children.[26,27] Although the WHO recommends the use of the Xpert MTB/RIF test for all children suspected of TB,[15] other studies show that the diagnostic value of the Xpert MTB/RIF in bronchoalveolar fluid (BALF) samples in patients with PTB has a high sensitivity and specificity, except for children.[28,29] In another study in children under 15 years of age, the Gene Xpert MTB/RIF test showed a sensitivity of 50% and a specificity of 96% in samples of gastric lavage, induced sputum and BALF, with a higher sensitivity than bacilloscopy.[30] Due to the above, molecular tests should be considered as a diagnostic tool in children without ruling out follow-up in children with negative tests.

In adults, the diagnosis is usually more timely and is based on microbiological tests such as bacilloscopy and the culture of *Mycobacterium tuberculosis* (*M. tuberculosis*), with the culture of *M. tuberculosis* being the gold standard test.[7,8] There are different diagnostic methods according to age, according to current reports and the Clinical Practice Guide *(Table 3)*.[8,11,15-17,31-34] Signs, symptoms and type of diagnosis may vary depending on age *(Figure 1)*.[1,6,7,9-11,24,26,31,35-37] Over time, more complex diagnostic methods have been developed and improved that allow us to approach the patient in a timely manner to carry out an adequate

Table 3: Diagnosis with chest X-ray, TST, nucleic acid amplification and IGRA in children and adults.[8,11,15-17,31-34]

	Data from other reports	Clinical Practice Guide	WHO consolidated guidelines on tuberculosis 2022. Diagnosis
Children	**Normal or lateral chest X-ray**		
	A primary complex, consisting of: opacification (mediastinal or subcarinal) and consolidation or a segmental lesion (infiltrate and atelectasis)	With unilateral infiltrate or pleural effusion not explainable by another cause	It has poor specificity and therefore very low performance for true positive TB
	Sputum bacilloscopy		
	Induction of sputum (warm saline) in cases of sampling is difficult.	In sputum and gastric juice with the disadvantage that it is paucibacillary	Basic diagnostic test, not very sensitive
	Tuberculin skin test		
	Immunocompromised children (including HIV positive children): > 5 mm and in all other children (with or without BCG vaccine): > 10 mm	Exposed to adults with active PTB ≥ 10 mm	> 5 mm in children with severe malnutrition, > 10 mm children exposed to adults with TB
	Xpert MTB/RIF or Xpert Ultra		
	Xpert MTB/RIF in pulmonary TB, and extrapulmonary detects 80%	It does not mention information about it	The Xpert Ultra test should be used as the initial diagnostic test for TB
	IGRA in children		
	It is limited, of low quality, little evidence of studies in neonates and schoolchildren. In children with HIV, sensitivity is low	It does not mention information about it	In children over 2 years of age
Adults	**Normal or lateral chest X-ray in adults**		
	Hilarlymph adenopathies, pleural effusion	Pulmonary consolidation, fibrous changes on chest X-ray suggestive of inactive PTB	Extensive cavernous disease may occur. It offers high sensitivity, but low specificity
	Sputum bacilloscopy in adults		
	Recommended, with 73% sensitivity	Rapid study, sensitivity (51.8%), specificity (97.5%) Nebulization with hypertonic sterile saline solution (3%) where it is not possible to obtain a sample spontaneously	It is a basic diagnostic technique It is not a very sensitive test Recommended for monitoring patients with treatment
	Tuberculin skin test in adults		
	People without risk factor: > 15 mm People where TB is endemic: > 10 mm People with recent contact or HIV: > 5 mm	≥ 10 mm or ≥ 5 in: close contact with active TB case, HIV, immunocompromise, corticosteroid use, immunosuppressive therapy	> 5 mm in recent contact with TB, > 10 mm in: injecting drug users, residents of high-risk groups * and > 15 mm in people without risk factors for contact with TB
	Xpert MTB/RIF in adults		
	High specificity (85-98%) High sensitivity for TB with positive bacilloscopy (96%) Lower sensitivity for TB with negative bacilloscopy (66%)	It does not mention information about it	It should be used as the initial TB diagnostic test and detection of rifampicin resistance
	IGRA in adults		
	> 95% specificity and better sensitivity when combined with TST	It does not mention information about it	Decreases exposure to TB preventive treatment

TST = tuberculin skin test. IGRA = interferon gamma release assays. WHO =World Health Organization. TB = tuberculosis. HIV: human immunodeficiency virus.
PTB = pulmonary tuberculosis. BCG = bacillus Calmette Guerin.
* People who are in jail, recent immigrants from countries that have a high TB burden.

treatment, although they also allow us to see that we still have a long way to go with the diagnostic methods used in children in PTB, which is complicated due to its variety of presentation and the damages that anti-tuberculosis drugs can generate in minors. This advancement of diagnostic methods has outpaced the Clinical Practice Guideline due to a lack of up-to-date information *(Figure 1 and Table 3)*.

The variety of signs and symptoms that patients may present according to the stage in which they are, together with the diagnostic methods that could be employed according to age, are shown in *Figure 1*.

As an alternative, different evaluations of both the hematological populations and the immune response of the host in response to *M. tuberculosis* infection have been proposed, which may be complementary to the diagnosis of TB and/or the follow-up of pharmacological therapy, although they are not routinely performed.[38]

HEMATOPOIETIC POPULATIONS IN CHILDREN AND ADULTS

Because hematologic populations vary with age, reports of hematologic counts from healthy subjects compared to patients with PTB at different ages were analyzed. In neonates, the immune system is in an immature state, which develops during the first years of life. The maturation of the immune system will depend in part on antigen exposure. This is why both children and older adults are more susceptible to infections in general.[39,40] Although some patients may have variations in the absolute numbers of hematologic subpopulations, when these values are compared in patients with PTB without comorbidities such as HIV, the number of hematologic cells is not significantly different in the different groups *(Table 4)*.[41-45]

Overall, monocyte, lymphocyte, and eosinophil counts in TB patients are within the normal range relative to healthy controls; however, in some patients, hematological alterations such as monocytosis, eosinophilia, lymphopenia, and neutrophilia have been reported,[5,46] some of these alterations have been associated with HIV co-infection.[43]

It is unclear how much variations in hematological values contribute to TB. What has been observed to a greater extent is susceptibility to TB in children attributed to an immature immune status.[47]

IMMUNODIAGNOSIS OF PULMONARY TB IN CHILDREN AND ADULTS

Because existing conventional diagnostic methods are often limited in time to diagnosis, sensitivity, and/or specificity, and are sometimes too costly or complex for resource-limited settings,[25,48] immunological studies based on host response to *M. tuberculosis* infection have been conducted, predicting treatment efficacy, reactivation of infection, and immune responses by vaccination.[49] Over the past few decades, different host response-based markers (biomarkers) have been proposed for the diagnosis of PTB, which have focused on diagnosing active PTB, latent TB, and measuring the efficacy of treatments.[38,49]

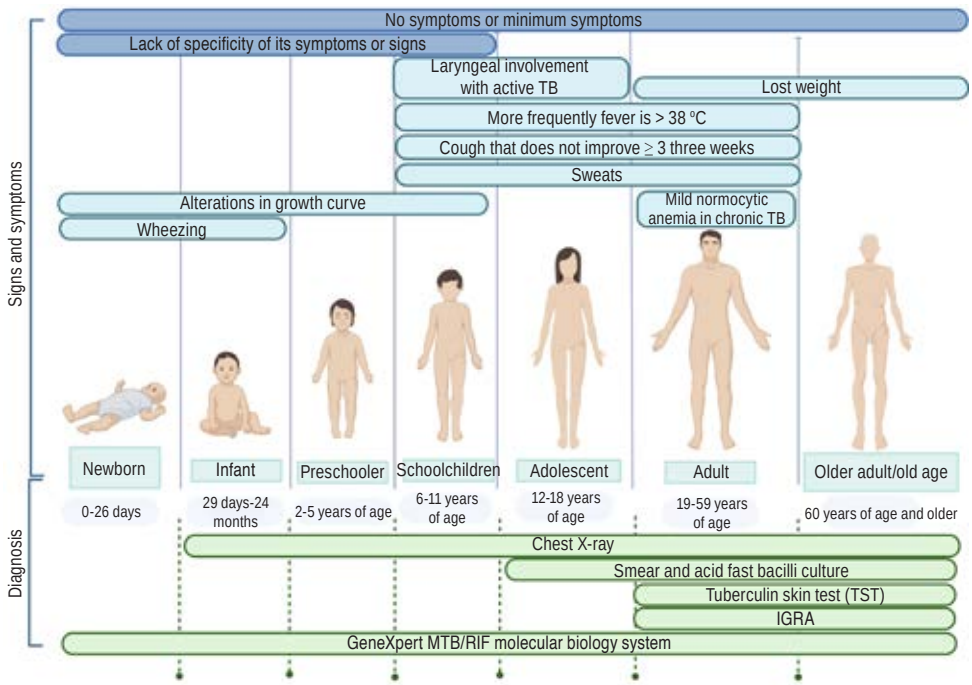

Figure 1:

Signs, symptoms and diagnostic according to age for pulmonary tuberculosis.[1,7,10,17,26,28,34,38-43]

Table 4: Comparison of hematopoietic cell counts in healthy and tuberculosis patients during neonatal-preschoolers and adult age.[5,41-47]

Cells	Condition	Neonatal-preschoolers* (× 10^3/mm^3)	Adolescents-adults** (× 10^3/mm^3)
Monocytes	Healthy	0.5-1.1	0.3-1.1
	Tuberculosis	0.83	0.41-0.69
Neutrophils	Healthy	1.5-8.5	1.8-7.7
	Tuberculosis	9.7	4.0-5.2
Eosinophils	Healthy	0.3	0.2-0.5
	Tuberculosis	0.2	1.7-3.8
Lymphocytes	Healthy	2.0-8.0	1.0-5.2
	Tuberculosis	4.7	1.5-2.1

* 0-5 years of age. ** > 11 years of age.

Table 5: Biomarkers for immunodiagnosis of tuberculosis in children and adults.[25,47,49-68]

Biomarker	Neonatals-infants	Adolescents and adults
Extracellular vesicles (EV)	Blood: LAM and LprG have been detected by immunoassay	Urine: LAM and CFP-10 (Rv3874) have been detected by I-PCR Serum: *M. tuberculosis* peptides by MRM-MS
Cytokines	Sputum: IFN-γ and IL-2 detection by ELISPOT Blood: detection of IFN-γ, IP-10, (TNF)-α, IL-1ra, IL-2, IL-13 and MIP-1β by multiplex immunoassay	Blood: Detection of IL-2 IL-1ra, IL-10 and TNF-α by multiplex immunoassay
miRNAs	Blood: the combined identification of: miR-1, miR-155, miR-31, miR-146a, miR-10a, miR-125, miR-150, miR-29 up regulated with 95.8% sensitivity and miR-29 down regulated with 95% sensitivity Serum: detection of let-7e, miR-146a, miR-148a, miR-192, miR-193a-5p, miR-451, miR-532-5p, miR-590 -5p, miR-660, miR-885-5p, miR-223, miR-30e, miR-25, miR-146	Pleural fluid: the combined identification of miR-3615, miR-4616, miR-378i that are expressed upwards in patients with active and latent TB Serum: A promising biomarker for the diagnosis of MDR-TB is Let-7e-5p, miR-155, miR-21-5p, miR-92a-3p and miR-148b-3p, miR-21-5p, miR-92a-3p and miR-148b-3p Sputum: miR-151, miR-409-3p, miR-1204, hsa-miR-376c, miR-23a Serum/Sputum: miR-1270, miR-371-3p, miR-380, miR-582-3p, miR-618
IP10/CXCL10	Blood: Detection of IP-10 using a sandwich ELISA	Urine: detection of IP-10 associated with treatment efficacy by ELISA
Lipoproteins	Plasma: *M. tuberculosis* lipoprotein (TLP) by ELISA	Serum: lipoprotein capture assay by ELISA
75 metabolites	Serum: detection of metabolites (leucine and kynurenine) by mass spectrometry	Urine: N-acetylhexosamine, neopterin, diacetylspermine and sialic acids by mass spectrometry

ELISPOT = enzyme-linked immunosorbent spot. I-PCR = immuno-polymerase chain reaction. MRM-MS = multiple reaction monitoring mass spectrometry assays. Bioplex = multiplex immunoassay. ELISA = enzyme-linked immunosorbent assay.

From these findings, new tools have been developed such as immunoprofiles or immunological profiles, miRNAs, measurement of soluble metabolites (such as cytokines, chemokines or growth factors) and the use of new tools such as transcriptomics and multiomics that improve the diagnosis of TB based on biomarkers present in accessible samples such as peripheral blood, saliva or urine *(Table 5)*.[47,49-65] The use of miRNAs in adults has proven to be effective in discerning between PTB and other types of pathologies (lung cancer and pneumonia).[25] Regarding other methods such as the use of biomarker cytokines, it has demonstrated potential in the detection of PTB in children with high levels of sensitivity and specificity.[66] Although these TB biomarkers are still in the experimental and preclinical stage, few progress to a validation stage,[67] so they are only alternatives for the

detection of *M. tuberculosis* and seek to solve the problems represented in diagnosing.

Timely and accurate diagnosis of PTB is a determining factor for early detection and essential for achieving compliance with global TB control programs.[16] That is why it is important to validate new biomarker-based TB diagnostic methods.[65,67,68] Unfortunately, few biomarkers progress to a developmental stage, so validation and application design studies for the use of biomarkers in PTB diagnosis and drug treatment monitoring are required to be funded. So far, only the measurement of biomarkers has been used as alternatives for the detection of *M. tuberculosis* in difficult to diagnose patients, such as the diagnosis of PBT in children.

CONCLUSIONS

Diagnosis of TB in children and adults requires a high index of suspicion, a thorough assessment of clinical and radiological features, and judicious use of diagnostic tests. Although the clinical and immunological characteristics of TB are similar in both populations, there are differences that must be taken into account when making the diagnosis. Further research is required to develop more accurate and reliable TB diagnostic tests, especially in children.

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Review
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Radiological features of non-neoplastic lesions of mediastinum

Características radiológicas de las lesiones no neoplásicas del mediastino

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ABSTRACT. Non-neoplastic mediastinal lesions of the mediastinum comprise a heterogeneous group of diseases that do not show a specific compartmental location; Radiologically, its characteristics can guide the diagnosis, the best follow-up method, as well as treatment and prognosis. Computed tomography (CT) and magnetic resonance imaging (MRI) features provide better patient selection for therapeutic interventions. The present review provides the radiological findings of this group of diseases.

Keywords: mediastinum, mediastinitis, lymphangiomatosis, pneumomediastinum, hemorrhage.

RESUMEN. Las lesiones no neoplásicas del mediastino comprenden un grupo heterogéneo de enfermedades que no muestran una localización compartimental específica; radiológicamente sus características pueden orientar el diagnóstico, el mejor método de seguimiento, así como el tratamiento y pronóstico. Las características por tomografía computada e imagen de resonancia magnética proporcionan una mejor selección de pacientes para intervenciones terapéuticas. La presente revisión proporciona los hallazgos radiológicos de este grupo de enfermedades.

Palabras clave: mediastino, mediastinitis, linfangiomatosis, neumomediastino, hemorragia.

INTRODUCTION

The group of diseases that make up the non-neoplastic lesions of the mediastinum have in common characteristics associated with increased thickness of the bands, displacement of lines or morphological modification of mediastinal recesses. Anatomical knowledge facilitates the decision making of the best diagnostic method that provides the most clinical information possible and the following therapeutic and/or prognostic procedure. The purist anatomical descriptions of the mediastinum have allowed, according to the structures included in it, to provide diagnostic possibilities based on compartments. However, nowadays the diagnostic tools have evolved technologically, allowing better image quality, better resolution of the anatomical structures and, therefore, descriptions with a broad semiological support that reduces the diagnostic options.

In the present review, we objectively provide the findings that best orient radiologically in the clinical-therapeutic approach, given that most non-neoplastic lesions are not limited to a mediastinal compartment.

MATERIAL AND METHODS

We conducted a review of the literature. Only studies published in English were considered. The databases used included UpToDate, Medline and PubMed. The types of articles included in the search criteria were retrospective, prospective, randomized controlled trials, case report studies, original research, meta-analysis, abstracts, and previous related reviews. Search terms used to identify relevant articles during screening included: mediastinal cysts, mediastinal granulomatous disease, mediastinitis, lymphangiomatosis, pneumomediastinum, mediastinal hemorrhage, and diaphragmatic hernias.

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RADIOLOGICAL FEATURES OF NON-NEOPLASTIC LESIONS OF THE MEDIASTINUM

Mediastinal abnormalities are frequently detected on chest radiography by identification of abnormal mediastinal contour or displacement and/or increased thickness of mediastinal lines and bands. Approximately 10% of mediastinal contours are vascular and include anomalous vessels and aneurysms.[1] Mediastinal abnormalities can be focal, unilateral or diffuse and bilateral; once the abnormality is identified, its location is corroborated in lateral projection and, according to this, its exact location is determined. Computed tomography (CT) and magnetic resonance imaging (MRI) allow the characterization of the lesions, evaluate their component in density or signal intensity, the effect on adjacent structures and their enhancement behavior.

Non-neoplastic pathology of the mediastinum can be classified according to its main etiology: 1) infectious type lesions: granulomatous lymphadenopathy and acute and chronic mediastinitis; 2) congenital type lesions: mediastinal lymphangiomatosis; 3) acquired non-infectious inflammatory lesions, post-birth: pneumomediastinum, mediastinal hemorrhage, diaphragmatic or hiatal hernia, esophageal dilatation and mediastinal lipomatosis; 4) cystic and pseudocystic lesions: congenital or acquired including bronchogenic cyst, esophageal duplication cyst, celomic cyst; intrathoracic pancreatic pseudocyst and hydatid cyst.

1. INFECTIOUS LESIONS

a. Granulomatous lymphadenopathy

When a mediastinal lymph node is visible in the chest X-ray, it modifies the mediastinal bands or lines depending on its origin and vascular drainage, they are generally larger than 10 mm, lose their kidney-shaped morphology and show a characteristic postcontrast enhancement. Most frequently, the paratracheal bands increase in thickness, modify the trajectory of the anterior pleural junction line, the azygoesophageal recess is convex and the contour of the aortopulmonary window is convex towards the parenchyma.

Non-metastatic or neoplastic nodal disease may have different radiologic findings depending on its etiology. When an organism can be identified, granulomatous lymphadenopathy in the mediastinum is usually caused by tuberculosis or endemic fungi such as histoplasmosis. Granulomas may result from a mass of lymph nodes that may compress adjacent structures, may induce an inflammatory reaction leading to sclerosing mediastinitis.

Mediastinal lymphadenopathy occurs in 7% of adults with tuberculosis, although lymph node enlargement is more common in AIDS. Lymphadenopathy may demonstrate low central attenuation; these areas of low density within the lymph nodes correspond to caseous necrosis *(Figure 1)*.[2] The right paratracheal area is most common, but may involve the anterior mediastinum or hilum. Lymph nodes may coalesce into poorly defined masses and adhere to adjacent vascular structures and mediastinal structures.

Between 5 to 13% of patients with histoplasmosis and nodal disease have esophageal involvement, particularly in the subcarinal region. Other less common causes include coccidioidomycosis, blastomycosis and cryptococcosis.[2]

Another effective imaging method for the evaluation of mediastinal and hilar lymph nodes is MRI, which has a lower spatial resolution than CT, but the use of paramagnetic contrast medium makes it possible to easily identify the lymph nodes. There are mediastinal levels that can be assessed more easily in MRI studies, the lymph nodes located in the aortopulmonary window are observed in coronal section, and the subcarinal lymph nodes are better seen in sagittal section.

b. Acute mediastinitis

It is an infection that is becoming less common since the advent of more effective antibiotics, it can be primary or secondary. Primary cases of mediastinitis are rare. Although the infection itself is self-limiting and resolves completely, it can also spread to the neck or broad ligament of the lung; 90% of mediastinitis is secondary to esophageal perforation or rupture.[3]

Descending necrotizing mediastinitis has an incidence of 1 to 2% and mortality between 30 to 67%. It is more frequent in men than in women, with a 6:1 ratio, the average age is 38 years, with a range of 28 to 30 years.[4]

The most frequently affected sites are superior (60%), anterior (60%), middle (20%) and posterior (20%) mediastinum. The most frequent finding on chest radiography is mediastinal widening (sensitivity of 77% and specificity of 66%) and pneumomediastinum (specificity of 100%).[5]

Chest CT is considered the modality of choice, it delimits the location and extent of the pathology, aiding clinical decision making when patients require immediate surgical intervention and cannot be managed conservatively by demonstrating pleural association and parenchymal disease.

The incidence of mediastinitis as a complication of cardiac operations is between 0.4 and 5% with a high mortality between 27 and 50% depending on the extent of the infectious process.[3]

Respiratory tract infections are rare causes of mediastinitis. However, oropharyngeal infections, such as tonsillitis, Ludwig's angina and retropharyngeal abscess, are cause for concern since they tend to spread along the fascial planes.

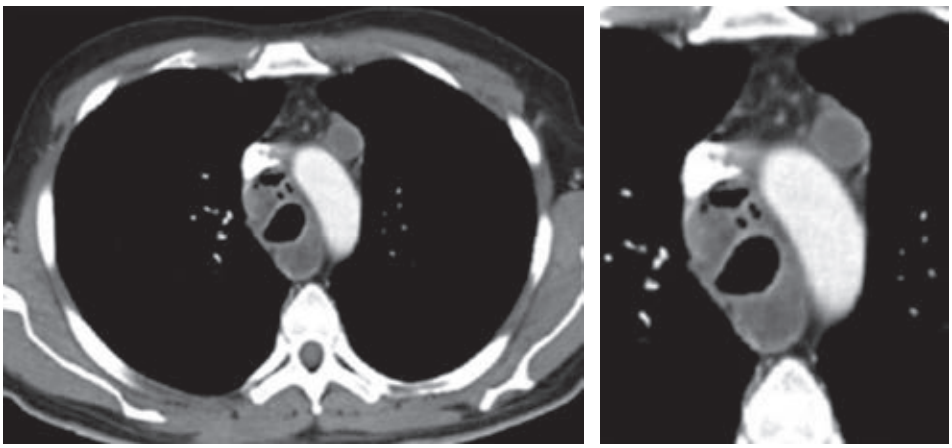


Figure 1:

Granulomatous lymphadenopathy. Observe in computed tomography, axial section, the annular postcontrast enhancement of the lymph nodes in the prevascular, right paratracheal and retrotracheal region.

These infections can cause necrotizing mediastinitis. The lateral parapharyngeal space is a transfer point for infections originating in the mandible, parotid glands, tonsils and cellulitis of the sublingual and submaxillary spaces.[3,6]

Tomographic findings include fluid collections, mediastinal gas, increased mediastinal fat attenuation, mediastinal widening, pleural effusion, pericardial effusion and presence of lymphadenopathy, in association with peristernal abnormalities such as soft tissue edema, sternal separation with marginal bone resorption, sclerosis and osteomyelitis *(Figure 2)*. The first two findings are characterized in the literature as highly positive.[7]

Mediastinal collections of 20 HU or less is indicative of the presence of fluid contents; however, high densities suggest the presence of blood which does not exclude the presence of a concomitant infection.

The differential diagnosis of loculated fluid collections includes postsurgical seromas, which show no enhancement of their wall with contrast medium. However, liquid collections of mediastinitis may not show enhancement if they occur within the first postoperative week.

CT performed up to day 15 after surgery has a low specificity due to the short period of time elapsed. Therefore, pathologic findings are difficult to differentiate from those expected in the postoperative period in these types of procedures. Frequent postoperative symptoms such as fever or chest pain may justify a tomographic study for the investigation of mediastinitis.

c. Chronic mediastinitis (sclerosing or fibrosing mediastinitis)

Fibrosing mediastinitis is defined as diffuse fibrotic infiltration throughout the anterior, middle and posterior mediastinum. Organisms are difficult to demonstrate, and cultures are usually negative. The gap of differential diagnoses includes histoplasmosis, tuberculosis, coccidioidomycosis, actinomycosis, sarcoidosis, blastomycosis, syphilis, and various malignancies (carcinoma, sarcoma, mesothelioma, and lymphoma).

Fibrous tissue may proliferate within the mediastinum as a consequence of infection, usually histoplasmosis. Sclerosing mediastinitis may be related to systemic vasculitis and may have an immunologic pathogenesis. It has also been reported in autoimmune disease such as Behcet's, rheumatic fever, radiation therapy, trauma, and drugs such as methysergide. In addition, it may occur in association with other fibroinflammatory disorders such as retroperitoneal fibrosis, sclerosing cholangitis, Riedel's thyroiditis and orbital pseudotumor.

Neoplasms that frequently produce fibrosis and can then be included in the differential diagnoses include sclerosing non-Hodgkin's lymphoma and nodular sclerosing variant Hodgkin's disease.

Symptoms are caused by obstruction of the superior vena cava, esophagus, trachea, bronchus or pulmonary veins, pulmonary arterial hypertension due to direct compression of the pulmonary arteries, or secondary to pulmonary venous compression.[8]

Approximately 30% die from complications caused by obstruction and fibrosis.[9] The worst prognosis is related to bilateral or carinal involvement. It is the most common cause of superior vena cava syndrome of benign origin. Central airway obstruction is by far the most common typical manifestation in patients with fibrosing mediastinitis presenting with cough and dyspnea. Causes of death are recurrent infection, hemoptysis, or cor pulmonale.

Fibrosing mediastinitis manifests as nonspecific mediastinal widening, with distortion and obliteration of recognizable mediastinal interfaces or lines. The middle mediastinum is most frequently affected, particularly the right subcarinal and paratracheal regions. Calcifications within the mediastinum or hilar are seen in 86% of patients.[10]

Central airway involvement may result in segmental or lobar atelectasis or recurrent pneumonia in the affected portions of the lung. The area of narrowing usually occurs at the level of the carina and in most cases in both bronchi.

Pulmonary arterial obstruction is typically unilateral and may result in an appreciable decrease in vessel size and number and localized regions of oligohememia in the affected segments. Venous obstruction manifests radiologically with findings of localized pulmonary venous hypertension, peribronchial cuffing, septal thickening or localized edema.

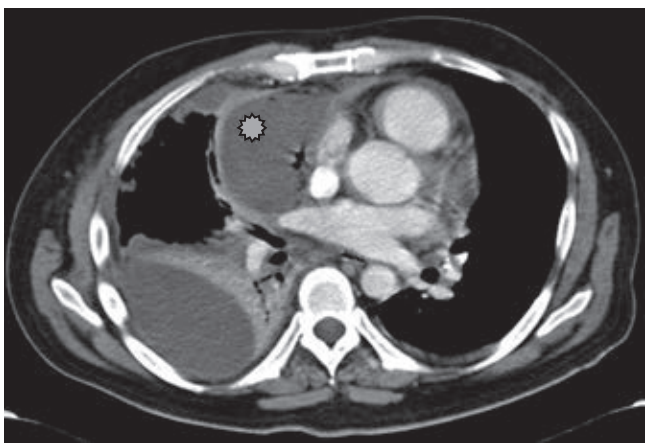


Figure 2: Contrast-enhanced computed tomography, axial plane, demonstrates liquid collection in paracardiac situation, with some air densities inside, minimal enhancement, with displacement of adjacent structures (asterisk).

On CT, it typically manifests as soft tissue attenuation masses that obliterate mediastinal fat planes and encase or invade adjacent structures. Sherrik et al[8] identified two patterns of tomographic invasion: a focal pattern and a diffuse pattern. The focal pattern *(Figure 3)* seen in 82% of cases, manifests as a mass with soft tissue attenuation that frequently calcifies (63%) and is usually located in the right paratracheal or subcarinal regions or in the hilum. The diffuse pattern *(Figure 4)*, seen in 18% of cases as a non-calcified infiltrative mass affecting multiple mediastinal compartments. The diffuse pattern occurs in the setting of other idiopathic fibrosing disorders such as retroperitoneal fibrosis.

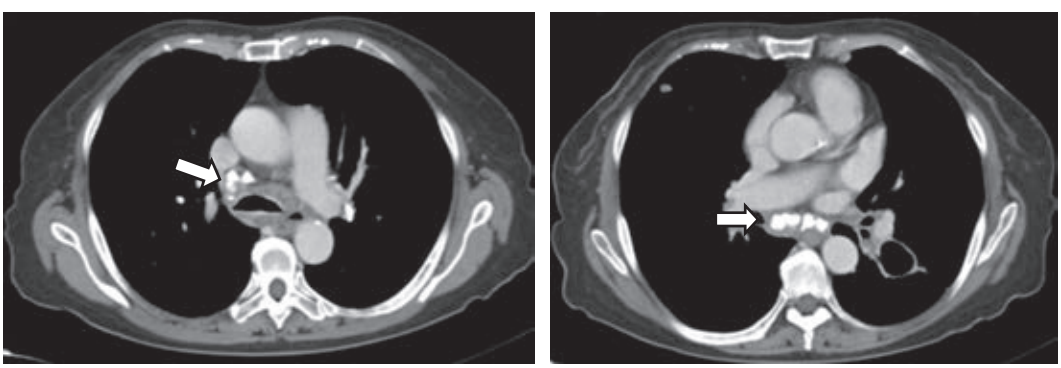
The degree of enhancement is variable and is useful to describe pigeonholing or obstruction of pulmonary arteries and veins. Two- or three-dimensional reconstructions can facilitate the surgical approach or local therapy of these lesions.

Venous obstruction frequently results in parenchymal abnormalities visible on CT, such as focal or diffuse regions of increased focal or diffuse parenchymal attenuation, ground-glass attenuation, and interlobular septal thickening.

CT also helps to evaluate the site, length and severity of airway stenosis. Esophageal invasion by fibrosing mediastinitis is best demonstrated by esophagogram. The

Figure 3:

Computed tomography, postcontrast, showing soft tissue density in the carinal and subcarinal region, which decreases the airway lumen, with the presence of irregular dystrophic calcifications (arrows), characteristic of focal sclerosing mediastinitis.



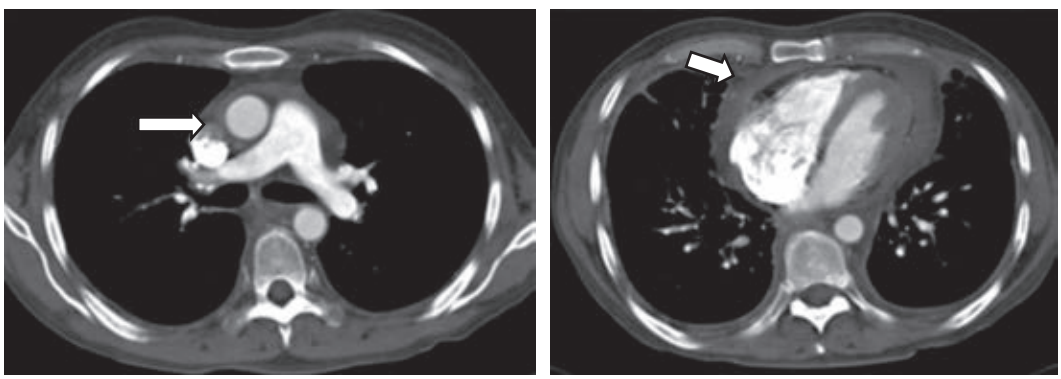


Figure 4:

Diffuse sclerosing mediastinitis. Chest tomography in axial plane, postcontrast, showing obliteration of mediastinal fatty tissue by a soft tissue attenuation mass, without evidence of enhancement, involving the middle mediastinum (white arrow).

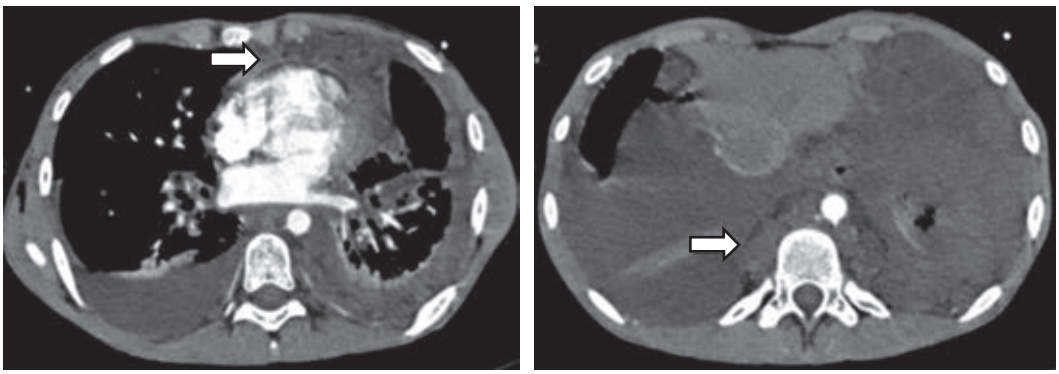


Figure 5: Pulmonary lymphangiomatosis. Contrast tomography shows infiltration of mediastinal fatty tissue and towards the retroperitoneum by soft tissue density lesion that does not enhance the passage of intravenous contrast medium, involving the anterior, middle and posterior mediastinal space (white arrow), pleural effusion coexists.

junction of the upper and middle thirds of the esophagus is frequently affected, although extensive invasion can also occur. The affected segment of the esophagus is usually adjacent to invaded regions of the trachea or main bronchi. Typical findings include circumferential narrowing and large segmental strictures.

MRI shows features ranging from heterogeneous and infiltrative mass appearance in T1-weighted sequences, to areas of hyperintensity and hypointensity visualized in T2-weighted images. These T2 hyperintense areas are considered to be related to areas where there is more active inflammation, while those T2 hypointense areas represent areas of fibrosis and calcifications; with paramagnetic contrast medium, heterogeneous enhancement of the affected mediastinum can be observed.

2. CONGENITAL LESIONS

a. Lymphangiomatosis

It is a diffuse proliferation of lymphatic vessels in multiple sites. It is more common in children. The mediastinum may be affected as well as the lung and pleura, presenting with chylothorax. In 60% of cases it is present at birth and in 90% the diagnosis is made during the first or second year of life.[11]

Radiological findings are: generalized mediastinal widening on CT with increased mediastinal fat attenuation (water-like). A focal mass is not visible. The involvement may be associated with interlobular septal thickening. Pleural thickening or pleural effusion is seen in almost all patients *(Figure 5)*.

3. NON-INFECTIOUS INFLAMMATORY ACQUIRED LESIONS

a. Pneumomediastinum

It was described in 1819 by Laennec. Macklin described the physiology of pneumomediastinum in 1939.[12] Pneumomediastinum is manifested by lucent lines or gas bubbles that demarcate mediastinal structures, elevate the mediastinal pleura and frequently extend to the neck or chest wall.

The findings basically depend on the delimitation of the anatomical structures by air both radiologically and on CT. If there is sufficient air, the thymus may be elevated producing the «flying thymus» sign. Air anterior to the pericardium (pneumopericardium) is a frequent manifestation and requires a lateral chest view for diagnosis. Air surrounding the pulmonary artery or its main branches may result in a ring around it (artery sign). When there is air adjacent to the main branches of the aorta both sides of the vessels are demarcated; mediastinal air demarcates the medial side, and aerated lung margins the lateral side («tubular artery sign»).

Occasionally, air may be in front of a major bronchus, allowing clear distinction of the bronchial wall producing the «double bronchial wall contour sign». The continuous diaphragm is produced by air trapped posterior to the pericardium, which gives the appearance of a continuous collection of air on the anteroposterior radiograph. Mediastinal air may extend laterally between the parietal pleura and the diaphragm producing the extrapleural sign.

Air may also migrate into the mediastinum within the pulmonary ligament to rupture into the distal esophagus *(Figure 6)*. Other names for pneumomediastinum include the «V of Naclerius» sign, in which gas delimits the margin of the descending aorta and extends laterally between the parietal pleura and the left medial hemidiaphragm. Although this finding was originally described in association with esophageal rupture, it is not specific for any other condition. A second «V-sign» is formed by gas delimiting the superior margin of the brachiocephalic veins at their confluence.

b. Mediastinal hemorrhage

Anterior mediastinal hematoma may occur as a sequela of rupture of a mediastinal vein (such as the internal mammary

vein) after trauma or coronary artery catheterization. It may also be seen with aortic damage from blunt trauma, such as in a motor vehicle accident. In addition, anterior mediastinal hematoma has been reported to occur spontaneously in patients receiving hemodialysis.[2]

CT demonstrates a liquid collection, which has high attenuation and may or may not have air densities within it. Soft tissue edema in the chest wall, sternal or rib fracture and other findings are due to trauma and may be seen in these patients. Pseudoaneurysms can be carefully excluded in cases of anterior mediastinal hematoma; therefore, any evaluation of the chest in the trauma patient should be performed with bolus administration of intravenous contrast material.

When there is suspicion of mediastinal hemorrhage in MRI we can visualize a mass-like lesion with increased signal in FLAIR (fluid attenuated inversion recovery) enhanced images, which does not lose signal intensity in fat-suppressed sequences, and signal restriction in diffusion sequences, which expresses different stages of hemorrhage.

c. Hiatal hernia

The esophageal hiatus is formed by the decussation of muscle fibers originating from the diaphragm around the lower esophagus. Sliding hernias account for 90% of them, the remaining 10% are paraesophageal hernias.[10]

In a patient with a sliding hiatal hernia, the most common abnormality identified is dehiscence of the diaphragmatic crura and stretching of the esophageal brachial ligament. These findings manifest as widening of the esophageal hiatus identified when the medial margins of the diaphragmatic crura are not closely opposed. The current standard esophageal hiatus width measurement, defined as the distance between the medial margins of the crura, averages 10.7 mm with a maximum width of 15 mm.

Sliding hiatal hernias are commonly associated with an apparent increase in mediastinal fat surrounding the distal esophagus secondary to omental herniation through the phrenic-esophageal ligament. Radiologically, the presence of a mediastinal mass with a hydroaerial level inside *(Figure 7)*, allows the diagnosis of hiatal hernia, it can extend to the right, left or bilaterally, it displaces the azygoesophageal recess. Tomographic findings with a wide esophageal hiatus, direct visualization of abdominal contents, identification of the esophageal-gastric junction, may be associated with atelectasis, consolidation by microaspiration of gastric contents.

The main differential diagnosis is Bochdalek's hernia, which occurs through the remnant of the pleuroperitoneal canal.

d. Esophageal dilatation

It may occur with esophagitis and strictures, esophageal carcinoma or other tumors, fibrosing mediastinitis, scleroderma, achalasia and leiomyomatosis. Marked dilatation may result in a mediastinal mass apparent on radiographs. In patients with known esophageal dilatation, CT may be used in identifying the mass *(Figure 8)*.

Esophageal dilatation in achalasia and scleroderma is usually associated with normal wall thickness. An air-fluid level and retained food may be visible in patients with achalasia, stricture or carcinoma, but is less common with scleroderma. Esophageal dilatation is present in 80% of patients with scleroderma and is often asymptomatic.

Few descriptions exist on the application of MRI in the diagnosis of pathologies affecting the esophagus, but with the advent of real-time acquisition it has been possible to demonstrate some findings such as the classic bird's beak sign in achalasia, esophageal dilatation, the diameter of the esophageal sphincter and motility disorders by visualizing the dynamics of the transit of the bolus or saliva.

e. Mediastinal lipomatosis

It is a benign condition in which abundant amounts of histologically normal, unencapsulated fat accumulate in the mediastinum. It may be associated with Cushing's syndrome, steroid treatment or obesity. It has no symptoms. It is relatively common and is frequently detected in patients with chest CT.

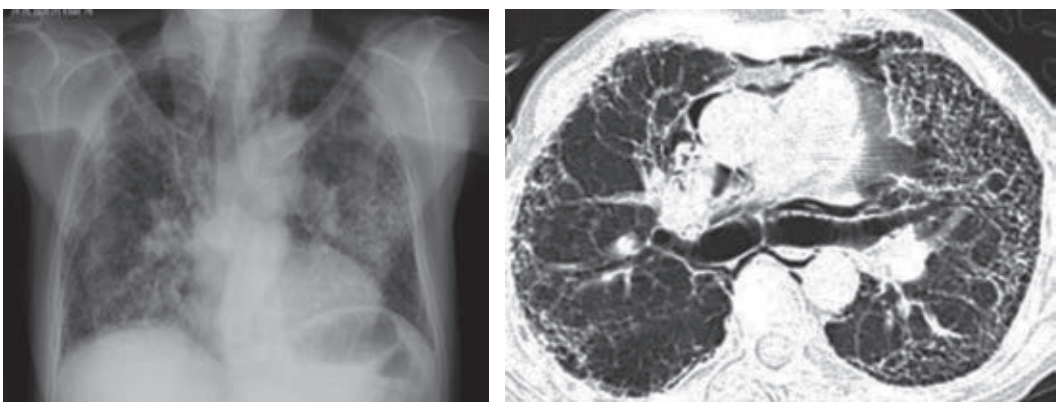


Figure 6:

Pneumomediastinum. Posteroanterior projection of the thorax and high-resolution tomography showing delimitation of the mediastinal structures and dissection of the facial planes due to the presence of air, corroborated in the axial tomography.

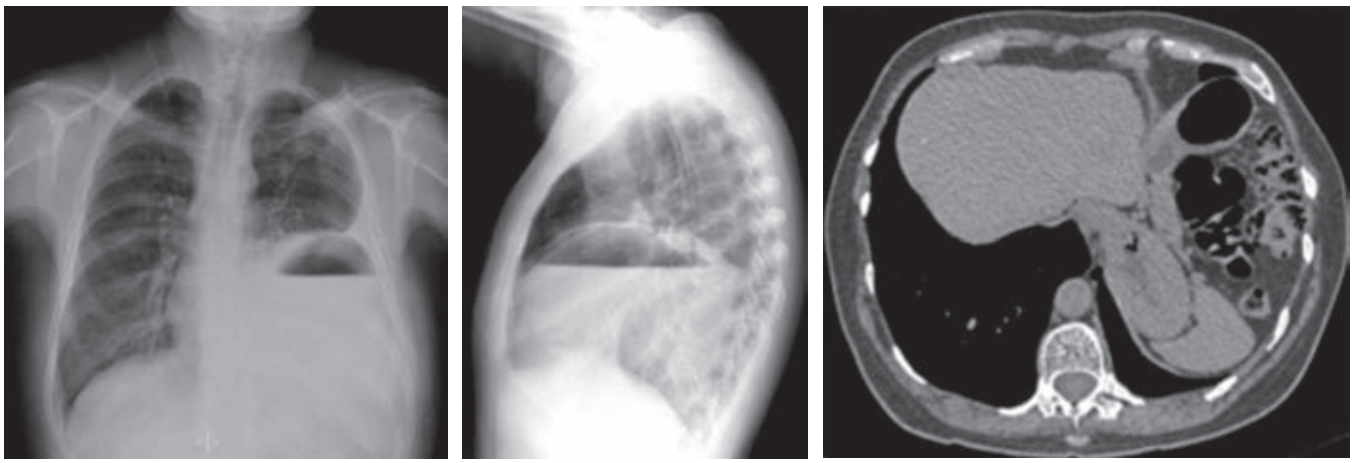


Figure 7: Hiatal hernia. Posteroanterior and lateral projection of the thorax showing passage of the stomach through the esophageal hiatus, with distension of its lumen by barium contrast material, air-liquid level in its interior and passage of the gastric fundus through the hiatus in the tomography image.

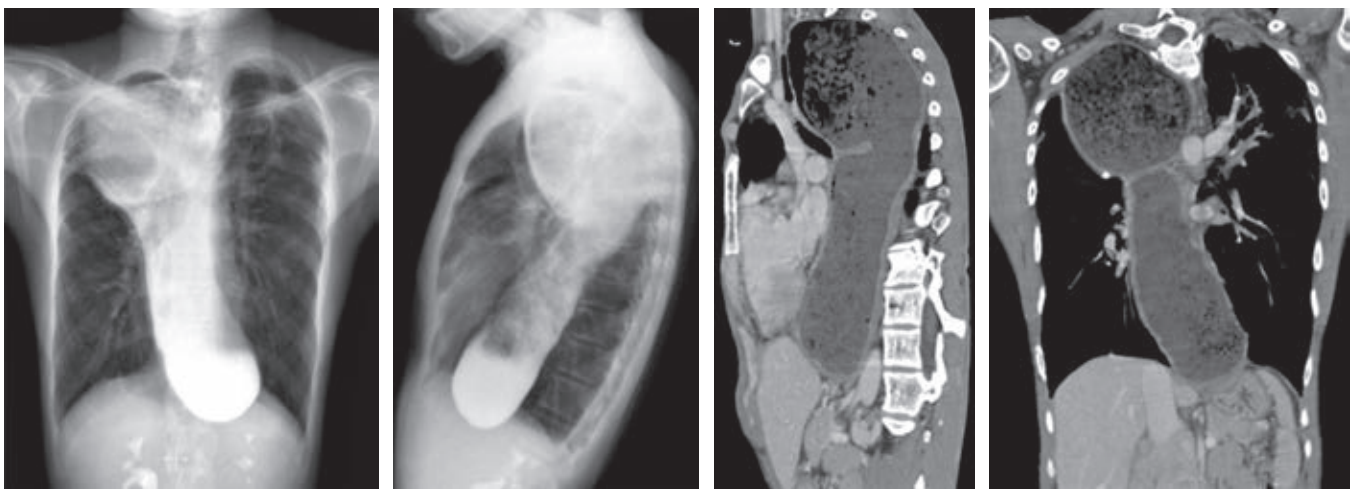


Figure 8: Esophageal dilatation. There is a large retrocardiac mediastinal mass with a hydroaerial level inside, the multiplanar, sagittal and coronal projections show the extension, as well as the identification of the esophageal dilatation in specific.

Excess fat deposition is more prominent in the superior mediastinum resulting in smooth mediastinal widening as shown on chest radiograph and convex or bulging pleural surfaces on CT. Tracheal compression or displacement is absent. Less common is fat accumulation in the cardiophrenic angles and paraspinal regions.

In patients with lipomatosis, the fat should appear homogeneously low attenuating, sharply delimiting the mediastinal vessels and nodes.

Among the differential diagnoses are mediastinal fatty masses, as well as focal fatty lesions such as mediastinal fat necrosis, characterized by a nidus of juxtapericardial fat attenuation surrounded by inflammatory tissue, it is the analogue of epiploic appendagitis in the abdomen, and is accompanied by pericardial effusion and adjacent atelectasis. Mediastinal fat necrosis occurs frequently in men between 40 and 50 years of age, it is self-limited, the symptoms are similar to those perceived in pulmonary thromboembolism and acute myocardial infarction, they disappear in 48 to 72 hours.[13] It is histologically normal fat, very easy to identify in MRI studies, increased signal intensity is observed in T1 and T2 sequences, with similarity to subcutaneous fat when compared.

4. CYSTIC AND PSEUDOCYSTIC LESIONS OF THE MEDIASTINUM

Mediastinal cysts form a group of rare benign lesions of congenital and inflammatory nature, accounting for 20-32% of all primary mediastinal masses.[14] They include different

pathologic entities with overlapping clinical and radiologic features. They are seen in both adult and pediatric populations and their classification is based on the cause.

a. Bronchogenic cysts

Bronchogenic cysts constitute 50-60% of all mediastinal cystic lesions. These types of cysts are sometimes found together with other congenital lung malformations, such as pulmonary sequestration and lobar emphysema, thus calling them hybrid malformations.[15]

Cysts may have clear fluid, serous or mucoid material. They occur anywhere in the mediastinum, but frequently near the carina in the middle or posterior mediastinum. Less frequently they appear in the parenchyma, pleura or diaphragm. They are frequently connected by fibrous tissue to the trachea or bronchus. Cysts are spherical and usually unilocular, but may be multilocular. They have a thin wall with a smooth outer surface and a trabeculated inner lining.

On CT a bronchogenic cyst appears as a single smooth, round or elliptical mass with an imperceptible wall and uniform attenuation *(Figure 9)*. The value, in Hounsfield units,

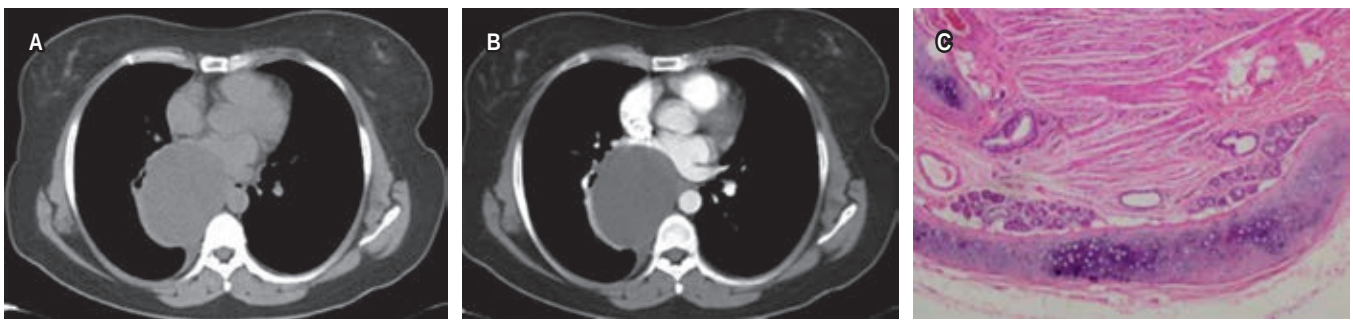


Figure 9: Thorax tomography in axial plane, showing liquid attenuation image **(A)**, without postcontrast enhancement **(B)** and histopathological finding where cartilage is identified in the wall of the lesion **(C)**.

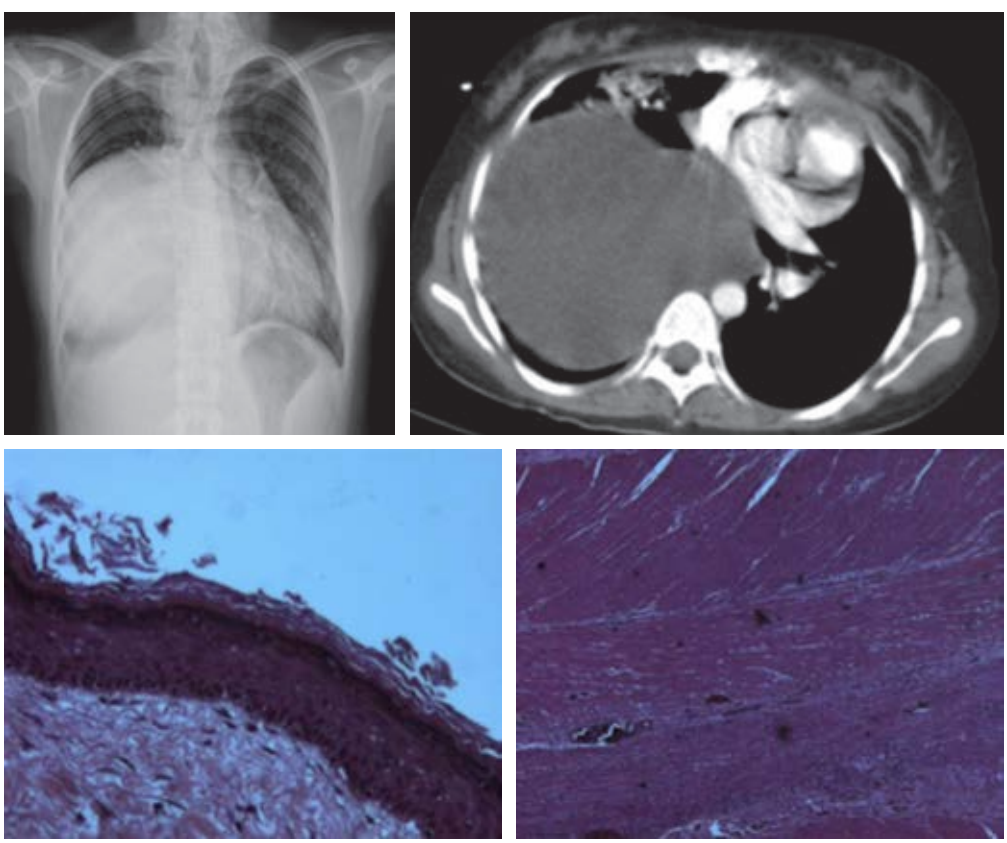


Figure 10:

Esophageal duplication cyst. Posteroanterior projection of the thorax shows a mediastinal cystic lesion, unilocular, retrocardiac location, exerting compression and displacement of mediastinal structures. The histopathological finding showed stratified flat epithelium and three muscular layers, compatible with the diagnosis.

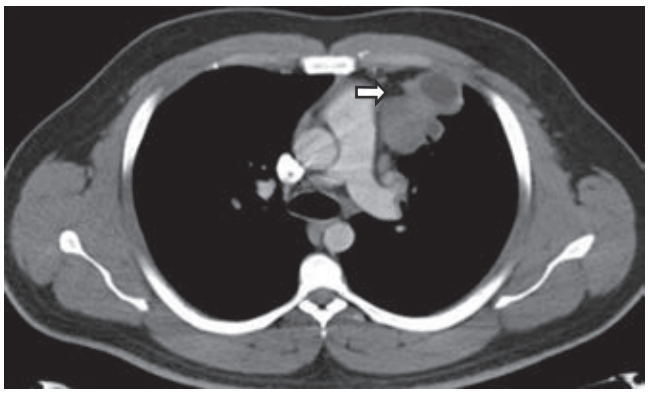


Figure 11: Hydatid cyst. Mediastinal cystic lesion with thick wall and faint enhancement to the passage of contrast medium. It shows adjacent cysts of smaller size, daughter cysts (white arrow).

may be greater than 100 HU if they have an elevated protein level and calcium oxalate in a mucoid cyst. Air within the cyst suggests infection and communication with the airway.

In MRI, in T2 bronchogenic cysts present increased signal due to their liquid content; in T1 enhanced images there is variation in the signal pattern, due to the presence of protein, hemorrhagic or mucous content inside the cyst, even up to the presence of liquid-liquid level.

b. Enteric duplication cyst

Mediastinal enteric cysts, also called enteric duplication cysts, are esophageal or gastroenteric cysts. They are mainly diagnosed in children under 15 years of age. A male predominance has been described. Patients have respiratory symptoms, other symptoms present include dysphagia, cough and vomiting. Cysts covered by gastric epithelium may ulcerate and perforate. These cysts are differentiated from bronchogenic cysts by location, absence of cartilage and the presence of muscularis propria. The nature of the cyst sometimes cannot be determined due to the absence of distinctive features.

They are frequently reported in association with malformations of the thoracic and cervical vertebrae. They are visually identical to bronchogenic cysts, except that the wall of the lesion is thick and in contact with the esophagus *(Figure 10)*, they are located in the posterior mediastinum near the esophagus, typically in the retrocardiac position. On T1-weighted MRI images they are hypointense, while on T2-weighted images they are hyperintense and, occasionally, liquid-liquid levels are identified.

c. Coelomic cysts

Pericardial or coelomic cysts originate in the embryologic development of the pleuropericardial membranes, some are attached by a pedicle. They are usually reported in adults, but can also appear in children, many patients are asymptomatic. The cysts have fibrovascular tissue with a smooth, thin wall, contain fluid, are spherical and unilocular. The cyst contents are clear watery or straw colored. They are bounded by a plate or sheet of cuboidal mesothelial cells supported by loose connective tissue. Coelomic cysts can be treated surgically or by percutaneous aspiration of the contents.[15]

They usually originate in the cardiophrenic angle, they are more frequent in the right angle than the left. Some are in the superior mediastinum and connected to the pericardium. On CT, they can be seen as well-demarcated, unilocular, oval or round or triangular masses and can be 30 cm in diameter, the attenuation is similar to that of water. In MRI they present similar findings to the other cystic lesions of the mediastinum.

d. Hydatid cyst

They are acquired cystic lesions, representing 0.1% of all mediastinal cysts. They are composed of a fibrous capsule: pericyst. The true cyst has a thin wall composed of two adherent layers, the laminated endocyst and the delicate tapetum endocyst, from which the daughter cysts hang. They have a predilection for the anterior mediastinum and appear as cystic lesions with daughter cysts *(Figure 11)*.

In MRI the findings are very characteristic, the pericyst is hypointense in T1 due to its fibrous component. The mother or true cyst is of intermediate signal intensity on T1 and the daughter cyst will have lower signal intensity on T1 than the matrix of the mother cyst. On T2-weighted images, the pericyst will remain hypointense, and on T2 the mother and daughter cysts will have the same high signal intensity.

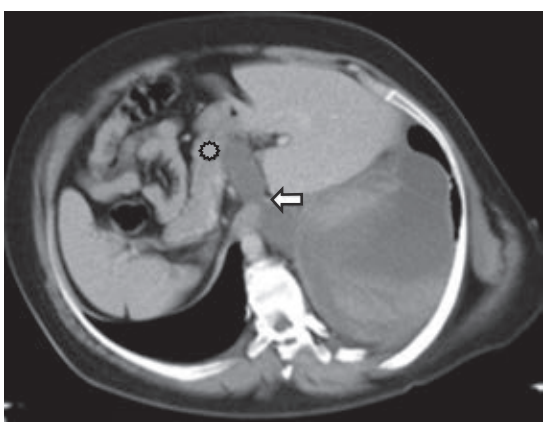


Figure 12: Intrathoracic pancreatic pseudocyst. Oblique axial projection showing dehiscence of the diaphragm (white arrow) through which the cystic lesion crosses to the pancreatic head (asterisk).

e. Lymphatic cysts

Cystic lymphangioma or cystic hygroma is a cystic lesion of lymphatic vessels. Thoracic duct cysts can have several mediastinal locations: below the azygos vein in the posterior mediastinum, above the aortic arch, at the level of the hilum, in the epiphrenic area and above the heart. They can measure 15 cm in diameter or more. The microscopic appearance is characteristic of fibrous connective tissue with endothelial cells. On CT, the lymphangioma typically appears as a multiloculated, smooth-margined mass with homogeneous water-like attenuation. On T1 and T2 MRI, adequate characterization of serpentiginous or vascular shaped septa are identified within.

f. Pancreatic pseudocyst

Alcoholism is a common factor in adults and trauma in children. In many cases, the pseudocyst extends from the pancreas to the posterior mediastinum through the esophageal hiatus. Less commonly, it can penetrate through the aortic hiatus, Morgagni's foramen or a diaphragmatic erosion.

It represents an encapsulated collection of pancreatic secretions, blood and necrotic material. It always occurs in the lower posterior mediastinum, gaining access from the thorax via the esophageal or aortic hiatus. Tomography shows a thin-walled, low-attenuation cyst in the posterior mediastinum or adjacent to the thoracic cavity associated with compression or displacement of the esophagus, may be hyperattenuating depending on whether there is hemorrhage or infection *(Figure 12)*.

CONCLUSION

The theoretical boundaries of mediastinal compartments are not so clear, and identification of the close anatomic relationships of a mass is often instructive.

In most cases, the initial use of chest radiography instructs the next diagnostic method upon suspicion of a visible mediastinal abnormality; however, tomography is a tool that in most cases is diagnostic in the context of a non-neoplastic lesion of the mediastinum, in short and long-term follow-up for clinical management and treatment.

There are several clues in the differential diagnosis, most of the time based on previous clinical knowledge.

Acknowledgments

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Procedures and recommendations

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Spirometry: update of the procedure and post pandemic perspectives

Espirometría: actualización del procedimiento y perspectivas pospandemia

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ABSTRACT. Spirometry is the most widely used and standardized respiratory function test. In 2019, the American Thoracic Society and the European Respiratory Society updated the international guidelines for its execution. The COVID-19 pandemic forced the establishment of better biosafety parameters and has renewed interest in respiratory medicine in the world, including physiological evaluation. The present manuscript summarizes these changes incorporating recommendations and suggestions for countries with limited resources.

Keywords: spirometry, lung function, vital capacity, bronchial obstruction.

RESUMEN. La espirometría es la prueba de función respiratoria más utilizada y estandarizada. En el año 2019, la Sociedad Americana del Tórax y la Sociedad Respiratoria Europea actualizaron los lineamientos internacionales para su ejecución. La pandemia de COVID-19 ha obligado a establecer mejores parámetros de bioseguridad y ha renovado el interés por la medicina respiratoria en el mundo, incluyendo la evaluación funcional. El presente manuscrito es una propuesta de procedimiento de espirometría ajustado a los cambios e incorpora recomendaciones y sugerencias para países con recursos limitados.

Palabras clave: espirometría, función pulmonar, capacidad vital, obstrucción bronquial.

Abbreviations:

ATS/ERS = American Thoracic Society/European Respiratory Society.
COVID-19 = disease by coronavirus 2019.
EOFE = end of forced expiration.
EOTV = end of test volume.
F/V = flow/volume.
FET = forced expiration time.
FEV_1 = forced expiratory volume in one second.
FVC = forced vital capacity.
FIVC = forced inspiratory vital capacity.
IC = inspiratory capacity.
PEF = peak expiratory flow.
RV = residual volume.
SVC = slow vital capacity.
TLC = total lung capacity.
V/T = volume/time.

INTRODUCTION

Forced spirometry is a respiratory function test that assesses components of lung mechanics. It measures the maximum

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volume of air that an individual can forcibly inhale and exhale as a function of time.[1-3]

The main variables measured in forced spirometry are: forced vital capacity (FVC), which is the maximum volume of air, measured in litres, that can be exhaled through the mouth with maximum effort after a full inspiration; and forced expiratory volume in one second (FEV_1), which is the volume of air exhaled during the first second of the FVC manoeuvre.[1-3]

The FEV_1/FVC ratio, expressed as a percentage of the absolute value, is the defining variable for obstruction, as it represents a disproportionate reduction in the maximum FEV_1 of a forced manoeuvre relative to the total volume that a subject can exhale during the FVC manoeuvre. Therefore, a decreased FEV_1/FVC ratio implies airflow limitation, i.e. airway obstruction during exhalation.[2]

Other spirometric variables briefly addressed in this paper are $FEV_{0.5}$ and $FEV_{0.75}$, which represent the forced expiratory volume in the specified fraction of a second,[1,4] as well as the slow vital capacity (SVC) which is the maximum volume of air measured in litres, that can be exhaled through the mouth in a relaxed manner after a full inspiration.[1]

This document aims to adjust the spirometry procedure according to the new recommendations published in the 2019 ATS/ERS standard for forced spirometry,[1] as well as the challenges and protocols assumed in its execution in the wake of the COVID-19 pandemic.[5]

INDICATIONS

Spirometry is a fundamental test in respiratory assessment.[1] Indications are shown in *Table 1*, updated according to current evidence on the usefulness of the test in multiple settings.

CONTRAINDICATIONS[1]

The FVC manoeuvre directly increases intrathoracic pressure and indirectly increases intra-abdominal and intracranial pressure, and physical exertion can increase myocardial demand. Therefore, the potential risks when performing forced spirometry are due to the impact of these changes on thoracic organs, abdominal, venous return and arterial pressure. The international standard for spirometry[1] states that there are no absolute contraindications for performing forced spirometry and that its performance will depend on the risk-benefit of performing the test.

Patients with contraindications should ideally be evaluated in a pulmonary function laboratory by expert personnel. Slow spirometry may sometimes be performed to assess the subject's vital capacity, although the result is not interchangeable. It is also important that the patient is cooperative and follows instructions in order to avoid submaximal manoeuvres. The appearance of pain, presyncope or discomfort during the test is a criterion for suspension of the test.

Contraindications, all relative, are shown in *Table 2*.

MATERIAL RESOURCES

Spirometer

A device that records physiological ventilatory volumes, in the vital capacity range, as well as the flow generated by them through a sensor.[27]

ATS/ERS 2019[1] states that this equipment must meet the minimum requirements of the latest update to ISO: 26782,[27] which are summarised below:

1. Measuring range from 0 to 8 litres, under BTPS (Body Temperature and Pressure and Saturated) conditions.
2. Maximum permissible error in volume measurement of ± 3% or 0.050 L (whichever is greater).
3. Minimum expiratory time recording of 15 seconds.
4. Real-time graphs with a ratio for the F/V (flow/volume) graph of 2 L/s: 1 L and for the V/T (volume/time) graph of 1 L: 1 s.
5. Recording of the extrapolated volume as well as the volume at the end of the forced exhalation (to identify start and end criteria).
6. Impedance of the equipment, with all its accessories, less than 0.15 kPa/(L/s) with flow rates up to 14 L/s.
7. Have a weather station for temperature measurement, which must have an accuracy of ± 1 °C to properly calculate the BTPS correction factor; in case of not having a weather station, the calculation of the correction factor to BTPS units will have to be done manually.
8. Appropriate reference equations for the population.[3]
9. Real-time display of F/V and V/T graphs at the time of manoeuvres.[1]
10. The report generated should have both F/V and V/T graphs for each of the manoeuvres performed; a volume scale ≥ 10 mm/L and a time scale ≥ 20 mm/s is recommended.[3]

Volumetric spirometers have fallen into disuse and flow spirometers, which measure air displacement velocity and calculate volume by integration, now predominate. These spirometers are portable, easy to clean, and some use disposable sensors, reducing the risk of cross-contamination; features that have facilitated the incorporation of spirometry in the office, hospital, laboratory and even the patient's home.

Table 3 summarises the different types of flow spirometers, their advantages and disadvantages, virtually all of which are available in Mexico.

Table 1: Indications for spirometry.

Diagnosis[1]

- **In suspected COPD:**
  - Presence of post-bronchodilator FEV_1/FVC < LIN or Z-score with symptoms and risk factors[6,7]
- **In suspected asthma:**
  - It helps during the diagnostic process to document FEV_1/FVC below LIN, especially if it reverses post-bronchodilator. Also an increase of > 400 mL post-bronchodilator in FEV_1 or FVC
  - Repeated spirometry (or PEF) in occupational settings may suggest occupational asthma that worsens at work and improves outside of work
  - If FEV_1 increases more than 12% and 200 mL from pre-bronchodilator value or from baseline after four weeks of anti-inflammatory therapy[8]
  - In suspected severe asthma, one of the criteria is the presence of pre-bronchodilator FEV_1 < 80% pred (or $\leq$ 1.64 in Z-score)[9]
- **In suspicion of other respiratory pathology with one or more of the following data:**[1]
  - Symptoms: dyspnoea, cough, wheezing, stridor
  - Signs: rales, thoracic deformity
  - Abnormal laboratory and laboratory studies: hypoxaemia, hypercapnia, polycythaemia, abnormal chest X-ray
- **Assessment of pulmonary impact of systemic disease:**[1]
  - In any patient with suspected ILD
  - In any patient with neuromuscular disease and suspected respiratory muscle weakness (SVC may be a better indicator of respiratory muscle weakness than FVC as it is not affected by the coexistence of airflow obstruction)[10,11]
  - Difference > 10% in FVC performed in the sitting-supine position (FVC delta) suggests diaphragmatic weakness; unilateral diaphragmatic paralysis may have delta between 15-25% and bilateral up to 50%[12]
- **Screening:**
  - Not indicated in screening asymptomatic subjects without risk factors[13,14]
  - It is indicated in the intentional search for cases: presence of respiratory symptoms or signs and risk factors (> 35 years and smoking rate > 10 p-a, occupational or occupational exposure to biomass or toxic substances)[15]
  - Decreased FEV_1 is a cardiovascular risk factor independent of age, sex and smoking[16]
- **Preoperative risk assessment:**[1,17]
  - Respiratory function tests have not been shown to be superior to anamnesis and physical examination in predicting postoperative pulmonary complications in the absence of symptoms and risk factors
  - Perform in suspected lung disease without prior diagnosis and in procedures close to the diaphragm (thoracic or upper abdominal surgery)
  - Indispensable before lung resection and transplantation surgery

Follow-up[1]

- **Response to therapeutic interventions in lung disease**
- **Prognosis of already diagnosed lung disease:**[1]
  - In COPD, at least once a year to identify 'rapid decliners' (FEV_1 drop > 50-90 mL/year)[7,18]
  - In asthma, at the start of treatment, 3 to 6 months after achieving control (better lung function) and periodically[8]
  - The presence of FEV_1 < 60% pred and/or a very significant response to BD in asthmatic patients (even if asymptomatic or with few symptoms) are risk factors for crises[8]
  - In CF, at the start of treatment and every 3 months to identify the pattern of lung function decline[19]
  - The presence of persistent FEV1 < 40% pred in patients with CF is a criterion for advanced lung disease[20]
  - In interstitial lung diseases (of any aetiology) at least during the first 2 years of diagnosis, as it identifies progressive fibrosing phenotype: fall in FVC $\geq$ 10% or fall in FVC between 5 and 10% and worsening of respiratory symptoms and/or extension of fibrosis on HRCT[21]
  - In muscular dystrophies; if the patient is still walking and < 12 years old, annual is recommended. If the patient is > 12 years, wheelchair user or has an FVC < 80% pred, every 6 months is recommended (FVC < 40% pred is indication for volume recruitment manoeuvres and assisted cough and FVC < 30% pred for non-invasive mechanical ventilation)[22-24]
- **Assessment of functional status during and after an exacerbation of the underlying lung disease:**[1]
  - The presence of FEV_1 < 60% pred in a patient with an asthma flare-up after 48 hours of inhaler titration is an indication for initiation of OCS[8]
- **Occupational monitoring of subjects exposed to noxious agents:**[1]
  - Recommended on admission and annually thereafter. An excessive fall in FEV_1 identified by any of the following methods: % from baseline (> 15%), limit of longitudinal decline or linear regression suggests further evaluation of the worker[18]
- **During or after the use of drugs with known pulmonary toxicity:**
  - Patients on chemotherapy regimen (bleomycin, gemcitabine, paclitaxel, platinums, cyclophosphamide, doxorubicin). The presence of a spirometric pattern suggestive of restriction usually occurs in advanced cases, so it is suggested to perform serial DLCO in conjunction with spirometry[25]

- **Disability assessment**[1]
  - Admission to rehabilitation programmes
  - Initial assessment by insurers for risk of respiratory pathology
  - Initial assessment of lung health in physically demanding occupations
  - Medico-legal assessments

Contents

Continued Table 1: Indications for spirometry.

• **Other**[1] ○ Clinical research ○ Epidemiological studies ○ Generation of population reference equations ○ Assessment of health status prior to strenuous physical activity ○ General routine respiratory assessment

COPD = chronic obstructive pulmonary disease. FEV_1 = forced expiratory volume in the first second. FVC = forced vital capacity. %pred= predicted percentage. SVC = slow vital capacity. p-a = pack year. BD = bronchodilator. CF = cystic fibrosis. HRCT = high-resolution tomography. OCS = oral corticosteroids. DLCO = pulmonary diffusion of carbon monoxide. LLN = lower limit of normal.

Table 2: Relative contraindications to spirometry.[1]

Due to increased myocardial demand or changes in blood pressure
• AMI: one week prior*
• Symptomatic hypotension
• Severe hypertension (MAP > 130 mmHg)[26]
• Uncontrolled atrial or ventricular arrhythmia
• Decompensated heart failure
• Untreated pulmonary hypertension
• Acute cor pulmonale
• Acute PTE
• History of cough or exertional syncope
Due to increased intracranial/intraocular pressure
• Cerebral aneurysm
• Cranial or brain surgery: 4 weeks*
• Recent cranial contusion with persistent symptoms
• Eye surgery: one week
For increased intraotic pressure
• Sinus or middle ear surgery: One week*
• Otic infection: one week*
For increased intrathoracic and intra-abdominal pressure
• Unresolved pneumothorax
• Thoracic surgery: four weeks*
• Abdominal surgery: four weeks*
• Late pregnancy
Infection control
• Confirmed or suspected active respiratory infection (COVID-19, tuberculosis or other)
• Physical conditions predisposing to transmission of infection (active haemoptysis, presence of significant secretions, oral lesions or active oral bleeding)

AMI = acute myocardial infarction. MAP = mean arterial pressure.
PTE = pulmonary thromboembolism.
* In acute events, forced spirometry is not recommended.

Other equipment and consumables[3]

1. Computer and printer (some equipments do not require).
2. Scale, stadiometer.
3. Stable chair with side armrests. Avoid chairs with wheels to prevent falls.
4. Room thermometers with an accuracy of 1 °C and hygrometer for relative humidity measurement.
5. Mouthpieces recommended by the manufacturer, diving mouthpieces can be used for those patients who are unable to make a good lip seal.
6. Nasal forceps.
7. Certified three-litre syringe.

Infection control supplies:

1. Access to hand washing and gel-alcohol.
2. Disposable in-line filters with > 99% efficiency for filtration of viruses, bacteria and mycobacteria; dead space < 100 mL and resistance less than 1.5 cm H_2O at 6 L/s flow rate.
3. N95 respirator with leakage of less than 10% and a filtration efficiency of > 95% at a flow rate of 50 L/min.
4. Protective eyewear.
5. Natural water should be available, as well as facial tissues to be offered to the patient in case of coughing or secretions.

Bronchodilator consumables:

1. Salbutamol in metered dose inhaler (100 mg by atomisation).
2. Ipratropium bromide aerosol (20 mg per atomisation).
3. Reservoir chamber (spacer) with a recommended volume of at least 300 mL.

QUALITY CONTROL AT THE WORKPLACE *(Figure 1)*

There are requirements that any laboratory or site, where spirometry is performed, must meet to ensure good practice.

Logbook[2]

We recommend an auditable quality control report. The log should include the results of calibration

Table 3: Types of flow spirometers.[1,27]

Type of spirometer	Principle of action	Advantages	Disadvantages
Pneumotacograph (differential pressure)	Measure the pressure difference generated by passing a laminar fluid through a known resistance, where flow = Δpressure/resistance The resistance may be a mesh or a tube formed by a set of capillaries; it is usually heated to 37 °C to prevent condensation of water vapour from the exhaled gas	• Highly accurate at different flow rates • Portable • Automated • Available with disposable sensors	• Requires recalibration during the same day if ambient conditions change significantly • Accumulation of secretions or condensation of exhaled vapour changes the resistance and hence the flow measurement • Susceptible to resistance contamination if used without a filter. Change in gas composition requires calibration
Electronic turbine	It consists of a helix inside the tube that receives the flow. A light emitting diode (LED) is mounted on one side of the propeller and a photodetector on the other side. Each time the propeller rotates, it interrupts the light from the LED reaching the detector. These pulses are counted and summed to calculate the gas flow	• Portable • Useful in cardiopulmonary exercise testing (CEPPT) • Automated • Available with disposable sensors	• At high flows, the propeller is subject to distortion • At low flows, inertia may lead to misestimation of the flow rate • Susceptible to turbine contamination if used without a filter • Fragile moving parts with a tendency to accumulate dirt that impedes free rotation of the turbine
Thermistor (or hot-wire thermistor)	It consists of two metal filaments (usually platinum) heated by an electric current. The flow of gas through the filaments causes them to cool. In one filament, the current increases to maintain a constant temperature; the other filament acts as a reference. The change in current is proportional to the gas flow	• Portable • No moving parts • Measurement not susceptible to ambient temperature and pressure or fluid viscosity • Automated	• Sensor resistance connected in series, any modification to the components could be erroneously measured as a flow
Pitot tube	Based on the measurement of the fluid pressure at a given point in the pipe and using the relationship between the pressure and the area the fluid passes through, the fluid flow can be calculated		
Ultrasonic	Ultrasound waves travel through membranes on both sides of a tube at an angle to the gas stream. The sound waves speed up or slow down depending on the direction in which the gas is flowing. By measuring the transit time of the ultrasonic waves (which is modified by the passage of the gas) the flow can be accurately measured	• Portable • Highly accurate • Measurement not susceptible to ambient temperature and pressure or fluid viscosity • Air exhaled by the subject is not in contact with the sensor • Measures molar mass, with several additional applications possible	• Piezoelectric material very sensitive to shocks or falls • In absence of HEPA filter (high efficiency particle arrester) favours aerolisation • High cost sensors

processes, dates of spirometer maintenance (repairs and/or adjustments) and calibration syringe, software/hardware updates (dates on which procedures were performed and check that reference equations are included). Logbooks should be under the custody of the responsible technical professional and always available. Each spirometer should have its own physical or electronic logbook.

Contents

Evaluation of spirometer accuracy

All spirometry equipment must be validated prior to release and subsequently calibrated or verified (before manoeuvres are performed) to meet accurate flow and volume measurements for consistent clinical decisions. The following is a breakdown of the concepts describing these processes:

Validation: assesses the reproducibility of expiratory manoeuvres using a computerized curve generation system. The spirometer must faithfully reproduce the model curve generated by the computer system. It is not part of standard laboratory procedures; it is performed before spirometers are marketed.[28]

Calibration: a procedure by which a relationship is established between the volume or flow measured by the sensor and the actual flow or volume of the calibrator (syringe) under Ambient Temperature, atmospheric Pressure, Saturated (ATPS) conditions. It is an electrical gain adjustment manoeuvre of the device.[1] Spirometers whose sensor is affected by gas characteristics (condensation, etc.) such as pneumotachographs should always be calibrated.

Calibration verification: procedure that verifies that the spirometer is within the accuracy limits (± 3%, corresponding to: ± 2.5% of the equipment and ± 0.5% of the calibration syringe) under ATPS conditions. If the device fails, the verification must be repeated and the possible causes (leakage at the syringe junction with the spirometer, zero flow error, error in the syringe filling and injection process, or malfunction of the syringe) must be analyzed. If the failure is repeated, the equipment should be sent for recalibration and maintenance. The procedure should be performed daily by discharging the calibration instrument (certified three-litre syringe) through the sensor at least three times, in a flow range between 0.5 to 12 L/s (with injection times between 0.5 to 6 seconds). The final result should yield a volume of 3 L ± 90 mL (± 3%). If spirometry is intended to be performed with filters, then this procedure should also use filters. There are spirometers that are pre-calibrated by the manufacturer and cannot be recalibrated by the spirometer operator, however, it is advisable to carry out the calibration verification process on all equipment (even ultrasonic) and generate the corresponding reports that will be filed in the logbook.[1]

Biological control: performed with the participation of a healthy pulmonary subject, without risk factors, with normal spirometry; usually a laboratory technician

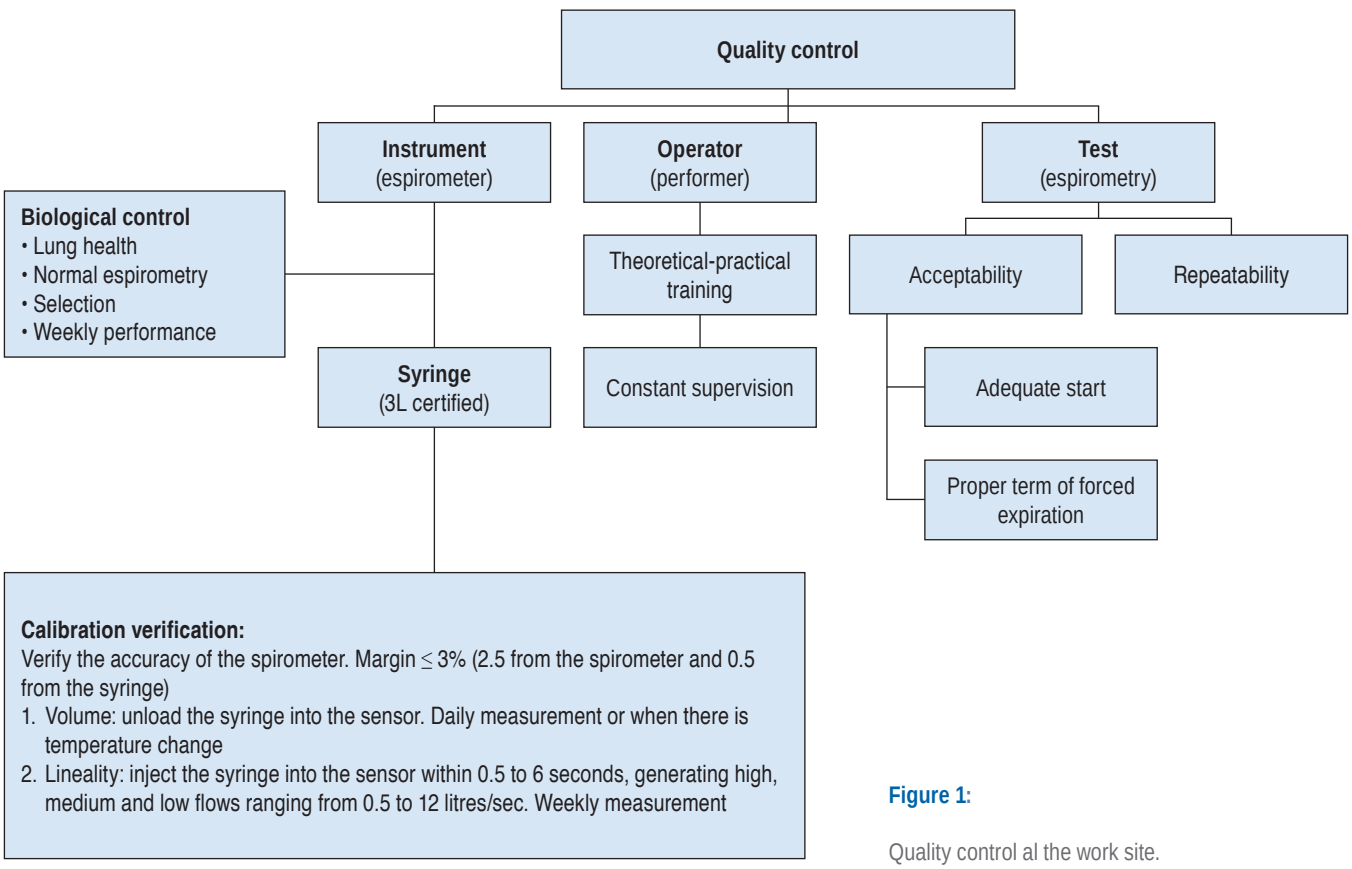

Figure 1:

Quality control al the work site.

who has the ability to perform the procedure in a highly repeatable manner. It does not replace the use of the calibration syringe. The subject to be designated as the biological control is given serial spirometry for a specified number of days at the same time, averaging the highest FEV_1 and FVC values.[1] Some machines provide the option of automated calculation of the SDs (standard deviations) within which the measurements obtained are considered to be correct. Subsequently, the subject should perform weekly spirometry to compare the measured value against the maximum expected error.

Standardized calibration instrument[1]

Corresponds to a three-litre syringe with an accuracy of ± 15 mL or ± 0.5%, with a current certificate. It should be checked according to the manufacturer's recommendations and ideally once a month, looking for possible leaks, performing a manoeuvre that attempts to fill and empty the syringe (at different volumes) with the outlet blocked. Similarly, it should be stored away from moisture or heat. A damaged or knocked syringe is considered potentially out of calibration and should not be used for this procedure.

Procedure conditions[1-3,28]

1. ATPS: ambient temperature, barometric pressure and ambient water vapour saturation. All procedures involving the input and output of volumes from a calibration syringe to the sensor must be performed under these conditions.
2. BTPS correction: given that exhaled air is at a body temperature of 37 °C and saturated with a water vapour pressure of 47 mmHg; the partial pressure in the lungs is 760-47 mmHg = 713 mmHg (at sea level). All procedures involving the performance of manoeuvres on subjects must conform to these conditions.
3. The work site should ideally meet the following characteristics: temperature between 17 to 35 °C, relative humidity between 30 to 75%. Changes in temperature or humidity during the working day should be recorded in the logbook as this may be a source of variability in spirometry results. In situations where the ambient air temperature changes rapidly > 3 °C in < 30 min, the appropriate correction should be made in the spirometer. Artificially air-conditioned laboratories allow better control of environmental variables.
4. Some spirometers have built-in sensors that automatically measure temperature and barometric pressure, but it is recommended that the operator verify the accuracy of these parameters.[1]

Ongoing staff training

Staff performing spirometry should maintain competence through regular training to safeguard the quality of results. Lack of ongoing training and infrastructure contribute to lack of knowledge about this test.[29] A short course improves competence;[30] learning is reinforced by a second training of longer duration and close monitoring.[29] It is recommended that staff develop skills to cope with special situations including: non-English language (dialects), hearing or visual impairments, and uncooperative patients.[1]

Quality of manoeuvres. Review the relevant section.

Improving patient experience[31]

The European Lung Foundation (ELF) conducted a virtual survey in 2018 in 52 countries among patients who regularly underwent spirometry. Of the 1,760 respondents, only 17% of them rated the test as difficult to perform, the rest rated it as tolerable. The most important suggestions from patients were the following: clear and concise information before, during and after the test (regarding drug cessation, contraindications, etc.), as well as access to and explanation of the results obtained in the context of their pathology.

FORCED SPIROMETRY PROCEDURE WITH BRONCHODILATOR[1,3]

Recommendations for the patient prior to the test

1. No smoking, vaping, or using water pipes at least one hour beforehand.
2. No use of drugs that affect consciousness within eight hours before.
3. No strenuous exercise one hour before.
4. Avoid wearing restrictive chest or abdomen garments.
5. If the indication for the test is diagnostic, bronchodilators should be discontinued according to the time of action of each *(Table 4)*.

Preparation of equipment prior to testing

1. All components (hoses, sensors, connectors, etc.) must be properly disinfected and/or sterilised and assembled according to the manufacturer's instructions.
2. Perform calibration or calibration verification.
3. The spirometer must be coded to the altitude or barometric pressure and average relative humidity of the site where the study is performed.
4. Verify that the spirometry report is properly configured.

Table 4: Bronchodilator withdrawal time in diagnostic spirometry.[1]

Type of bronchodilator	Example	Withdrawal time (hours)
SABA (short-acting beta-agonist)	Salbutamol/phenoterol	4-6
SAMA (short-acting muscarinic antagonist)	Ipratropium bromide	12
LABA (long acting beta-agonist)	Formoterol/salmeterol	24
LAMA (long acting muscarinic antagonist)	Tiotropium bromide/umeclidinium/aclidinium/glycopyrronium bromide	36
Ultra-LABA (ultra long acting beta-agonist)	Indacaterol/vilanterol/olodaterol	36-48

Staff actions on arrival of the patient

1. Introduce yourself to the patient and check that your details are correct (check name and date of birth).
2. Review the indications.
3. Evaluate the presence of possible contraindications, vital signs and the patient's adherence to the recommendations.
4. Enter patient data into the spirometer: full name, date of birth, anthropometric parameters: age in years at the day of testing, sex at birth (patients may provide their gender identity, but should be informed that sex at birth is required as it is a determinant of predicted lung size). It is important to enter, as notes or observations, any additional data that may help in the further interpretation of the study (such as smoking, exposures, history of previous lung disease, etc.).
5. Obtain the weight in light clothing, on a precision scale and record it in kilograms in closed units to the nearest 0.5 kg.
6. Obtain height with a stadiometer (should be measured without shoes, with feet together, standing as upright as possible, facing forward, with back and heels against the wall or stadiometer.)
7. In patients unable to stand or with rib cage deformity, measurement of arm span may be used to estimate standing height; measure the distance between the tips of the middle fingers (wingspan). For Caucasian males: height = arm span/1.03, for African-American males: height = arm span/1.06 and for females height = arm span/1.01. For patients who cannot be measured standing and also do not have an arm, the mid-span can be measured as the distance between the tip of the middle finger and the prominent cervical vertebra. And in patients with significant body posture deformity in whom it is not possible to measure the wingspan linearly, the composite wingspan shall be calculated.
8. Place the patient in a seated position, in a chair without wheels and with arm support, with the chest and neck in an upright position. If the test is performed in a different position (e.g. decubitus) it should be recorded.
9. Explain to the patient, in simple words, the purpose of the test. The following sentence is recommended: «*Spirometry is a blowing test to measure the size of the lungs and to find out whether or not there is obstruction of the bronchial tubes. You are going to blow hard and steady through this mouthpiece several times until you get at least three proper manoeuvres*».
10. A video or picture can be used to reinforce the explanation. It is not advisable to remove eye or respiratory protection to demonstrate the manoeuvre.

Forced vital capacity (FVC) manoeuvres

Manoeuvres that assess both phases of the respiratory cycle (inspiration and expiration), also known as «closed circuit», are preferred.

The four basic steps of a good manoeuvre are as follows:

1. Maximal inspiration to total lung capacity (TLC).
2. Explosive, immediate and unhesitant exhalation.
3. Continuing exhalation until the end of forced expiration criteria are met. At this point the motivation given by the performer is important.
4. Breathe in again until TLC. This closes the inspiratory curve and allows assessment of the forced inspiratory vital capacity (FIVC).

In spirometers that do not record the inspiratory phase, open circuit manoeuvres can be performed by placing the mouthpiece immediately after inspiration (step 1) and removing it after meeting end of forced expiratory criteria (step 3).

Figure 2 outlines the steps of a closed-circuit manoeuvre.

Bronchodilator administration[32]

The administration protocol should be recorded in writing in the site's internal procedures manual; it should contain the following elements:

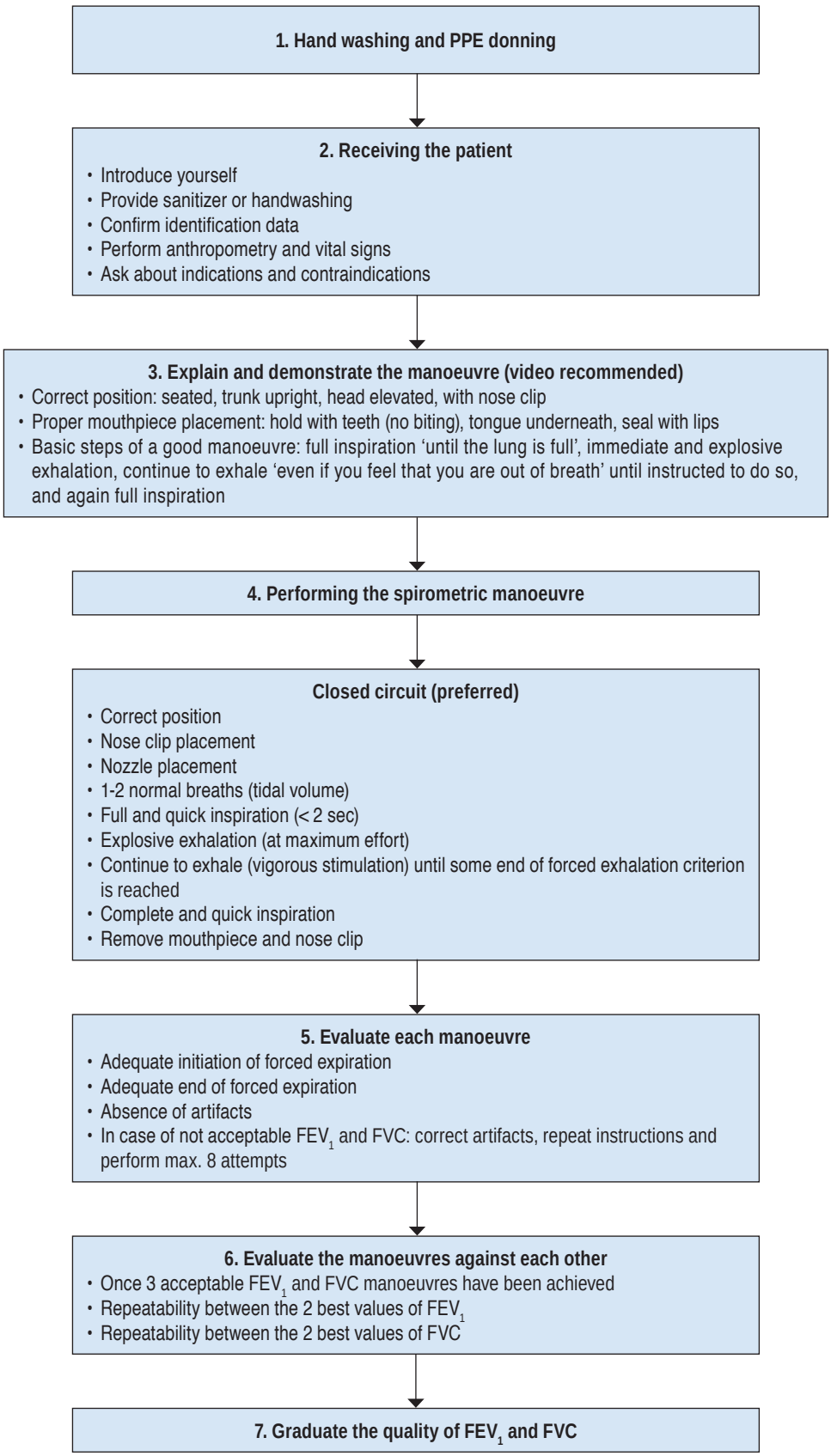

Figure 2:

Spirometric manoeuvre.

PPE = personal protective equipment. FEV_1 = forced expiratory volume in the first second. FVC = forced vital capacity.

Contents

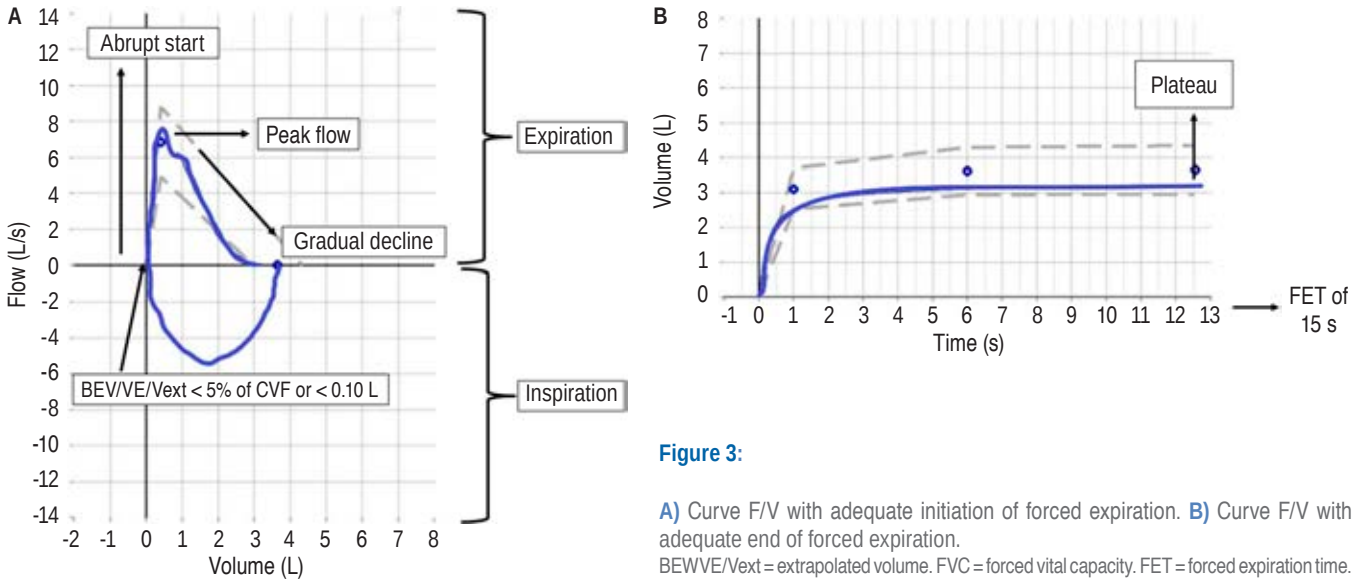

Figure 3:

A) Curve F/V with adequate initiation of forced expiration. **B)** Curve F/V with adequate end of forced expiration.
BEWVE/Vext = extrapolated volume. FVC = forced vital capacity. FET = forced expiration time.

1. Type of bronchodilator (salbutamol, fenoterol, ipratropium bromide or combinations).
2. Dose to be administered in children (salbutamol: 200 μg) and adults (salbutamol: 400 μg, ipratropium bromide: 80 μg).
3. Method of administration: metered dose inhaler (MDI) with or without mask, nebuliser. In this regard, MDI with air chamber is recommended; the use of nebulisers should take into account air flow, equipment pressure and not use oxygen while administering the drug.
4. Waiting time for post-bronchodilator manoeuvres: when using salbutamol wait at least 15 minutes and in the case of ipratropium bromide at least 30 minutes.

QUALITY OF MANOEUVRES[1]

Evaluation of each manoeuvre

At the end of each manoeuvre, it should be assessed for compliance with the following technical acceptability criteria:

1. **Adequate onset of forced expiration *(Figure 3A)*.** An explosive onset, with maximal effort, ensures that we are obtaining the patient's true FEV_1.
   The following two indicators must be assessed and met to ensure that the manoeuvre had a correct onset:

   a. The extrapolated volume, which is the amount of gas that is exhaled in a hesitant manner from peak inspiration at time 0, should be < 5% of the FVC or.
   b. The flow/volume (F/V) curve should be triangular in morphology, with steep, vertical rise to peak flow and gradual decline to 0.

2. **Adequate end of forced expiration *(Figure 3B)*.** A proper end of the manoeuvre ensures that the patient's true FVC is obtained.
   At least one of the following three indicators must be assessed and met to ensure that the manoeuvre was properly terminated:

   a. Plateau. This is the best indicator of the end of forced expiration; it refers to an absent increase in volume on the V/T or EOFE curve.
   b. Expiratory time of 15 seconds. This indicator is more likely to be achieved in older adults or in patients with lower airway obstruction. For patient safety, if the plateau has not been reached, but 15 seconds of expiratory time has been reached, the manoeuvre should be terminated.
   c. The subject is unable to continue exhaling. In this case, the FVC of the previous and subsequent manoeuvres shall be assessed to ensure that they are repeatable with respect to each other.

3. **Absence of artefacts affecting technical acceptability** *(Figures 4 to 11)*.

a. Baseline errors. Occurs when the operator or patient generates some flow while the equipment is establishing the baseline; affects both FEV_1 and FVC *(Figure 4)*. This artefact is common when spirometry is performed outdoors or near an air conditioning device.
b. High extrapolated volume. This is generated when the patient takes too long between maximal inspiration and expiratory effort. Its presence renders both FEV_1 and FVC unacceptable and not useful *(Figure 5)*.

c. Mouthpiece leak or obstruction. Occurs when the patient does not seal the mouthpiece properly with the lips, sticks the tongue in or bites down hard on the mouthpiece. If after verifying proper mouthpiece placement, subsequent manoeuvres still show the «artefact» of obstruction, it is important to rule out true intra- or extrathoracic central airway obstruction. Patients with facial paralysis or edentulous patients without prostheses may require support in sealing *(Figures 6 and 7)*.
d. Coughing. If it occurs during the first second it affects the FEV_1 result; however, FVC may be usable in such cases *(Figure 8)*.
e. Glottic closure. The individual pushes instead of exhaling, closing the glottis and suddenly obstructing outflow; if it occurs during the first second it affects both FEV_1 and FVC making the manoeuvre not usable, if it occurs after the first second FEV_1 may be usable *(Figure 9)*.
f. Repeated exhalations. Occurs when the patient reinhales through the nose and exhales again, falsely increasing the FVC of that manoeuvre. The FEV_1 may be usable if the second exhalation occurred after the first second *(Figure 10)*.
g. Variable efforts. Occurs when the patient does not exhale at maximal effort, which may be suspected in the presence of variable peak flows and non-overlapping traces on the F/V curve *(Figure 11)*.
h. FIVC-FVC subtraction greater than 0.10 L (100 mL) or 5% of FVC (whichever is higher). If the volume inspired to close the circuit after completion of the forced expiration (FVIC) is much greater than the FVC for that manoeuvre, it means that the patient did not fully inspire at the start of the test, which affects the FVC result.

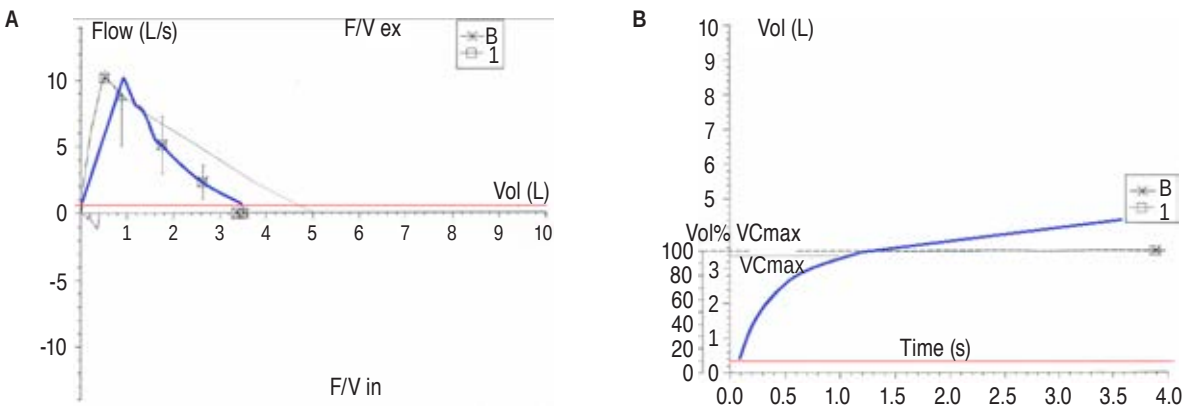

Figure 4: Baseline error. **A)** The F/V graph starts above flow 0 and does not return to flow 0 at the end of the manoeuvre. **B)** The V/T graph also does not start at 0 and shows a progressive and infinite increase in volume.
VCmax = maximum vital capacity.

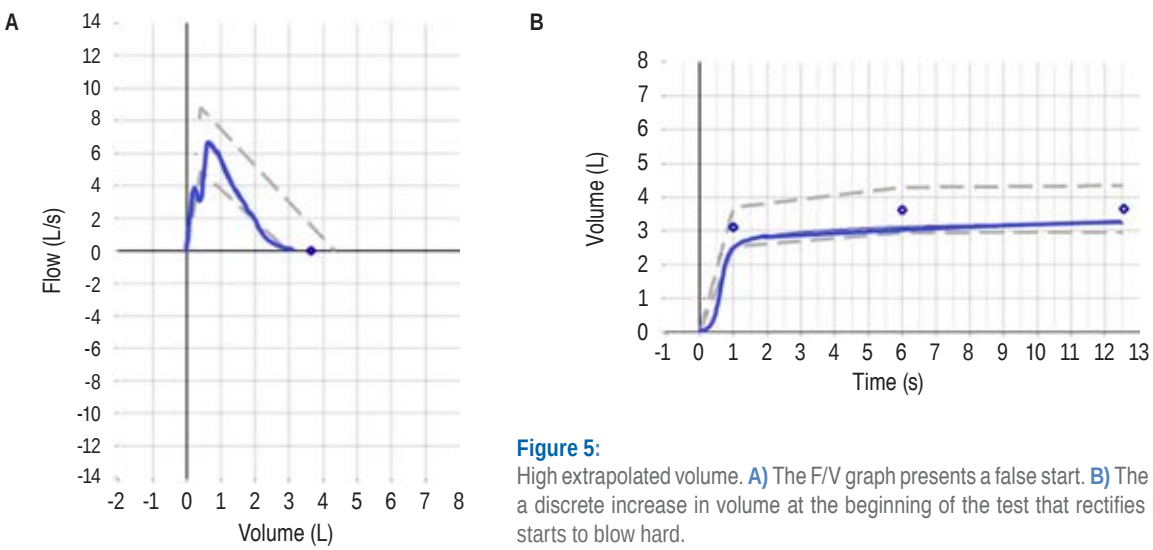

Figure 5:
High extrapolated volume. **A)** The F/V graph presents a false start. **B)** The V/T graph may present a discrete increase in volume at the beginning of the test that rectifies itself when the patient starts to blow hard.

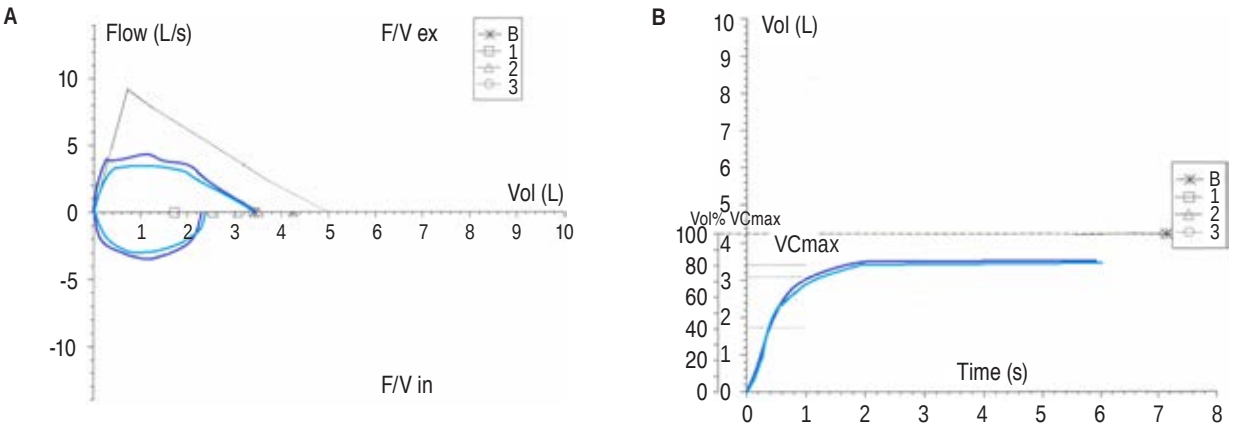

Figure 6: Nozzle obstruction. **A)** The F/V graph does not have a peak flow despite adequate patient effort. **B)** The V/T graph discreetly flattened prematurely. VCmax = maximum vital capacity.

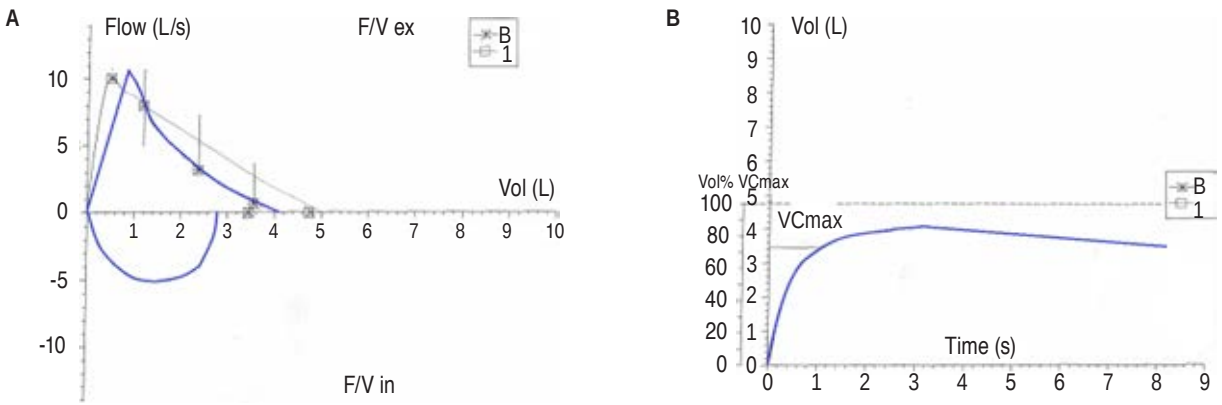

Figure 7: Volume leakage. **A)** The F/V graph may remain unchanged. **B)** The V/T graph shows a progressive drop in volume as the subject continues to exhale. VCmax = maximum vital capacity.

ASSESSMENT BETWEEN MANOEUVRES[1]

Acceptability implies that each manoeuvre is well executed (from start to finish), while repeatability means that the manoeuvres resemble each other, which is an indicator of measurement consistency. The more consistent a phenomenon is, the lower the probability of error.

Therefore, once three acceptable manoeuvres (both FEV_1 and FVC) have been obtained, repeatability should be assessed under the following criteria: the difference between the two highest FEV_1 values and the two highest FVC values should be ≤ 150 mL (maximum ≤ 200 mL) in subjects older than six years, and ≤ 100 mL or ≤ 10% of the highest value in patients younger than six years *(Figure 12 and Table 5)*.

Test quality grades[1]

After obtaining three acceptable and two repeatable manoeuvres (in FEV_1 and FVC) the quality of the test should be graded *(Table 6)*. It is important to note that automated quality does not always match that of the expert observer, so automated algorithms should be used with caution.

Test quality considerations[1]

1. Acceptability may be achieved in FEV_1 but not in FVC, and vice versa, in the presence of certain artefacts that are difficult to correct for.
2. Repeatability is analysed until three acceptable efforts have been completed.
3. Eight attempts is a practical limit, but some people, especially those with little testing experience, may get their best manoeuvre after the eighth, especially if they do not show fatigue, in order to get three acceptable ones. Patients who are getting poorer tests or lower measurements with new manoeuvres will generally not benefit from going beyond the eighth manoeuvre.

4. In case no acceptable manoeuvres in FEV_1 and FVC are obtained, despite our and the patient's efforts, an expert assessor can use the quality score U and issue some interpretation.
5. In patients with bronchial hyperresponsiveness, repeated FVC manoeuvres may cause decreased flows.

Reporting the results[1-5]

It is recommended that it includes sufficient information to assess the quality of the test, as well as a standardised interpretation by an expert. It should include the following components *(Figure 12 and Table 5)*:

1. Patient's full name.
2. Patient's date of birth.
3. Anthropometric parameters (age, gender, ethnicity, weight and height).
4. Significant respiratory history.
5. Origin of reference values.
6. Date of last calibration.
7. The values of three acceptable spirometry manoeuvres: FVC, FEV_1 and PEF in units (L or L/s) to two decimal places and the FEV_1/FVC ratio in percent to one decimal place. Depending on the case, FEV_6 and FEV_1/FEV_6 can also be included, and in the case of preschoolers, $FEV_{0.5}$ and $FEV_{0.75}$, with absolute values and the percentage of the predicted value. It is essential to include the numerical value of the extrapolated volume (BEV, BEV or Vext) and end-expiratory volume (EOTV or EOFE), as well as the expiratory time (FET).
8. All three volume-time and flow-volume graphs, both baseline and post-bronchodilator, should be visible.

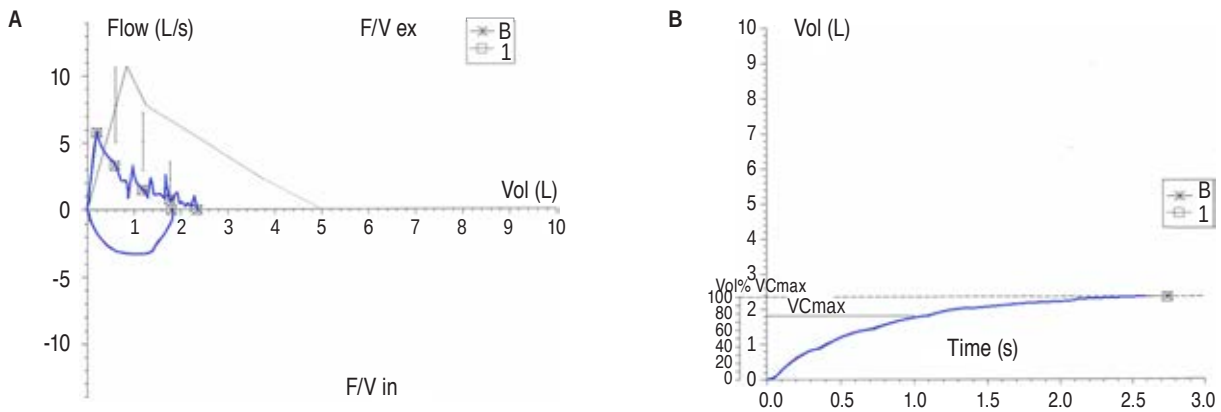

Figure 8: Cough. **A)** The F/V graph shows sudden fluctuations in flow. **B)** The V/T graph shows step-like irregularities.
VCmax = maximum vital capacity.

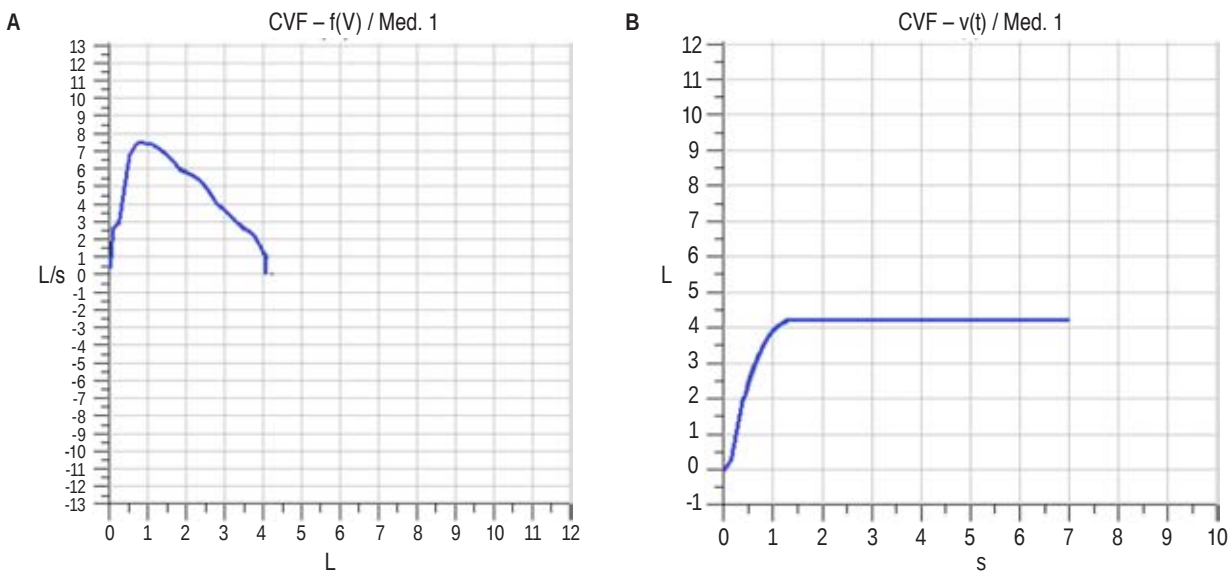

Figure 9: Gothic closure. **A)** The F/V graph shows a sudden volume drop to 0. **B)** The V/T graph shows a platou completely flat from the first second.

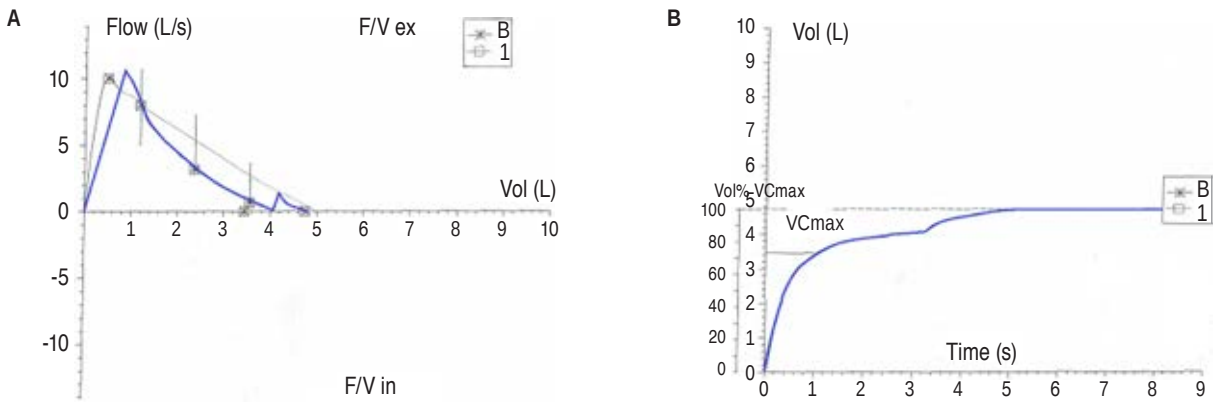

Figure 10: Repeated exhalations. **A)** The F/V graph shows an additional volume flow curve at the end of the exhalation. **B)** The V/T graph shows an artificial increase in the forced vital capacity
VCmax = maximum vital capacity.

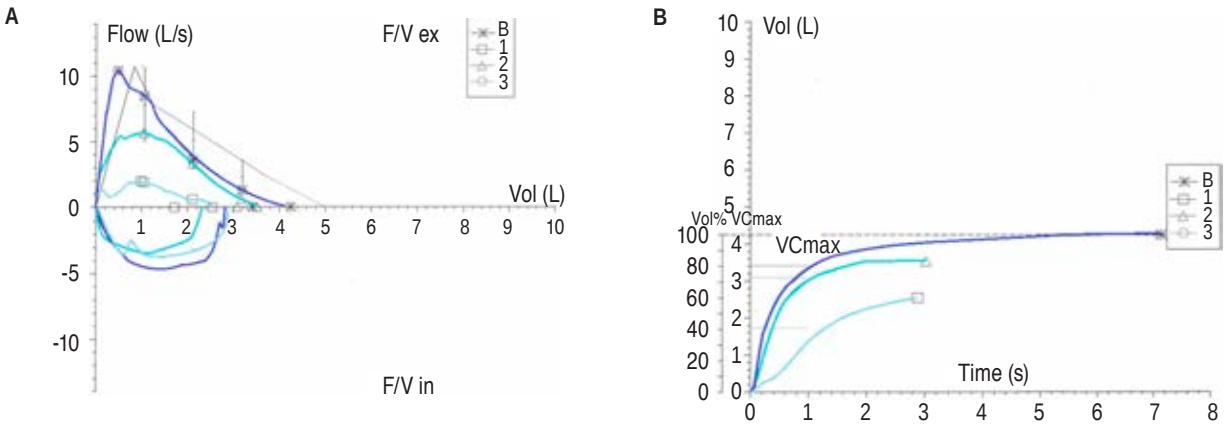

Figure 11: Variable efforts. **A)** The F/V graph shows no peak flow in two of the manoeuvres, only one is acceptable. **B)** The V/T graph has a more gradual increase in volume, although the artifact may go unnoticed on the V/T graph.

9. The three best values at baseline and the three best values after bronchodilator administration should be displayed. Some outdated spirometers report only the best baseline and best post-bronchodilator values.
10. Ideally the change in FEV1 and FVC between the best baseline and best post-bronchodilator test should be reported.
11. Column of predicted, lower limit of normal and Z-score.

BIOSAFETY CONSIDERATIONS

Precautions and processes that reduce the risk of personnel exposed to a potentially infectious agent[33] have always been indispensable, but often ignored in healthcare procedures. Potential micro-organisms involved in cross-infection within a pulmonary function laboratory are mainly transmitted by droplets and aerosols; there is also a risk of contact transmission in immunocompromised patients.[34]

With the emergence of COVID-19, numerous expert consensus proposed limiting the performance of respiratory function tests according to pandemic phase.[35-37] In a survey of laboratories registered with the American Thoracic Society, only 70% of them continued to perform spirometry in all phases.[38] Although there is no similar information from Latin America, the National Institute of Respiratory Diseases in Mexico established biosafety guidelines that ensured the continuity of respiratory physiology services throughout the pandemic.[39]

Spirometry, like other respiratory function tests, is an aerosol-generating procedure, which requires active breathing manoeuvres in close proximity to the personnel performing the test and may induce coughing. In addition, asymptomatic and pre-symptomatic patients are difficult to detect, regardless of the screening performed.[40] The pandemic itself has shown us how important it is to assess patients in the respiratory setting, and this includes

spirometry.[5,38] For full and urgent reactivation of centres performing this test, a hierarchy of risk control must be established, giving priority to processes that protect the collective workforce, without neglecting the surveillance of individual measures.[41]

In post-pandemic times, all hygiene and disinfection procedures should be documented in the internal procedures manual. Similarly, the scheduling of each study should consider extending the time between patients, thus avoiding prolonged waiting time and

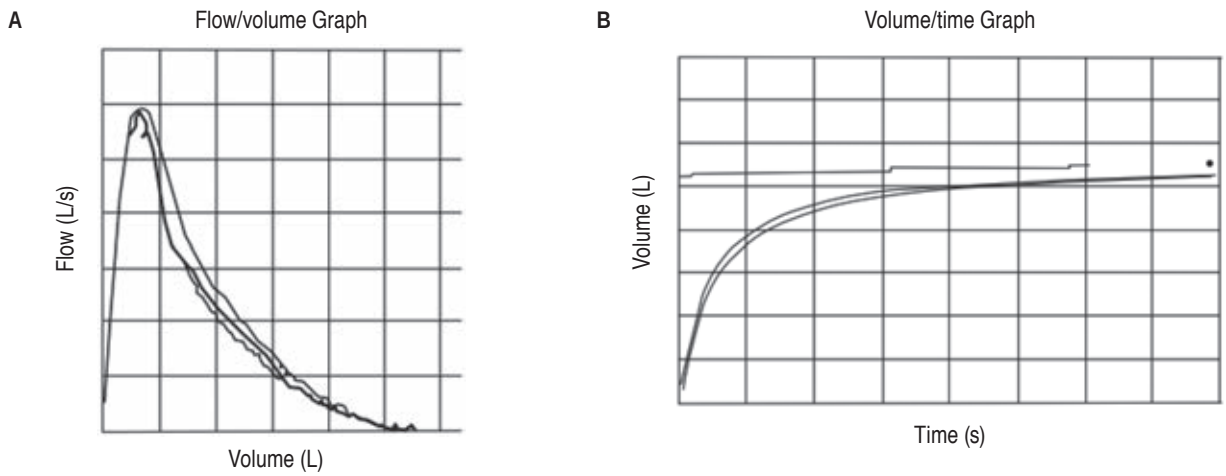

Figure 12: Acceptable single forced spirometry (good onset: F/V graph with abrupt onset, peak flow and gradual decline, extrapolated volume or BEV/Vext less than 0.10 L or 5% of FVC. Good termination of forced exhalation: EOTV or EOFE less than 0.02 L) Repeatable in FVC (4.28-4.16 L = 0.12 L) and FEV_1 (2.96-2.88 L = 0.8 L).

Table 5: Complete spirometric report.

Forced spirometry Name of the execution site								
Patient's full name			ID			Age (years)		
Sex			Ethnic origin			Height		
Weight (kg)			Date of the test			Predicted (NHANES III...)		
Date of last calibration			Initials of the performing technician			Smoking rate/asthma...		
	Pre-bronchodilator values							
Parameter	**Pred**	**LIN**	**Best**	**Test 1**	**Test 2**	**Test 3**	**% pred**	**Z-score**
FVC (L)	3.73	3.00	4.28	4.28	4.16	4.11	115	1.24
FEV_1 (L)	2.87	2.25	2.96	2.96	2.88	2.75	103	0.24
FEV_1/FVC	0.78	0.69	0.69	0.69	0.69	0.66	88	-1.63
PEF (L/s)	7.80	5.67	6.96	6.62	6.71	6.96		
FET (s)			9.6	9.6	10.9	9.3		
FIVC (L)	3.73	3.00	4.00	4.00	3.91	3.74		
EOTV (L)				0.00	0.00	0.00		
BEV or Vext (L)				0.12	0.09	0.08		
FEV.75 (L)			2.62	2.62	2.56	2.42		
FEV.75/FVC (L)			0.61	0.61	0.61	0.58		

NHANES = National Health and Nutrition Examination Survey. Pred = predicted. LIN = lower limit of normal. FVC = forced vital capacity. FEV_1 = forced expiratory volume in the first second. PEF = peak expiratory flow. FET = forced expiratory time. FIVC = forced inspiratory vital capacity. EOTV = end of test volume. BEV or Vext = extrapolated volume. FEV.75 = forced expiratory volume at 0.75/s.

Table 6: Quality grades for FEV_1 and FVC.[1]

Grade	Acceptable manoeuvres	ΔFEV$_1$ and ΔFVC, mL		Commentary
		Over 6 years old	Under 6 years of age	
A	3	< 150	< 100	Technically highly reliable
B	2	< 150	< 100	Technically reliable
C	2	< 200	< 150	Technically acceptable
D	2	< 250	< 200	Technically with reserve
E	2 o 1	> 250	> 200	Technically not recommended
U	0 acceptable and 1 useful	N/A	N/A	Rating recommended only for expert assessor
F	0 or 1	N/A	N/A	Technically not recommended

FEV_1 = forced expiratory volume in the first second. FVC = forced vital capacity. N/A = not applicable.

Table 7: Control of occupational hazards when performing spirometry.[5,38]

	Engineering control	Administrative control	Personal protective equipment
Objective	Isolate personnel from exposure	Modify work processes to reduce exposure	Directly protect the exposed worker
Organizational Impact	Collective		Individual
Actions	**Prioritise implementation by category:** • Category 1. Urgent or essential (needed for life-threatening treatment) • Category 2. Life-limiting (needed to initiate treatments that improve quality of life) • Category 3. Routine • Category 4. Vulnerable patients Categories 3 and 4 should be reserved for the post-pandemic phase **Infrastructure:** • Ventilation rates of at least 6 air changes/HR • HEPA filters with adequate maintenance • Negative pressure room for active TB patients **Consumables:** • Disposable mouthpieces (do not reuse) • Mandatory use of high efficiency filters	**Screening for active respiratory infections:** • Signs and symptoms questionnaire (re-agendize for active infection data) • Immunocompetent do not need negative PCR vs. SARS-CoV-2 30 days after infection • Immunocompromised 2 PCRs recommended versus SARS-CoV-2 (-) after illness **Organisation of schedule and patient flow:** Earmarking first shifts or specific areas for vulnerable patients **Physical distance (at least 2 metres) in waiting area** **Minimise patient exposure time during testing** **Mandatory mouth cover on patient between manoeuvres** **Cough or sneeze etiquette when performing the manoeuvre** **Mandatory handwashing of staff and patient** **Aerosol break** **Cleaning and disinfection between patient and patient**	**Eye protection:** • Goggles or face shield **Respiratory protection:** • Respirators with more than 95% particulate filtering (FFP2 or N95) • Seal test • The use of fabric, surgical or other masks is not recommended when testing

HR = 6 air changes/hour. HEPA = high efficiency particle arrester. PCR = polymerase chain reaction.

overcrowding of subjects, and reducing the risk of infection. *Table 7* summarises the measures according to the international consensus published by the European Respiratory Society.

CONSIDERATIONS IN PAEDIATRICS

With proper training, children as young as two and a half years can perform acceptable spirometry.[1]

It is suggested that tidal volume manoeuvres (such as impulse oscillometry) be performed first, followed by forced spirometry, as deep inhalations may change bronchial tone in children with asthma. Children have a high elastic recoil, so these patients may not reach a plateau, in these cases the indicator of adequate EOFE is the repeatability of FVC. Practitioners involved in the performance of pulmonary function testing of young children should be trained to work with this population. *Table 8* summarises some recommendations in this type of patient.[42,43]

SLOW SPIROMETRY

Spirometry can also be performed in a relaxed or quiet manner, which is referred to as slow spirometry. The slow manoeuvre is comfortable to perform, does not require strenuous physical effort and provides additional information to the forced manoeuvre.

The main measurements obtained from slow spirometry are SVC, which is the slowly exhaled volume from TLC to residual volume (RV), and inspiratory capacity (IC), which is the slowly inspired volume of air from expiration at tidal volume to maximal inspiration at TLC. It is recommended to be performed before any forced manoeuvre. The manoeuvre consists of the following steps *(Table 9)*:

1. Tidal volume breaths (at least three steady ones) and then ask the patient to perform one of the following:

a) Deep breath in to TLC without hesitation and relaxed exhalation to RV *(Figure 13A)*.
b) Relaxed exhalation to RV and subsequent deep inspiration to TLC *(Figure 13B)*.

The manoeuvres are relaxed and unforced. Peak inspiratory and expiratory levels are usually achieved within the first six seconds, some patients may require more time. The manoeuvre should not be excessively slow, as this may underestimate the SVC. As with forced spirometry, at least three acceptable manoeuvres should be obtained. A

Table 8: Recommendations for spirometry in paediatric patients.[44]

1. Establish a patient-friendly environment	Greet the child, encourage conversation (compliment the way they are dressed, ask about holidays, school)
2. Use analogies to explain the test	Instruct the child to play a «blowing game» on the computer Demonstrate the test by blowing into a handkerchief, blowing into a kerchief, blowing into a kettle, or blowing into a spittoon
3. Maintain correct patient position	Encourage the child to stand upright and hold the flow sensor vertically Use nose clips, but if they are too uncomfortable avoid them
4. Encourage the patient to perform the manoeuvre properly	Position yourself at the same visual level as the child Be expressive with your body language (change the intonation of your voice, use your hands) Use words the child can understand and simple instructions: «Breathe in», «Breathe out»; «Breathe in until you feel like you're bursting», «Breathe out» Use visual incentives (such as birthday candles)
5. Train your frustration tolerance	Be prepared to try different techniques (open vs. closed manoeuvre) Establish rest periods Offer incentives (stamps, prizes, recognition) Know when to stop. Sometimes it will not be possible to obtain technically acceptable or repeatable spirometry

Table 9: Slow spirometry manoeuvres.

	Prebronchodilator values							
Parameter	Pred	LIN	Best	Test 1	Test 2	Test 3	% pred	Z Score
VC (L)	3.80	3.09	3.73	3.73	3.64	3.58	98	-0.15
VCex (L)	3.80	3.09	3.70	3.65	3.70	3.69	97	-0.16
VCin (L)	3.80	3.09	3.73	3.73	3.64	3.58	98	-0.15
IC (L)			2.86	2.97	2.88	2.75		
VT (L)			1.03	1.02	1.03	1.02		

LIN = lower limit of normal. VC = vital capacity in litres. VCex = expiratory vital capacity in litres. VCin = inspiratory vital capacity in litres. IC = inspiratory capacity. VT = tidal volume.

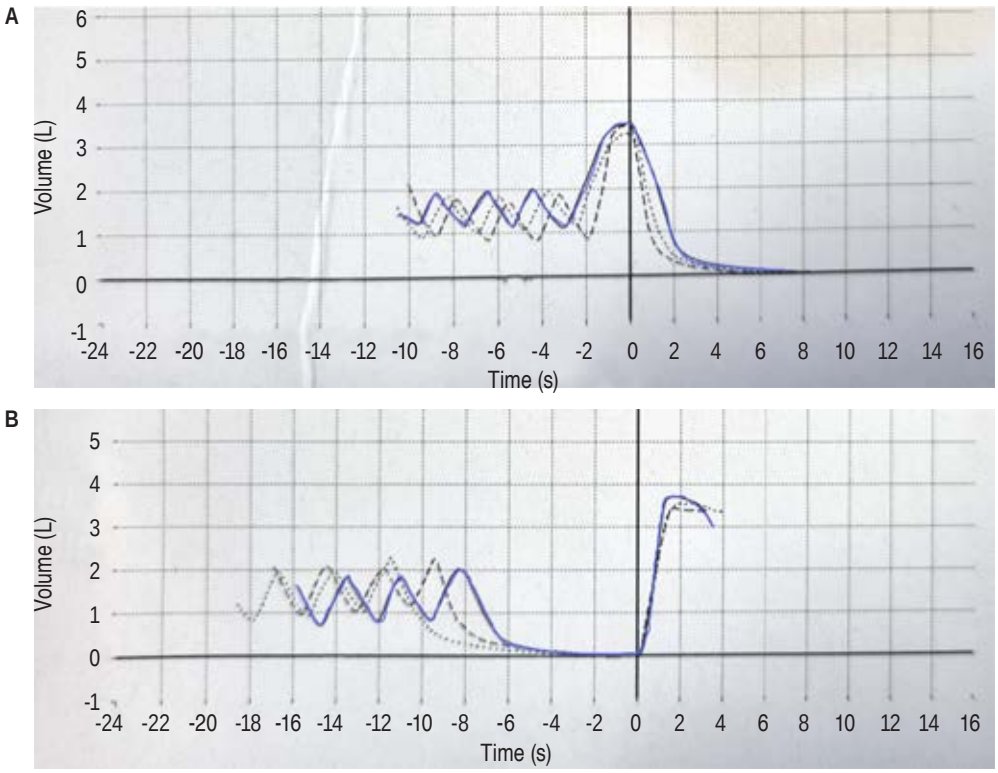

Figure 13:

A) Manoeuvres of slow expiratory vital capacity. **B)** Inspiratory slow vital capacity manoeuvres.

maximum of eight attempts is recommended. The criteria for acceptability are the same as for the forced manoeuvre. Repeatability is assessed by subtracting the values of the two best SVCs, and these should be < 150 mls.

The lack of repeatability in this study is, in most cases, due to incomplete inspiration. For SVC, the highest value of the acceptable manoeuvres should be reported. For IC, the average of the acceptable manoeuvres should be reported. SVC and CI are useful for assessing bronchodilator response, using as criteria for significant response an improvement in 200 mL and 12% in either variable.

FVC and SVC in subjects without airflow obstruction show similar values; however, in obstructed subjects, small airway collapse and air trapping in the forced manoeuvre mean that FVC is lower than SVC.

Limitations of slow spirometry are its lower reproducibility with respect to the forced manoeuvre, less standardisation and fewer reference values available; but, on the other hand, it may be more sensitive in detecting airflow obstruction.

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Clinical case

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Complicated pleural effusion in Kartagener syndrome: clinical case presentation

Derrame pleural complicado en síndrome de Kartagener: presentación de caso clínico

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ABSTRACT. The Kartagener triad; chronic sinusitis, bronchiectasis and *situs inversus totalis* occur in the syndrome of the same name, with a prevalence of one in every 20 to 40 thousand individuals. This syndrome corresponds to one of the causes of primary pulmonary dyskinesia in adults (unlike the majority present since childhood). These patients have the characteristic of suffering from repeated community-acquired pneumonia, consequence of alterations in ciliary movement to be able to eliminate mucus and the presence of chronic sinusitis that generates purulent secretion, which will move until it reaches the alveoli, reason that complicates the prognosis in this type of patients. We present a clinical case of a 40-year-old male patient with complicated pleural effusion secondary to repeated respiratory infections, as a consequence of primary pulmonary dyskinesia. This is a case of a rare disease since the complete triad characteristic of Kartagener's syndrome can be of extraordinary presentation.

Keywords: Kartagener, dyskinesia, bronchiectasis, pleural effusion, infection.

RESUMEN. La tríada de Kartagener: sinusitis crónica, bronquiectasias y *situs inversus totalis* se presentan en el síndrome del mismo nombre, con una prevalencia de uno por cada 20 a 40 mil individuos. Dicho síndrome corresponde a una de las causas de discinesia pulmonar primaria en el adulto (a diferencia de la mayoría presentes desde la infancia). Estos pacientes tienen la característica de cursar con neumonías adquiridas en la comunidad de repetición, consecuencia de alteración del movimiento ciliar para poder eliminar el moco y la presencia de sinusitis crónica que genera secreción purulenta, la cual va a desplazarse hasta establecerse en los alvéolos, motivo que complica el pronóstico en este tipo de pacientes. Se presenta el caso clínico de un paciente masculino de 40 años, con derrame pleural complicado secundario a infecciones respiratorias de repetición como consecuencia de una discinesia pulmonar primaria. Nos encontramos ante un caso de enfermedad rara, ya que la tríada completa característica del síndrome de Kartagener puede llegar a ser de presentación extraordinaria.

Palabras clave: Kartagener, discinesia, bronquiectasias, derrame pleural, infecciones.

INTRODUCTION

Kartagener syndrome is the cause of 50% of primary ciliary dyskinesias (PCD), as well as generating bronchiectasis in adult patients, mainly young.[1] It has an average age of presentation of 23 years of age, even though there are reported cases of adolescent patients and even up to the fifth decade of life.[2] The triad of Kartagener occurs in only one in every 20 to 40 thousand individuals with ciliary dyskinesia; it is characterized by the presence of chronic sinusitis that is almost always diagnosed in childhood. The *situs inversus totalis* is mostly incidental, since it usually does not generate clinical symptoms, however, a small proportion of patients can develop congenital heart diseases; bronchiectasis develops in adulthood as a result of repeated respiratory infections.[3] The classic clinic corresponds to recurrent respiratory infections that, if not adequately treated, can lead to complications such

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as severe pneumonia, complicated pleural effusion and even total lung transplants due to damage secondary to bronchiectasis.[4] In addition, patients experience infertility in 100% of cases, because the cilia of the reproductive systems are defective and do not confer adequate mobility to sperm in men, or adequate adherence of the ovary to the fallopian tubes women.[5]

CASE PRESENTATION

Male patient of 40 years of age, married, without children, with a history of essential arterial hypertension of six-month diagnose in treatment with ARA-II (angiotensin II receptor antagonists), adequate control. History of chronic sinusitis of 31 years of diagnosis without treatment; carrier of *situs inversus totalis* is reported at nine years of age. Recurrent hospitalization secondary to community-acquired pneumonia, that until now had not conditioned any complication. He began suffering from unquantified fever, shortness of breath and cough, therefore, he is admitted to the emergency area. Laboratory studies were carried out that reported slight leukocytosis at the expense of neutrophilia, increase in acute phase reactant (PCR 50.04), the rest of the paraclinical studies in reference values according to the laboratory. The chest X-ray (not available) showed desxtrocardia, atelectasis, and area of condensation at the base of the right hemithorax; it does not respect the anatomical plane, so it is considered an atypical image. Rapid test is performed for SARS-CoV-2 that is negative. A contrasted computerized axial tomography (CAT) of the chest and abdomen is requested with a report of *situs inversus totalis* *(Figure 1A)*, mass in the left based and in the anterior mediastinum *(Figure 1B and 1C)*, with slight contrast enhancement, in addition to bibasal bronchiectasis *(Figure 1D)*. Based on laboratory and imaging results, treatment is provided for community-acquired pneumonia (CAP), pneumonia severity index (PSI) of 70 points risk class III, with dual antibiotic treatment. Because the clinic, mainly the cough, did not yield a sputum culture was carried out, with a seven-day growth of *Granulicatella elegans*; a treatment scheme established by a decrease of 50% the initial PCR value is maintained. Complete course of complicated pleural effusion at the expense of loculations; endopleural probe was placed to try to drain effusion without any success, without obtaining a sample for cytological and cytochemical shipments of pleural fluid. He was moved to the chest surgery area for decortication due to complicated pleural effusion, of probable parapneumonic origin due to repeated infections, secondary to pulmonary dyskinesia with inadequate removal of the ciliary mucus that conditions encapsulation.

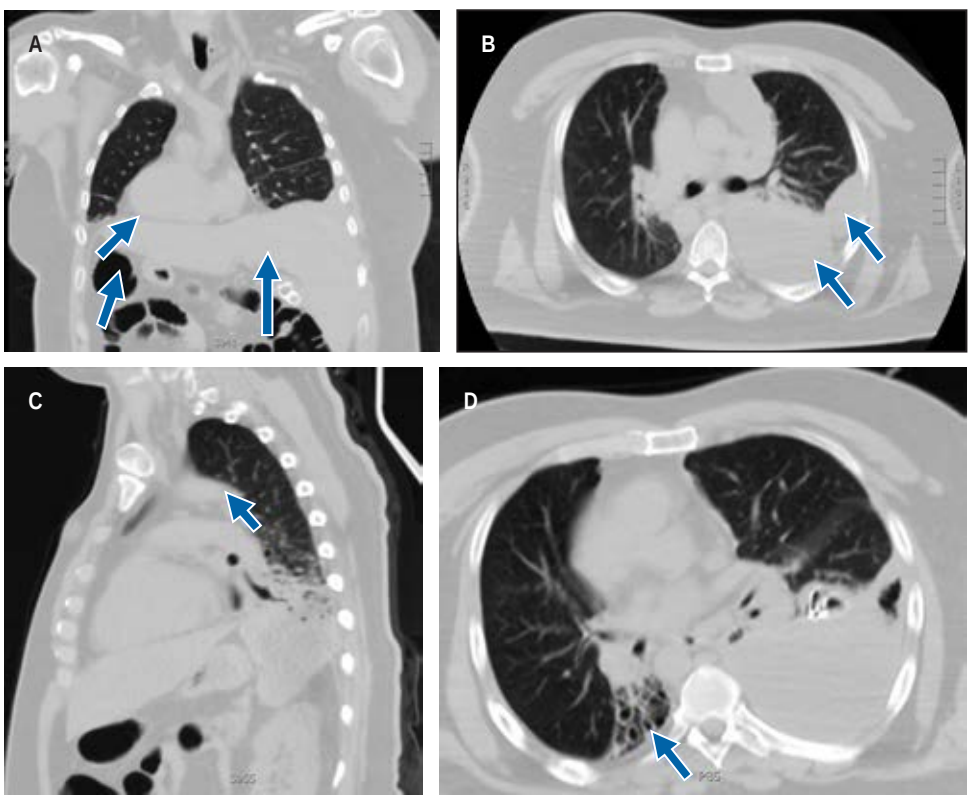

Figure 1:

A) *Situs inversus totalis* represented by mirror image of heart, liver and gastric bubble (arrows). **B)** Mass observed in the left hemithorax with view in axial section (arrows). **C)** Mass observed in the mediastinum in the sagittal section (arrow). **D)** Bronchiectasis based on right hemithorax (arrow).

DISCUSSION

Primary pulmonary dyskinesia corresponds to a genetic defect with autosomal recessive inheritance linked to the X chromosome, involving genes 4 and 12; since there is a defect in the embryonic nodal cilia, they determine the *situs inversus totalis*, since the location of the organs during embryogenesis depends on them. Kartagener syndrome is characterized by the triad of *situs inversus totalis*, bronchiectasis and chronic sinusitis; in addition, it is common to find infertility problems in adult patients due to lack of ciliary mobility in sperm.[5]

Clinically, it is characterized by the presence of recurrent upper respiratory infections that depend on the presence of chronic purulent sinusitis, and lower by the lack of mobility of the cilia that are the main determinants of the formation of bronchiectasis; this has allowed the development and research of new pulmonary physiotherapy techniques as part of the preventive approach.[6] In recent years, genetic techniques have been studied, which would reduce future complications by starting preventive treatment early. Treatment consists of treating the complications with pulmonary physiotherapy, pneumococcal and influenza vaccination. Antibiotic prophylaxis with azithromycin has been proposed for 6 to 12 months in individuals with recurrent complications, but there is still insufficient scientific evidence, despite the fact that it has been proven that morbidity and mortality have significantly decreased in the patients in whom it has been used.[4] Among the surgical options, lobectomy and lung transplantation stand out, which has been used successfully in patients with major complications that are life-threatening; the disadvantage is that highly specialized national health centers are required to perform them.[3] The preventive approach is the main objective in Kartagener syndrome; if all patients will have the possibility of performing ciliary video microscopy with ciliary sampling or genetic testing, prophylactic measures could be implemented early, and in this way avoid complications in the future.[4]

CONCLUSIONS

Kartagener syndrome corresponds to the main cause of pulmonary dyskinesias; the main complication corresponds to the course of recurrent respiratory infections.

The main therapeutic approach in the future should be prevention, as well as offering new early detection techniques to all patients detected with upper respiratory tract infection and *situs inversus totalis* or partial.

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Clinical case

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Mediastinal cryobiopsy: case report

Criobiopsia mediastinal: reporte de caso

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ABSTRACT. Bronchoscopy has become an essential diagnostic and therapeutic modality for a variety of lung diseases. With the addition of complementary techniques, such as taking a biopsy with a cryogenic probe, the role of the evaluation of pulmonary and mediastinal pathology is further expanded, allowing better diagnostic performance. **Case description:** 63-year-old male patient, with no history of direct family members with cancer, smoking rate of 50 packs/year, suspended three months prior to his evaluation due to dysphagia, without improvement, so he went to medical evaluation. A simple and contrast-enhanced chest tomography was performed, presenting a subcarinal mediastinal lesion measuring 58 × 51 × 74 mm and a mass in the apical segment of the right upper lobe, so it was decided to perform bronchoscopy to take a transcarinal biopsy. Which were performed using rigid tracheoscopy and flexible bronchoscopy, performing aspiration with a Wang needle, subsequently Forceps clamps and finally a flexible cryoprobe were introduced through the same puncture site with no evidence of hemorrhage after the procedures. Tissue measuring 0.6 × 0.3 × 0.2 cm was obtained through cryobiopsy, ideal for carrying out immunohistochemistry and mutation studies in pathology.

Keywords: mediastinal cryobiopsy, flexible bronchoscopy, transcarinal.

RESUMEN. La broncoscopia se ha convertido en una modalidad diagnóstica y terapéutica esencial para una variedad de enfermedades pulmonares. Con la adición de técnicas complementarias como la toma de biopsia con sonda criogénica, se amplía aún más el papel de la evaluación de la patología pulmonar y mediastínica, lo que permite un mejor rendimiento diagnóstico. **Presentación del caso:** paciente masculino de 63 años, sin antecedentes de familiares directos con cáncer, índice tabáquico de 50 paquetes/año, suspendido tres meses previos a su valoración por disfagia, sin mejoría por lo que acude a valoración médica. Se le efectúa tomografía de tórax simple y contrastada; presenta lesión mediastinal subcarinal de 58 × 51 × 74 mm y masa en segmento apical de lóbulo superior derecho, por lo que se decide realizar broncoscopia para toma de biopsia transcarinal. Las cuales se practicaron mediante traqueoscopia rígida y broncoscopia flexible, realizando aspiración con aguja Wang, posteriormente se introdujeron pinzas fórceps y, finalmente, criosonda flexible a través del mismo sitio de punción; no hubo datos de hemorragia posterior a los procedimientos. Se obtuvo tejido de tamaño de 0.6 × 0.3 × 0.2 cm mediante criobiopsia, ideales para realizar estudios de inmunohistoquímica y mutaciones en patología.

Palabras clave: criobiopsia mediastinal, broncoscopia flexible, transcarinal.

INTRODUCTION

Flexible bronchoscopy has become an essential diagnostic and therapeutic modality for a variety of lung diseases; the addition of transbronchial needle aspiration (TBNA) further expanded the role in the evaluation of mediastinal pathology. In 1949, Schieppati made the first description of mediastinal lymph node sampling through the carina using a rigid bronchoscope. In 1978, Wang and colleagues demonstrated that paratracheal lymph node sampling by TBNA was feasible.[1]

Bronchoscopic cryobiopsy has proven useful in both endobronchial and peripheral lung tumours as well as interstitial lung diseases; the most common side effects reported are pneumothorax and bleeding. Mediastinal cryobiopsy has shown improved diagnostic utility for molecular testing of genetic mutations.[2]

The first randomized trial, conducted in 2021 by Zhang and associates, included a total of 197 cases with mediastinal lesions ≥ 1 cm in which they used endobronchial ultrasound (EBUS)-guided TBNA and linear

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EBUS-guided cryobiopsy, alternating the order of initiation of these procedures. They recorded higher diagnostic yield in cryobiopsies 91.8% versus 79.9% (p = 0.001) and higher sensitivity in rare tumours (91.7% versus 25%, p = 0.001), with pneumothorax and pneumomediastinum in 1% and 0.5% of cases, respectively, resolving without intervention.[3-5]

In another prospective pilot trial, conducted in 2022 by Gershman E et al, 24 patients underwent EBUS-guided cryobiopsy following EBUS-guided TBNA. They obtained an anatomopathological result of 83.3% for cryobiopsy and 87.5% for TBNA. No complications were recorded in any of the patients.[4]

In both studies mentioned above, the procedures were performed under EBUS guidance. However, in the present study, the procedure was performed without ultrasound guidance because the lesion was of significant size and located in a relatively easily accessible site.

The performance of the first mediastinal cryobiopsy at our hospital is described below.

PRESENTATION OF THE CASE

Male patient aged 63 years, with no history of cancer in direct family members, smoking rate of 50 packs/year, suspended three months prior to hospital admission, recently diagnosed with systemic arterial hypertension.

His condition began three months prior to admission with dysphagia, for which he stopped smoking without improvement; he subsequently presented with non-productive cough and dysphonia. He went to the corresponding health centre where extension studies were performed, which revealed a mediastinal mass. He was referred to the third level for further treatment.

On admission, a simple and contrasted chest CT scan was performed; it showed a subcarinal mediastinal lesion measuring 58 × 51 × 74 mm, as well as a mass in the apical segment of the right upper lobe, a centrilobular micronodular pattern in the right upper and middle lobe, a subsolid nodule measuring 4. 3 × 5.2 mm in S7 and soft nodule of 5.4 × 5.1 mm in S8 of the right lower lobe, so it was decided to perform bronchoscopy with biopsy *(Figure 1A-D)*. The procedure was performed under full sedation with the use of rigid tracheoscopy, with a rigid Hemer Richar Wolf® tracheoscope model with a diameter of 14 mm, and flexible bronchoscopy with a 5.9 mm diameter vi deobronchoscope with a 2.8 mm working channel Olympus Medical Systems®. With fluoroscopy support, a 21G eXcelon™ Boston Scientific® transbronchial aspiration needle was introduced for aspiration at the level of the main carina. Subsequently, Radial Jaw™ 4 Boston Scientific® forceps, 100 cm in length, with 1.8 mm diameter forceps were introduced with a double purpose: first, to collect tissue sample and, second, to increase the diameter of the orifice; finally, through the same puncture site, a flexible cryoprobe of 1. 9 mm × 900 mm Erbe® flexible cryoprobe connected to the ERBECRYO 2® cryosurgery unit, with a freezing time of four seconds, was thawed in warm saline; a total of three samples were collected, with no post-procedure bleeding. Two tissue samples, each measuring 0.1 × 0.1 cm, were obtained using forceps and three samples were obtained by cryobiopsy, together measuring 0.6 × 0.3 × 0.2 cm, ideal for immunohistochemistry and mutational studies in pathology.

The samples were sent to the Pathology Service for review by a pulmonary pathologist for immunohistochemistry and mutational studies. The report indicated the following:

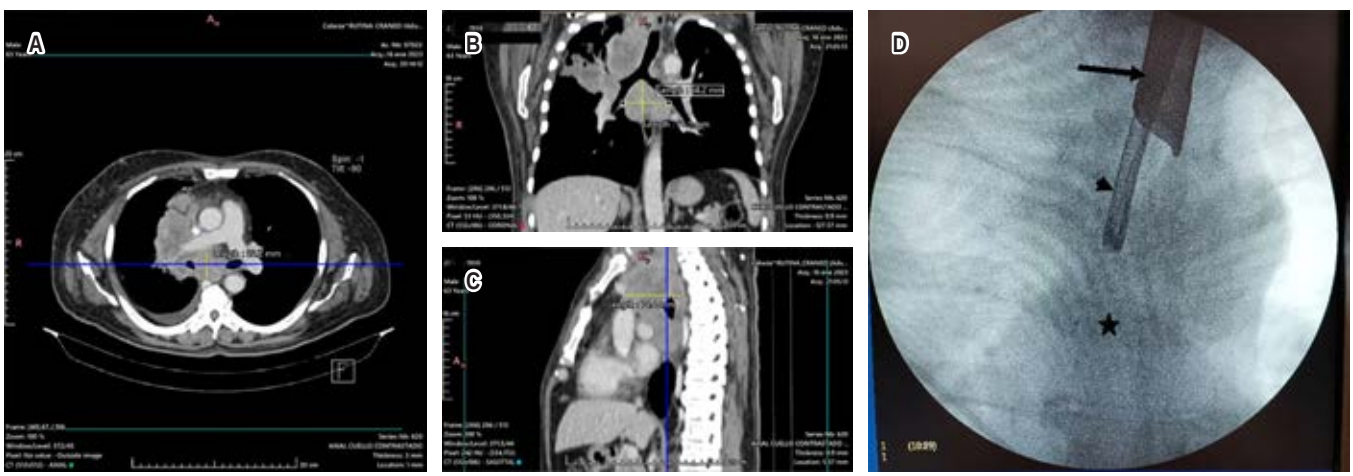

Figure 1: Contrast-enhanced chest CT scan mediastinal window with measurement of mediastinal node station VII in axial **(A)**, coronal **(B)** and sagittal **(C)** views. **D)** Fluoroscopy image showing rigid bronchoscope (arrow), flexible bronchoscope (arrowhead), mediastinal node at node station VII (star).

1. Biopsy station VII with forceps forceps: small cell carcinoma with crush artifact.
2. Cryobiopsy of station VII: small cell carcinoma. Immunophenotype CKAE1/ AE3+/ CK8-18+/ chromogranin +/ synaptophysin +/ TTF1+/ cell proliferation index KI-67: 50%.

DISCUSSION

Cancer treatment is evolving rapidly; therefore, bronchoscopists are providing increasing amounts of tissue to perform molecular testing for genetic mutations in a safe and minimally invasive manner. The implementation of these tests has led to improved diagnostic and therapeutic performance without the need to subject patients to surgical procedures.

Surgical mediastinoscopy is still considered a first-line procedure in certain situations, such as in cases of haematological malignancy, and in conditions where there is failure of bronchoscopic specimen collection. However, the complication rate is higher and the scarce availability of ultrasound bronchoscopic guidance at the institutional level in our country makes this procedure a minimally invasive diagnostic option. In the case presented, we dispensed with the use of EBUS due to the size (> 5 cm) and location (subcarinal level) of the lesion, with adequate results. It is necessary to continue performing this technique in order to standardize it and to know the profile of patients who would benefit from this procedure.

CONCLUSIONS

Rapid and correct diagnosis of mediastinal masses is mandatory for the clinical management and prognosis of patients; to this end, it is necessary that sufficient high-quality tissue samples are obtained for pathological, genetic, immunological and other evaluations, with increasingly less invasive methods. Mediastinal cryobiopsy is a promising technique for obtaining biopsies with sufficient material for pathological analysis.

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Pulmonary and endobronchial mucormycosis: a case report

Mucormicosis pulmonar y endobronquial: reporte de caso

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ABSTRACT. The case of a male patient who was admitted to the pulmonology department for a diagnostic protocol for left apical cavitation is presented. One of the risk factors he had was type 2 diabetes. His condition began with productive cough, whitish sputum, and dyspnea. During the diagnostic process, a bronchoscopy study was performed, revealing endobronchial invasion. Samples were taken, and in the initial assessment, tuberculosis was ruled out due to its high prevalence in our region. Ultimately, the diagnosis was established as pulmonary mucormycosis and an uncommon endobronchial mucormycosis, both of which have a high mortality rate.

Keywords: pulmonary mucormycosis, amphotericin B, air-crescent sign, mucormycosis endobronchial.

RESUMEN. Se presenta el caso de un paciente masculino que ingresó al servicio de neumología para someterse a un protocolo diagnóstico de cavitación apical izquierda. Uno de los factores de riesgo que presentaba era la diabetes *mellitus* tipo 2. Inició su padecimiento con tos productiva, expectoración blanquecina y disnea. Durante el proceso de diagnóstico se realizó un estudio de broncoscopia en el que se observó invasión endobronquial. Se tomaron muestras y, en primera instancia, se descartó la tuberculosis debido a su alta prevalencia en nuestro medio. Finalmente, el diagnóstico se estableció como mucormicosis pulmonar y mucormicosis endobronquial poco común, ambas condiciones con una alta tasa de mortalidad.

Palabras clave: mucormicosis pulmonar, anfotericina B, signo de la media luna, mucormicosis endobronquial.

INTRODUCTION

Mucormycosis is an opportunistic infection caused by mucoral fungi of the class *Zygomycetes*.[1] These mucoral fungi are ubiquitous, saprophytic and not very demanding; they are found in soil or decaying organic matter. Among them, three genera are known to be pathogenic to humans: *Rhizopus*, *Absidia* and *Mucor*. Their optimum growth temperature is 28 to 30 °C under aerobic conditions, with an incubation period of two to five days. Incubation may begin with inhalation of spores or direct inoculation of injured skin.[2] The most common types of mucorales isolated from patients with mucormycosis are *Absidia*, *Rhizopus* and *Rhizomucor*. These species are believed to be ubiquitous saprophytes and soil is their main habitat. Sporangiospores released by the mucorales range in diameter from 3 to 11 μm and can aerosolise, which disperses them into the environment and can lead to upper or lower respiratory tract infections.[2]

Pulmonary mucormycosis is the third most common presentation of this disease and is characterised by its aggressive clinical course, with a mortality rate of more than 50%.[3] In the United States, the estimated incidence of this disease is 1.7 cases per million people per year; according to a review of 116 cases of mucormycosis, 22% are pulmonary mucormycosis.[4] There are numerous predisposing clinical factors, such as uncontrolled diabetes mellitus, diabetic ketoacidosis, chemotherapy, haematological malignancies (leukaemia and lymphoma), immunosuppressive therapy, acquired or congenital neutropenia, antibiotic therapy, metabolic acidosis due to chronic salicylate intoxication, elastoplasty dressings, renal

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failure, prolonged postoperative period, solid tumours, solid organ transplantation, agammaglobulinaemia and burns.[5-8] In patients with haematological malignancies, mucormycosis most commonly affects the lungs (58-81%).[8]

The diagnosis of pulmonary mucormycosis represents a challenge, as late diagnosis can have serious consequences. Therefore, it is of utmost importance to consider this disease among the possible differential diagnoses, especially in immunocompromised individuals. This article presents the case of a patient diagnosed by culture with mucormycosis.

CASE PRESENTATION

A 68-year-old man presented to our hospital in July 2023 with a non-productive cough with whitish expectoration, accompanied by dyspnoea on medium exertion; he denied fever and suffered a weight loss of 6 kg in the last few weeks. After receiving anti-infective treatment in the emergency department for two days, with little improvement, he was admitted to pneumology for diagnostic and therapeutic protocol; a chest X-ray was taken on admission *(Figure 1)*; a chest CT scan was scheduled *(Figure 2)*, where a well-defined cavitated mass was found within the left upper lobe, with the sign of the air like a crescent moon. Due to a suspected diagnosis of pulmonary tuberculosis, a bronchoscopy study was requested for bronchoalveolar lavage and acid-fast bacilli (AFB) test, mycobacterial and fungal cultures, as well as bacterial cultures. During the fibrobronchoscopy study, a whitish exophytic mass was observed in the anterior wall of the left S3 segment, so

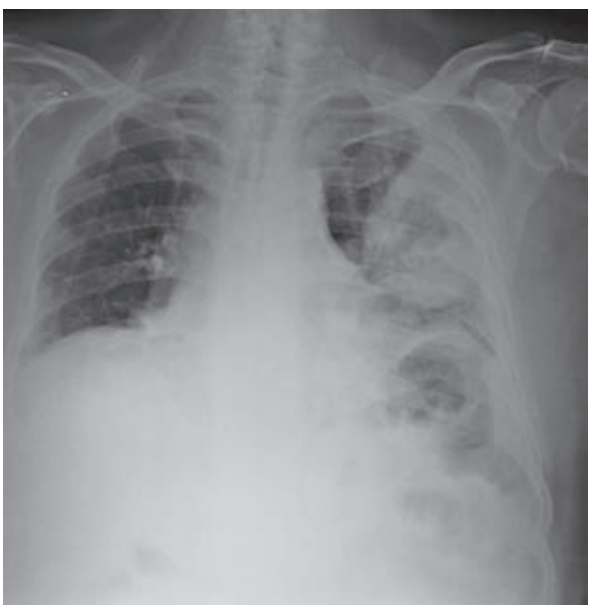

Figure 1: Chest X-ray. It shows a ball-shaped cavitated mass with crescentic cavitation in the posterior segment of the left upper lobe.

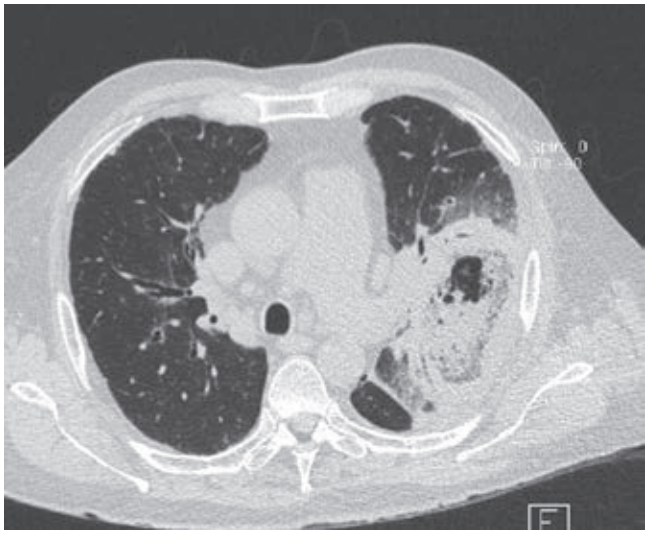

Figure 2: Chest CT scan. It shows a well-defined cavitated mass within the left upper lobe, with an air crescent sign. Nodules of different sizes are seen around the lesion and in the left upper lobe.

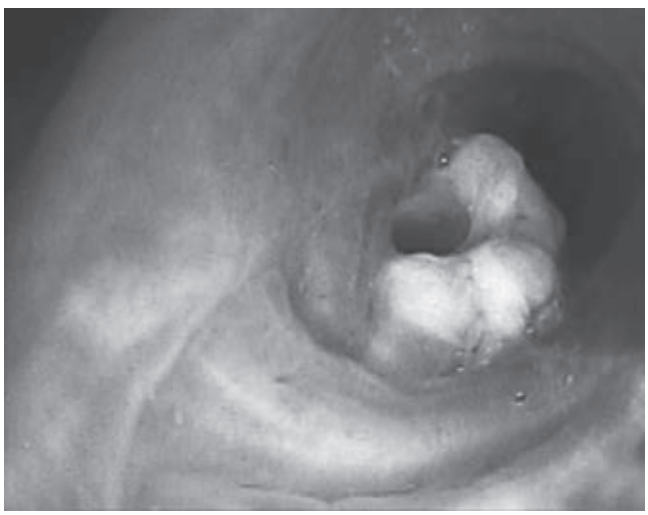

Figure 3: Fibrobronchoscopy. A whitish exophytic mass is seen in the anterior wall of the left S3 segment.

it was decided to take a biopsy and samples *(Figure 3)*; subsequently, by histopathological study, the diagnosis of mucormycosis was made and, by culture, *Absidia* mucormycosis. Management with amphotericin B was started; during the first three days of treatment, the patient's oxygen requirement increased, a new chest X-ray was requested; he arrived at the 15-litre reservoir mask with 90% saturation, tachypnoea, respiratory rate 30 per minute, with thoracoabdominal dissociation, and advanced airway management was decided. He died of septic shock in the first 12 hours of his stay in respiratory intensive care.

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DISCUSSION

We present the case of a 68-year-old male patient with a history of type 2 diabetes mellitus with poor control as the only risk factor. Initially, a possible *Mycobacterium tuberculosis* infection was considered, so it was decided to perform a bronchoscopy to obtain bronchoalveolar lavage samples, while awaiting the results of acid-fast bacillus (AFB) and GenXpert tests. The pulmonary infiltration progressed and, due to positive mycology culture results for mucor, treatment with antifungal agents, including continuous amphotericin B, was initiated. Unfortunately, the patient received a late diagnosis of pulmonary mucormycosis and his prognosis proved fatal during intensive respiratory therapy.

Pulmonary mucormycosis develops due to inhalation of fungal spores in the bronchioles and alveoli, usually leading to rapid progression to pneumonia or endobronchial disease. In rare cases, this infection can lead to endobronchial lesions and complications associated with airway obstruction. Haemoptysis is a common symptom when vascular invasion occurs, which can sometimes be fatal. Symptoms of pulmonary mucormycosis are usually non-specific, even in advanced stages of infection, and may include fever, dyspnoea, cough and chest pain. Rarely, the disease may manifest as progressive subcutaneous emphysema, Pancoast syndrome, Horner syndrome or chronic mediastinitis and bronchial perforation.[6,9]

Patient immunosuppression appears to be the most critical risk factor predisposing the patient to mucormycosis. Diabetes is also considered an important risk factor, as it significantly decreases the function of the immune system and increases the risk of various infections.[10]

Pulmonary mucormycosis can cause pulmonary embolism because mucorales species tend to invade the elastic intima of large and small blood vessels, which can lead to thrombosis, bleeding and infarction. This may be an important diagnostic clue when pulmonary embolism of unknown cause occurs in patients with signs of pulmonary infection. Therefore, physicians should be alert and consider the possibility of pulmonary mucormycosis in these cases.

Radiological manifestations of pulmonary mucormycosis are mostly non-specific; more than 80% of patients show abnormal findings on chest radiographs.[11] Findings may include consolidation, cavitation, air crescent sign, halo sign, inverted halo sign, multiple or solitary pulmonary nodules or masses, bronchopleural fistulas, pulmonary artery pseudoaneurysms, lymphadenopathy and pleural effusion. Cavitation is seen in up to 40% of cases, although the air crescent sign is rare. High-resolution computed tomography (CT) may be more sensitive in detecting the disease and may find evidence of infection earlier than conventional chest X-rays. The right lung is affected more frequently than the left, and there is a predilection for upper lobe involvement, although the reason behind this is unknown. The present case reported a right upper lobe lesion, as do the majority of cases in the literature.[11]

Histopathologically, vascular invasion with tissue necrosis and neutrophilic tissue infiltration is common to all types of mucormycosis. Diagnosis is made by demonstrating the presence of broad (6-16 μm diameter), non-septate (coenocytic), ribbon-like, right-angled branching hyphae in a routine haematoxylin and eosin stained tissue specimen. Special fungal stains are usually not necessary to establish the diagnosis. Less common and less specific features of pulmonary mucormycosis include bronchial invasion, pneumonia, lung abscesses and granulomatous pneumonitis.[7]

CONCLUSIONS

Pulmonary mucormycosis is primarily an opportunistic infection caused by mucorales. Such fungal infection occurs mainly in patients with immune system deficiency, although it may rarely attack immunocompetent patients. Due to its high mortality rate, clinicians must make judgements about suspected cases correctly and promptly to avoid misdiagnosis and delays in treatment. Early diagnosis of pulmonary mucormycosis remains a clinical challenge due to the lack of specific clinical manifestations. Firstly, clinicians need to be aware that pulmonary mucormycosis can occur in patients with normal immune function, especially when routine anti-infective treatments fail.

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Abstracts of free works

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Abstracts II International Mexican Congress of Sleep Medicine

Resúmenes II Congreso Internacional Mexicano de Medicina del Dormir

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Implementation of an animal model to analyze the effect of antiepileptic drugs on sleep disorders caused by generalized epileptic crisis+

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+Winning abstract in the basic/translational research category.

Introduction: epilepsy is a neurological disorder characterized by recurrent attacks caused by the synchronization of the discharge of thousands of neurons. Nocturnal epilepsy has a significant impact on sleep, as well as on the quality of life of individuals who suffer from it. The use of experimental animal models has contributed significantly to the understanding of the pathological processes and pathophysiological mechanisms underlying epilepsy. Administration of pentylenetetrazole (PTZ) results in the development of generalized epileptic crises. These models have been useful for testing the efficacy of different substances with antiepileptic potential. **Objective:** to implement an experimental model of epilepsy to compare the efficacy of antiepileptic drugs, with the purpose of protecting against sleep disturbances caused by epileptic crises. **Material and methods:** the experiments were carried out in white Wistar rats, chronically implanted for control sleep recording and under the effect of epileptic crisis provoked by the administration of PTZ. Subsequently, one group of rats was administered valproate, and another gabapentin (GBP) prior to PTZ administration. **Results:** PTZ administration, in addition to seizures, produced long-lasting insomnia; whereas pre-PTZ administration of both valproate and GBP reduced convulsive crises and improved sleep, making the action of GBP more effective. **Conclusions:** the experimental animal model implemented allows testing the efficacy of antiepileptic drugs on sleep disturbances caused by epileptic crises, as well as comparing the efficacy of different drugs, which will facilitate the selection of the appropriate drug for patients.

Sleep disorders in bed partners of patients with obstructive sleep apnea++

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++Winning abstract in the category of social-economic anthropological impact research.

Introduction: sleep disorders (SD) in our population are currently a public health problem. In Mexico, the most prevalent SD are: insomnia (22.1%), obstructive sleep apnea syndrome (OSAS) (6-32%), daytime sleepiness (19.1%) and poor sleep quality (45%). These disorders are known to directly affect the mental health of patients and may also affect that of the bed partner. Studies focused on sleep habits in older adults have demonstrated this phenomenon; however, this relationship is unknown in specific SD such as OSAS. **Objective:** to describe the prevalence of sleep disorders of bed partners of patients with obstructive sleep apnea syndrome. **Material and methods:** descriptive, observational, cross-sectional study. Twenty-one dyads of family members and patients diagnosed with OSAS were interviewed. Pittsburgh sleep quality index (PSQI), Epworth sleepiness scale (ESE) and insomnia severity index (ISI) were applied. **Results:** twenty-one

bed partners of patients with OSAS participated. The mean age was 54 ± 13.2 years; 15 (71.4%) were women. According to the ISI, nine (42.9%) had insomnia; according to the PSQI, 18 (85.7%) had some sleep problem; and with the ESE, six (28.5%) had moderate or excessive sleepiness. **Conclusions:** bed partners of patients with obstructive sleep apnea have more sleep disturbances than the general population. The importance of sleep assessment as a dyadic aspect and not as an individual component is noted.

Sleep quality and prevalence of probable sleep bruxism (PSB) in schoolchildren in León, Guanajuato, during 2023+++

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+++Winning abstract in the clinical research category.

Introduction: the sleep quality (SQ) is a determinant of daytime functioning. Among the functions of sleep are the maturation of the central nervous system and human development; one of the sleep disorders (SD) that affects SQ and is related to oral health is sleep bruxism (SB). **Objective:** to identify the association between SQ and probable sleep bruxism (PSB) in schoolchildren of the «Leona Vicario» elementary school in León, Guanajuato. **Material and methods:** cross-sectional, analytical study, in which a sample of 236 children (mean age 8.52 ± 1.82 years) was analyzed, 50.4% female. A Spanish-translated version of the children's sleep habits questionnaire (CSHQ) was applied. Tooth wear, indentation and furrowed tongue were evaluated with the «TWES 2.0» system. Mean and standard deviation were calculated for quantitative variables; and frequencies and percentages for qualitative variables; bivariate analysis was performed with χ^2. The statistical program IBM SPSS Statistics 24.0, 2016 was used. Informed consent was obtained from the responsible persons for each minor. **Results:** a prevalence of 18.2% of PSB was found, with a higher prevalence for the female sex of 9.3%. A significant relationship was found between PSB and the subscales of parasomnias ($p \leq 0.00$) and sleep fragmentation ($p \leq 0.02$); although there was no significant relationship with the subscales of sleep efficiency, total sleep time and obstructive sleep apnea. **Conclusions:** in the studied sample the prevalence of PSB was high and was related to indicators of other sleep disorders. Considering the negative impact of SD on development, early identification of PSB is very important.

Self-organizing maps to assess the effect of antiepileptic drugs on vigilance states in an experimental animal model of epilepsy

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Introduction: experimental animal models have been used to test the protective effect of antiepileptic drugs on wakefulness and sleep. One model involves the use of pentylenetetrazole (PTZ) as a generalized seizure-inducing agent. Generally, the efficacy of antiepileptic drugs is evaluated by inferential statistics, so the effect in each animal is not characterized separately. We believe that knowing the individual effect of drugs would contribute to assessing their efficacy. **Objective:** to use self-organizing maps (SOM) to evaluate the effect of diverse antiepileptic drugs on vigilance states in a PTZ model of epilepsy. **Material and methods:** data from previously published studies whose methodology consisted of the induction of epilepsy by PTZ and the use of antiepileptic drugs in adult male Wistar rats were evaluated. Valproate was applied to 10 rats, gabapentin to 24, phenobarbital to 10 and saline solution to eight. Under these conditions, three polygraphic recordings were made on three consecutive days to evaluate the surveillance states. For the SOM analysis, a multidimensional profile composed of waking, sleep-slow and sleep-REM values was determined in each rat for each day of recording. **Results:** four different groups of rats were identified, considering the effect exerted by antiepileptic drugs on the amount of wakefulness and sleep. **Conclusions:** SOM analysis allows to identify individual differences in the effect of antiepileptic drugs on vigilance states. These findings, at the clinical level, could contribute to explain the reaction of patients under treatment with different drugs.

Network science to assess the relationship between sleep quality, anxiety and depression levels of people during the COVID-19 pandemic

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Introduction: the COVID-19 pandemic had negative effects on levels of anxiety, depression and sleep quality. Although most studies report intensity levels ranging from mild to moderate, there are individual variations. Therefore, it is important to explore new methods of analysis that allow us to know the characteristics of the scores of these reports and to identify aspects that may be of clinical or epidemiological relevance. **Objective:** to evaluate the relationship between levels of sleep quality intensity, anxiety and depression using network science. **Material and methods:** a sleep quality questionnaire and the Beck anxiety and depression inventories were administered. The informed consent and questionnaires were placed on a digital platform whose link remained available during February-April 2021. The data were modeled with a bipartite network, one set of nodes was formed with the participants; the other set was formed with the responses of the three questionnaires, for which four categories were formed based on the level of intensity. Subsequently, a weighted projection was performed on the bipartite network over the set of questionnaires, and a modularity algorithm was applied to the resulting network. **Results:** three clusters were identified, each including the three variables that coincided with the level of intensity. **Conclusions:** network analysis

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corroborates the relationship between the severity levels of sleep quality, anxiety and depression. The better the quality of sleep, the lower the reported levels of anxiety and depression.

Cost-effectiveness economic evaluation of two treatments for obstructive sleep apnea-hypopnea syndrome from the perspective of the patient attended at the Sleep Disorders Clinic of the UNAM

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Introduction: obstructive sleep apnea-hypopnea syndrome (OSAHS) is characterized by intermittent and repeated collapse of the pharyngeal airway during sleep, which may be complete (apnea) or partial (hypopnea). The apnea-hypopnea index (AHI) is the frequency of apneas and hypopneas per hour during sleep that, in a healthy person, are less than five. The medical treatment for OSAHS is the administration of continuous positive airway pressure (CPAP) during sleep using a medical device of the same name. Lifestyle management is often recommended as a complement. It has been observed that treatment with CPAP combined with cognitive-behavioral therapy (CBT) can improve therapeutic outcomes. **Objective:** to economically evaluate CPAP therapy versus CPAP + CBT in the treatment of moderate to severe OSAHS in adult patients to determine if the implementation of combined therapy is cost-effective. **Material and methods:** a Markov model was performed that considered the stages of uncontrolled OSAHS, controlled OSAHS, stroke, myocardial infarction, vehicular accident and death. The time horizon of the model was 10 years. Health resource consumption and costs were determined by crude costing, using clinical practice guidelines and information reported in the literature. The effectiveness of the therapies was evaluated in terms of the probability: decrease in AHI < 5; other probabilities of occurrence of other clinical events included in the model were also included. The incremental cost-effectiveness ratio (ICER) was obtained. A multivariate and univariate sensitivity analysis was performed with a variation of ± 7% to evaluate the robustness of the model; a Monte Carlo simulation was performed, considering a willingness to pay of a GDP in Mexico. **Results:** the average cost-effectiveness ratio per patient resulting from the Markov model was $59,163.69 and $45,308.56 for CPAP therapy and CPAP + CBT, respectively. The most cost-effective therapy was CPAP + CBT. The ICER was $28,479.64, with the combined CPAP + CBT therapy being non-dominated, as it has an incremental effectiveness of twice that of CPAP monotherapy. Sensitivity analysis showed that the model is robust; the Monte Carlo simulation model showed that most iterations were below a cost equivalent to one GDP of Mexico. **Conclusions:** the implementation of combined treatment with CPAP + CBT is cost-effective versus CPAP monotherapy for moderate to severe OSAHS in adult patients, from the perspective of the patient treated at CTS-UNAM.

Level of anxiety and depression in chronic insomniac patients in the post-pandemic period at the UNAM Sleep Clinic

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D de la Orta-López,
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Introduction: insomnia associated with mood and/or anxiety disorders occurs in up to 70% of cases and is the main cause of consultation; it mainly affects women and the working-age population. During the acute phase of the pandemic, it was reported to have intensified worldwide. **Objective:** to assess the level of anxiety and depression in insomniac patients attending for consultation in the pre- and post-pandemic stages of the COVID-19 pandemic. **Material and methods:** observational, retrospective, comparative study. Non-randomized purposive sampling. Patient data registry from 2017-2019, pre-pandemic group (ADP); and 2022-2023, post-pandemic group (PDP). First-time patients with chronic insomnia and BAI (Beck anxiety inventory) and BDI (Beck depression index) tests were considered. The means of each scale were compared in univariate analyses with group, «sex», «anxiolytic and antidepressant medication use» as fixed factors and age as a covariate. Significance was considered with $p < 0.05$. **Results:** sample of 233 patients (160 ADP and 73 PDP), aged 56.3 ± 15.6 years; 132 (56.7%) female. Nine (5.6%) ADP and 14 (19.2%) PDP had indicated medication. In all comparisons, scale scores were higher in the ADP group compared to the PDP group, with BAI 18.6 ± 13 versus 14.9 ± 11.5, $p = 0.045$ and BDI 17.1 ± 11.6 versus 11.6 ± 8.5, $p < 0.001$. ADP versus PDP had low, 107 versus 55 (66.9% versus 75.3%); moderate (17.5% versus 15.1%) and severe (13.8% versus 9.6%) anxiety. ADP versus PDP had minimal or absent depression 48 versus 33 (30.0% versus 42.2%); mild (27.5% versus 31.5%), moderate (26.9% versus 17.8%) and severe (14.4% versus 5.5%). **Conclusions:** demographic data correspond to the population most affected by chronic insomnia, in the PDP a significant decrease in the intensity of anxiety and prevalence and intensity of depressive symptoms is observed; this effect should be contextualized to the end of mandatory confinement and the increased awareness of mental health during it.

Coherence analysis between brain and cardiac activity during sleep in children with Asperger syndrome

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Introduction: coherence is a method for quantifying the coupling between one or more biological signals in the frequency domain, so it has been used to investigate the relationship between brain and cardiac activity during sleep in children with Asperger syndrome, who have autonomic and cortical abnormalities, as well as comorbidity with sleep disorders. **Material and methods:** children aged six to 10

years diagnosed with Asperger syndrome (n = 11) and typically developing children (n = 11) were included. Polysomnographic recordings were made during two consecutive nights; the first night was for adaptation and the second night was considered for analysis. **Objective:** to determine whether there is coherence between parasympathetic cardiac activity and different brain frequency bands (delta, theta, alpha, beta and gamma) during REM and non-REM sleep in a group of children with Asperger syndrome and a group of typically developing children. **Results:** REM sleep latency, number of sleep cycles and time in bed were outliers in children with Asperger syndrome. On the other hand, typically developing children had higher coherence values between delta-RSA (respiratory sinus arrhythmia) during non-REM sleep compared to the group of children with Asperger syndrome. **Conclusions:** there is adequate parasympathetic functioning during non-REM sleep in typically developing children, reflected by a high coupling between the RSA and the delta band. Whereas, in children with Asperger syndrome, the communication between the cardiovascular center and the sleep generating circuits may be impaired, resulting in inefficient interaction between the brain and the heart during sleep, leading to poor coherence and outliers in some measures of sleep structure.

Sleep quality, associated respiratory disorders and the use of chronic noninvasive mechanical ventilation in children with neuromuscular diseases

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Introduction: neuromuscular diseases (NMD) affect 1 in 2,000 people. In children who suffer from them, sleep-disordered breathing (SDB) occurs in 40-70% of cases. Ventilatory compromise during sleep is a first step to chronic respiratory failure, so timely diagnosis and initiation of treatment is critical. **Objective:** to describe sleep disorders and their evolution with the use of non-invasive mechanical ventilation (NIMV) in patients with NMD attended at the INER Sleep Medicine Unit during the period from January/15 to January/20. **Material and methods:** cross-sectional, clinical research, with review of records from which demographic, clinical and polysomnographic information was obtained. The polysomnographies were basal and ventilatory; performed on the Grass, Alice and Neurovirtual equipment in children diagnosed with NMD. **Results:** 78 patients with an average age of 12 years were included. The main diagnoses were: Duchenne muscular dystrophy (65.3%) and spinal muscular atrophy type II (8.97%). Polysomnography reports altered sleep architecture with prolonged latency to REM sleep, increased N1 and N3 and decreased REM sleep. A total of 71.8% presented OSA, central apnea and hypoxemia during sleep were also reported. Of 43 patients, only 19 acquired NIMV equipment, the most commonly used being the Binivel ST (88.38%); in 89.47% an IPAP: 12, EPAP: 6, PS: 6 and backup FR: 18 were used; and of these, 51.61% had an adequate adherence to their use. **Conclusions:** SDB are frequent in patients with NMD. NIMV is a costly therapy that is not accessible to all, and adequate adherence to its use is relevant in order to make its benefits evident.

Complications and postoperative follow-up of patients undergoing adenotonsillectomy and nasal surgery with obstructive sleep apnea syndrome at the National Institute of Respiratory Diseases

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Introduction: nasal obstruction is common in patients with obstructive sleep apnea syndrome (OSAS); it contributes to increased negative airway pressure due to elevated nasal resistance and reduced nitric oxide production. The goals of nasal treatment are to reduce nasal obstruction and facilitate adherence to positive airway pressure therapy. OSAS in children is associated with neurobehavioral deficits and cardiovascular morbidity, highlighting the need for timely diagnosis and treatment. In healthy children, older than two years, with adenotonsillar hypertrophy, the first-line treatment for OSAS is adenotonsillectomy. **Objective:** to report surgical complications, as well as follow-up in patients with OSAS at the National Institute of Respiratory Diseases (INER for its acronym in Spanish). **Material and methods:** a search was made in the clinical records of INER patients with a diagnosis of OSAS who underwent nasosinusal surgery and adenotonsillectomy between March 2021 and May 2023. Data were analyzed according to their distribution as mean, median, standard deviation, interquartile range, percentage and proportions. **Results:** 288 nasal surgeries were performed, in which 30 (10.4%) patients had OSAS, 23 (76.6%) males and seven (23.3%) females; four (13.3%) with mild disease, eight (26.6%) with moderate disease and 17 (56.6) with severe disease. Among the types of nasal surgery, seven patients underwent rhinoseptumplasty, and the rest underwent functional surgery. Four of all patients with OSAS had the following complications: one late postoperative bleeding, one septal abscess, two intraoperative septal mucosal tears, of which none had septal perforation or any other late complication. A total of 104 adenotonsillectomy procedures were performed; of which 91 (94.65%) interventions had OSAS as a surgical indication; of this group of patients, 72 (65.5%) were minors and 19 (34.5%) were adults; four (3.6%) patients presented late surgical bleeding as a complication. **Conclusion:** nasal surgery and adenotonsillectomy in patients with OSAS are procedures that contribute to improve the clinical conditions of these patients, and also present a low incidence of complications.

An exploratory study of circadian activity patterns in individuals with major depression, primary insomnia, and good sleepers

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Introduction: in people with depression and insomnia, actigraphy has revealed lower daytime activity, higher wakefulness after sleep onset (WASO) and higher sleep fragmentation index. In primary insomnia, overestimation of sleep latency

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(SL), underestimation of total sleep time (TST) and phase delay in circadian activity have been found. Differences have also been found between subjective reporting and actigraphy reporting. Comparisons between the two groups are scarce, as are studies evaluating circadian activity patterns and not just sleep parameters. **Objective:** to evaluate the characteristics of circadian patterns of activity and rest in individuals with primary insomnia (PI), major depression with insomnia (MDI) and good sleepers (GS). **Material and methods:** observational, analytical, cross-sectional study. Using non-probability convenience sampling, three groups were obtained: patients with major depressive disorder and insomnia (MDI, n = 10), primary insomnia (PI, n = 11), and good sleepers (GS, n = 10). Actigraphs were used to measure activity and rest patterns for seven days. **Results:** in relation to the sleep indicators, there were no significant differences between the groups in TST, WASO, sleep efficiency and SL. Whereas, with respect to activity patterns, the GS started activity significantly earlier (< 6 a.m.) and their activity was higher between 5:30-6:30 a.m. compared to the PI and MDI groups; in turn, the PI group showed more activity at this time than MDI. Regarding activity time at different intensities, the three groups were mainly sedentary and the average number of minutes in daily activity types was similar among them. However, they differed in the average minutes of light activity; again GS had more minutes in light intensity compared to IP and MDI, and the IP group more than MDI. **Conclusions:** our results suggest that activity patterns are different between MD, IP and MDI. GS individuals start activity earlier and have more activity, mainly in the morning; at the other extreme are individuals with MDI, who start later and have less activity during the day. This is in the absence of significant differences in sleep indicators.

Prevalence of residual sleepiness and quality of life in adults undergoing CPAP treatment

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Introduction: obstructive sleep apnea (OSA) is caused by pharyngeal collapse resulting in episodes of total (apnea) or partial (hypopnea) airflow obstruction during sleep. The standard treatment is continuous positive airway pressure (CPAP), even with treatment, drowsiness may persist, impairing quality of life. Drowsiness can be assessed with the Epworth scale and quality of life by SAQLI, specific scales. In Mexico, the prevalence of OSA in adults is 27.3%, increasing due to BMI, age and living in urban areas. **Objective:** to describe the prevalence of residual sleepiness and quality of life in adults under treatment with CPAP at UMF No. 64. **Material and methods:** cross-sectional study in 207 subjects with OSA treated with CPAP for at least three months; after informed consent, they answered Epworth and SAQLI scales. Anthropometric, sociodemographic and last CPAP memory reading (programming, use and treatment efficacy) data were collected. Analysis: using SPSS version 25, descriptive statistics were performed according to the nature and behavior of the variables. Spearman's correlation coefficient was used to evaluate the relationship between sleepiness and quality of life. **Results:** 123 patients, 59.4% men; median age 58. 96% used it more than four hours/night, five (2.42%) with residual IAH > 10 E/h. The median Epworth score was six points; we found residual sleepiness in 47 patients (22.7%), quality of life was good (median 6.6 points). The Spearman correlation coefficient between Epworth and SAQLI was rs = -0.52. **Conclusions:** patients at UMF No. 64 are under optimal treatment with CPAP; however, 22.7% of them had residual somnolence. When presenting higher Epworth score, quality of life is lower.

Comparison of polysomnographic variables in older adults with and without sarcopenia

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Introduction: the number of older adults is increasing in Mexico; the years added to old age must be accompanied by good health. Muscle mass tends to decrease after the age of 40. Mexico shows one of the lowest values in muscle strength among older adults in the world; the prevalence of sarcopenia in the Mexican population is described at 32.8%. Sleep disturbances and malnutrition are two factors strongly associated with the presence of sarcopenia; a quarter of the adult population in Mexico is sleep deprived and is therefore at risk of developing sarcopenia. **Objective:** to compare polysomnographic variables in adults over 60 years of age with sleep disorder with and without sarcopenia. **Material and methods:** a prospective, prospective, prolective, comparative case-control study in which the sleep architecture of older adults with sleep disorder and sarcopenia was analyzed by polysomnography. Comparisons of patients with and without sarcopenia were performed with Student's t-test. **Results:** for sarcopenic, latencies were NREM 24.95 ± 18.72, REM 191.58 ± 114.35, NREM duration 295.76 ± 94.70, REM 49.05 ± 30.42, SWS 69.65 ± 32.41, SWS presentation frequency 3.06 ± 1.98 and micro arousals 272.81 ± 139.60. **Conclusions:** in sarcopenic older adults, REM latencies were prolonged, N1 and N2 stages are characterized by high frequency of micro awakenings and long-lasting apneas that increased hypoxemia during sleep.

Obstructive sleep apnea in patients with paroxysmal atrial fibrillation

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Introduction: obstructive sleep apnea (OSA) is highly prevalent among patients

with atrial fibrillation (AF). There are few studies analyzing heart rate variability (HRV) data in this association: OSA/paroxysmal AF (PAF). **Objective:** 1) to know the prevalence of OSA in a cohort of patients with PAF; 2) to establish the clinical characteristics and analysis of heart rate variability (HRV) assessed during sinus rhythm in patients with PAF and OSA, grouped by nutritional status; 3) to describe and compare the behavior of HRV in four time windows recorded during the night. **Material and methods:** patients diagnosed with PAF who attended the outpatient department of the Electrophysiology Department between 2019-2020 were studied. They underwent clinical apnea questionnaires, respiratory polygraphy (RP), 24-hour Holter and HRV analysis; transthoracic echocardiography and blood sampling to determine serum inflammatory markers. **Results:** of 57 patients studied, with mean age 62.5 ± 8.6, 60% were found to have clinically significant OSA. When divided into groups according to nutritional status, statistically significant differences were observed in body mass index (BMI) and STOP-BANG scale ($p = 0.005$ and 0.03, respectively). HRV analysis demonstrated that overweight/obese patients have greater LF activation ($p = 0.0143$) corresponding with sympathetic activity at the expense of the long postapnea window. **Conclusions:** there is a high incidence of OSA in FAP, with a positive STOP-BANG PR should be performed. In overweight or obese patients there is evidence of increased sympathetic activity during periods of apnea.

Validation of the pediatric sleep questionnaire in Mexican schoolchildren

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Introduction: sleep disorders (SD) in children and adolescents are highly prevalent: 18-25% of the child population. The main disturbances are respiratory, somnolence and sleep-related behavioral changes. Clinimetry is essential in the screening, diagnosis and follow-up of SD. The pediatric sleep questionnaire (PSQ) is the most widely used worldwide. In Mexico, the prevalence of SD in school children is unknown and we do not have a validated questionnaire. **Objective:** to validate the pediatric sleep questionnaire (PSQ) in Mexican schoolchildren. **Material and methods:** observational, prospective, descriptive and analytical study. The study included parents of children aged 6-12 years who attended the Sleep Disorders Clinic (CTS-UNAM) and two schools, one in the municipality of Iztapalapa and the other in the municipality of Magdalena Contreras in Mexico City. The Spanish version of the PSQ was administered, the reliability of the items was measured with Cronbach's alpha; the SPSS program was used in the statistical analysis with a statistical significance criterion of $p < 0.05$. **Results:** 280 parents participated, 263 met the inclusion criteria. The age of the children was 8.33 ± 1.96 years; 53.25% girls. The main sleep disturbances were: snoring, parasomnias, insufficient sleep time. Internal consistency was 0.906 for snoring, 0.743 for sleepiness, 0.810 for behavioral problems and 0.819 for the whole questionnaire. **Conclusion:** the Mexican version of the pediatric sleep questionnaire has good internal consistency and is reliable for use as a screening instrument in the clinic or for epidemiological purposes.

Heart rate variability during sleep in children with Asperger syndrome

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Introduction: Asperger syndrome (AS) is considered a neurodevelopmental disorder; its symptomatology has been associated with problems in the regulation of the autonomic nervous system (ANS) and with high comorbidity with sleep disorders. The information obtained by analyzing heart rate variability (HRV) is considered a strong indicator of autonomic functioning under different physiological and emotional conditions. **Objective:** describe the characteristics of HRV during sleep, using different analysis methods (time domain, frequency domain and nonlinear methods). **Material and methods:** included children aged six to 10 years diagnosed with AS ($n = 10$) and typically developing children ($n = 10$). Polysomnographic recordings were made during two consecutive nights; the first night was for adaptation and the second night was considered for sleep macrostructure and HRV analyses, of which five-minute blocks per sleep phase were analyzed for each child. **Results:** children with AS presented greater latency to REM sleep and a lower number of sleep cycles. In addition, they presented higher heart rate (HR) during all sleep phases, mainly during REM sleep. On the other hand, parasympathetic nervous system activity, evaluated with the three methods of analysis, was similar between both groups. **Conclusions:** in children with AS, HR was higher than in normotypic children; while parasympathetic activity was similar between both groups. The lengthening in the latency to REM sleep may be indicative of abnormalities in the generative circuits of this sleep phase, which is consistent with the presence of fewer sleep cycles in children with AS.

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