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Review Article

Pulmonary Gas Exchange in Chronic Obstructive Lung Diseases

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Abstract

Chronic obstructive pulmonary disease is defined as a situation of progressive airflow limitation, sometimes reversible, whose pathogenetic mechanisms responsible are to be attributed, on the one hand, to the progressive obstruction of the central and peripheral airways, with structural modification of their histological status and, secondly, to a progressive destruction of the elastic component of the parenchymal tissue, with loss of alveoli and pulmonary capillaries. It follows that such a combination of inflammatory insults at the level of the bronchial and bronchiolar airways and loss of alveoli and capillaries, inevitably, leads to a progressive inefficiency of intrapulmonary gas exchange, which may be different if we keep into account the different phenotypic manifestations of the disease, especially in its early onset. In this review, we try to go beyond what it is commonly declared in the GOLD statement thatrather than regular arterial blood gases analysis, it would be more sensible to use pulse oximetry as a screening test since this is a simple, cheap, painless and non-invasive technique which is fairly accurateand perform arterial blood gas analysis only on patients with an arterial saturation of less than 92% and in patients with suspected CO_2 retention, although this will rarely be present in the absence of arterial hypoxaemia and desaturation and in stable patients with FEV1< 50% predicted or with clinical signs of right heart failure. Since this statement seems to minimize the issue of gas exchange in COPD, with this review, which deals with all the aspects of gas exchange impairment and all the tests it is possible to execute, we would like to refresh the information on an issue as the complexity of gas exchange scenario in COPD.

INTRODUCTION

Chronic obstructive pulmonary disease, which by this point we define COPD, is understood as a situation of progressive airflow limitation, sometimes reversible, whose pathogenetic mechanisms responsible are to be attributed, on the one hand, to the progressive obstruction of the central and peripheral airways, with structural modification of their histological status and, secondly, to a progressive destruction of the elastic component of the parenchymal tissue, with loss of alveoli and pulmonary capillaries . It follows that such a combination of inflammatory insults at the level of the bronchial and bronchiolar airways and loss of alveoli and capillaries, inevitably, leads to a progressive inefficiency of intrapulmonary gas exchange . This inefficiency is initially reflected in evidences of slight reduction in arterial oxygen tension (hypoxia) and carbon dioxide (hypocapnia) . If the disease progresses, it can reach a level where it is established respiratory failure characterized by severe hypoxemia associated with hypo- or hypercapnia [1]. The alterations in gas exchange, even in the early stages of the disease, are supported primarily by the presence of a growing unequal distribution of ventilation, which is to be supported by pathological phenomena that increase airway resistance and increase the time of filling and emptying of the alveoli. To the unequal distribution of ventilation is associated also a progressive alteration of the distribution of perfusion, which in the phases of onset of the disease, may represent a sort of compensation reactive but that in the long run leads to an altered transfer of oxygen and carbon dioxide from side to another side of the alveolar-capillary membrane resulting in inefficiency of exchange [2].

If it is true that these changes are particularly frequent and more sustained in patients with very severe COPD, it is equally true that they also are established early in the course of the disease and sometimes in a subclinical way or before it is highlighted, with the common spirometry systems, the presence of airflow obstruction. It therefore arises of what methods the physiopathologist can have for an overall assessment of the efficiency of intrapulmonary gas exchange in COPD, keeping in mind that the lung by its nature has important factors of

compensation, both circulatory and biochemical, aimed at maintenance and optimization of the primary function and that is primarily to maintain the exchange of O_2 and CO_2 [3]. The answer is to accept that we should have tests easy to apply, accurate, sufficiently sensitive, and inexpensive, but the complexity of the phenomena that are investigated need to resort to more sophisticated measures, not easy to use clinical for routine purposes, sometimes expensive and invasive. In this context, a comprehensive assessment of gas exchange in COPD should be able to start from a simple measurement of respiratory gases dissolved in the blood by measuring the gradients of O_2 and CO_2 and related parameters (O_2 consumption and CO_2 production, respiratory quotient, minute ventilation, tidal volume, respiratory rate, anatomical and physiological dead space), or the alveolar-capillary diffusion through the carbon monoxide (which could also be placed before gas analysis), followed by the test cardio-respiratory stress, until arriving to employ more complex techniques such as those nuclear medicine study of ventilation [4,5] and the regional perfusion [6], which make use of gas or radioactive aerosols and particles of albumin labeled with isotopes, or by the method of inert gases with different solubility for the study of ventilation - perfusion ratio (VA / Q) and intrapulmonary shunt [7]. The combined use of these techniques allows us to understand the pathophysiological mechanisms responsible for the assessment of either hypoxemia, hypercapnia or hypocapnia and increase of alveolar to arterial gradients for oxygen and arterio-alveolar gradients for carbon monoxide and infer on their possible reversibility.

CONCENTRATIONS (TENSIONS) OF RESPIRATORY ARTERIAL GASES

A rapid assessment, as well as coarse, on the state of gas exchange can be achieved through the analysis of dissolved gases in the blood. Their determination includes the measurement of pH, PaO_2, $PaCO_2$. Other parameters that can be calculated are the values of oxygen saturation, bicarbonate, content of O_2 and CO_2 and other parameters of non-negligible utility in clinic. In the course of COPD, even in the presence of levels of severe obstruction, when you run blood gas tests, you may find yourself faced with values at least of normal gas dissolved in the blood or plaid variables hypoxemia, hypo and / or hypercapnia. This discrepancy between entities of abnormal obstruction and of arterial gas tensions has long been known. In fact, it has always been thought that if gas concentrations in the blood may be obtained by a simple aspiration of arterial blood, their interpretation is often difficult for the purpose of characterization of intrapulmonary gas exchange in COPD. It goes without saying that a proper interpretation of the blod gas data requires full knowledge of the physiological factors that may influence the result as the body temperature, the fraction of inspired O_2 and the temperature to which it is made the withdrawal, the values of barometric pressure and conditions patient clinics. Suffice it to point out as a condition of reduced PaO_2 below a value corrected for age [8-10], body mass index or posture [11], altitude [12] alwaysis expressions of an alteration of the function of exchange. Levels of hypoxemia or hypocapnia may be present not only in COPD but also, at the same time, in other pathological conditions, as reported in Table 1 .

Table 1: Pathological conditions associated with reduced levels of amount of oxygen and carbon dioxide dissolved in the blood.

Hypoxemia	Hypocapnia
Anemia	Hyperventilation Syndrome Hypoxia heart failure
Pulmonary Embolism	Pulmonary embolism
Primary or secondary pulmonary hypertension(PH) COPD	Primary or secondary PH
Restrictive lung diseases Left ventricular failure	COPD with emphysema
Hypoventilation syndrome	Heart Failure
Age	liver disease

It has to be oulined as a state of hyperventilation, that can be observed in cases of emphysema, may present a normal value of PaO_2 . In these cases you can use the adjustment formulas that allow us to be able to quantify the actual state of oxygenation [13]. At the same time we may be faced with conditions of patients with COPD in whom you can have an increase in CO_2. In this case, you configure the framework of alveolar hypoventilation by reduced ventilatory response that occurs in the natural history of the disease. When compared with normocapnic patients with COPD, hypercapnic COPD patients usually tend to have a lower PaO_2, a higher hemoglobin with a lower resting ventilation [14]. On the basis of these considerations, the GOLD guidelines set improperly, that for monitoring the obstructive disease, the measurement of gas analysis should be performed in all patients whose FEV1 is less than 40 % or when there are clinical signs of respiratory failure heart or lung disease [15]. Rather than using a regular blood pressure of dissolved gases in the blood would be much more sensible to use pulse oximetry as a screening test for subjects with disease less demanding, for example, and to address to blood gas analysis patients with a more severe obstruction, being the pulso-oxymetry testing much easier non-invasive, inexpensive and fairly accurate except for information regarding carbon dioxide [16]. Also according to the GOLD, re-edited in 2003-2004, and the document ATS- ERS 2004 (www.thoracic.org), a reasonable strategy would be to measure the pulse oximetry in all patients with COPD with airflow obstruction grade initial and limited to perform the blood gases to patients with oxyhemoglobin saturation less than 92-94 %, corresponding to a level of PaO_2 equal to 8 kPa or about 60 mm Hg on the hemoglobin dissociation curve. The same statement appears on the GOLD 2011. Finally, according to these documents, the arterial blood gas analysis should be performed in all patients suspected of CO_2 retention, this framework is infrequent finding in the absence of characteristic clinical signs.

The incompleteness of these claims resides in the fact that pulse oximetry is insensitive to minor degrees of hypoxemia and that the relationship between the degree of airflow obstruction as measured by FEV 1 and hypoxemia or intrapulmonary gas exchange, is weak [17], from which the claims on which patients bring blood gases. These considerations have been taken from the more recent Guidelines for the Diagnosis and Treatment of Respiratory Diseases (COPD and respiratory failure) indicating pulse oximetry monitoring as an examination of nocturnal oxyhemoglobin saturation by placing it at the same level gas

analysis, that is instrumental investigations of II level in the diagnosis and evaluation of COPD patient [18].

The structural and morphological changes that take place in the course of COPD are responsible of mild or moderate hypoxemia, hypercapnia, or even in the absence of relevant hypoxemia and hypercapnia, when the anatomical alterations of alveoli and capillaries become severe. In emphysema, for example, there can be only moderate hypoxemia with $PaCO_2$ often normal. In chronic bronchitis hypoxemia may be too severe with a $PaCO_2$ that may increase in the later stages by configuring the framework of respiratory failure in its various expressions clinics. Do not forget that the alterations in gas exchange can also be present in the early stages of the disease [19] because they are relating to alterations of the peripheral distribution of ventilation and perfusion. It turns out from these considerations that should be used much more frequently to the simultaneous measurement of respiratory gases dissolved in the blood and those of mixed exhaled air, using automated techniques that allow the complete calculation of the gradients of O_2 and CO_2 and ventilatory parameters related: these techniques may contribute to help you understand more fully of certain features evidenced to the blood gas analysis [20]. Composition of alveolar mean gas and gradients of O_2 and CO_2.

It is well known as in patients with COPD to have correct information about concentrations of alveolar gas is of crucial importance for the measurement of the gradients of O_2 and CO_2 and parameters of ventilatory efficiency [20]. The average concentration of the alveolar gas is closely influenced by the dynamics of filling and emptying of joined alveoli affected by inflammatory processes, but also by the uneven distribution of alveolar ventilation, in turn closely dependent on the extent of the obstruction and or distortion of the bronchi small caliber, alterations of intra-regional volumes of air in relation to both the intraalveolar ventilation and perfusion, or altered diffusivity of respiratory gases, amplified in COPD [21-23]. Since in COPD patients factors such as amount of current volume, the anatomical dead space, asyncronous emptying of different airways with different ventilation perfusion ratios influence the composition of alveolar gas, the determination of end-tidal respiratory gases may be misleading for the purposes of determination of concentrations of alveolar gas medium (Figure 1) [24], but unfortunately, it is seen to continuously use in literature and on case studies of COPD patients and for monitoring of gas exchange by anesthesiologists. At the same time as important parameters for the characterization of COPD, such as anatomical dead space, should not be estimated with the prediction formulas, but actually measured [25]. Moreover it has been shown as anatomical dead space is reduced in COPD and not as it is believed that increases [26]. At the end of the '90s it has been put in place an automated technique using a mass spectrometer, which aims to decompose the profile of expiratory gases in COPD patients, showing that the measurement of the realmean alveolar gas is made possible, in a breath by breath way, thanks to the identification of the moment in which the average respiratory quotient of a respiratory cycle equals the instantaneous value [20]. If this occurs, as seen in COPD before the end of the respiratory cycle and after anatomical dead space was entirely washed, the extent of alveolar gas results definitely correct and can be used for the calculation of gradients

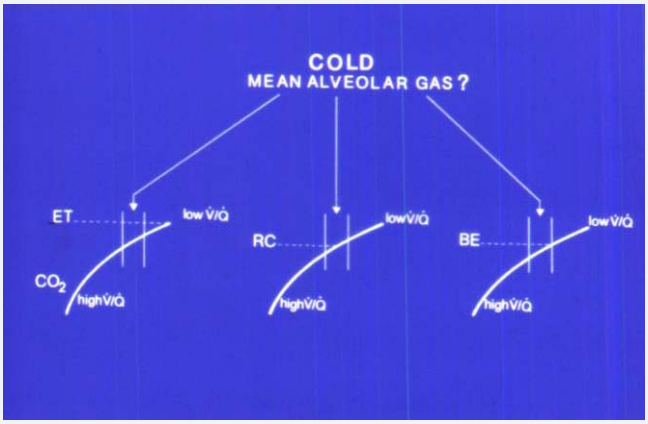

Figure 1 Representation of expiratory CO_2 behaviour in COPD patients. Using the determination of end-tidal values as point representative of alveolar concentration may be misleading; instead using the determination obtained by the method of Rahn or by the method of Bohr, due to the slope of capnogram in COPD patients which is increasing from resting level to residual volume due to the different time constant of alveolar units, is more correct. End-tidal measurement is representative of the low VA/Q units, since it collects the alveolar units with a long resistance emptying phase whereas according to Rahn'method it is possible to have information on the units with a low time constant that empty early. In this condition the mean alveolar gas seems more representative of mean alveolar gas since is able to collect the intermediate between alveolar units with different VA/Q units.

O_2 and CO_2, which are, however, still high even earlier, indicating the altered ratio VA / Q depending on several mechanisms (venous admixture resulting from lung regions with low ratio VA / Q, shunt perfusion, wasted ventilation, dead space effect). The normal values of the gradients of O_2 are around 15 mmHg in proportion to the age [27] and any increase them over this limit suggests the presence of an alteration of the transfer of O_2 from the airways to the alveolar-capillary membrane, for the presence of regions of low ratio VA / Q (obstruction and / or peripheral distortion of the bronchi). The normal values of the gradients of CO_2 are around 5 mm Hg and any increase in the combined presence of COPD suggests alveolar high ratio VA / Q, for the presence of alveolar units poorly perfused as emphysema or presence of alveolar ventilation totally wasted for the purposes of the exchange. It is also interesting to emphasize that in COPD patients the extent of the gradients of CO_2 correlates significantly with the current volume to prove the thesis that a decrease in tidal volume being obstructive disease is always considered an expression of wasted ventilation and ineffective and as expressive parameters of this phenomenon (physiologic dead space with technique of mass spectrometry and alveolar dead space and anatomical technique with inert gas), measured independently with different techniques, show significant correlations [28]. In particular this last result indicates the strength of simple techniques such as gradients with mass spectrometry in revealing pathophysiological mechanisms certainly detectable with more complex techniques not be proposed for routine use.

DIFFUSION OF ALVEOLAR-CAPILLARY CARBON MONOXIDE

One of the instrumental analysis which allows to classify the

patient with COPD in a proper and fast way is the diffusion test to CO in a single breath, which also had a recent standardization within the International Scientific Societas [29]. This test, one of the most commonly used in the world, allows physiopathologists to open " a window on the pulmonary microcirculation " because it gives accurate information on the transport of gas to the level of the alveolar-capillary membrane. Moreover it permits to monitor disorders of the lung parenchyma and the pulmonary capillary circulation [30]. The test of the transfer of CO represents one of the most important in the field of the respiratory physiopathology in discriminating between pulmonary emphysema (or obstructive pattern), chronic bronchitis, interstitial (or restrictive patterns), when it is related to alveolar volume in which it is measured. In the early stages of COPD, when it begins to establish the mechanism of progressive inhomogeneity of ventilation, which, subsequently, for reactive elements, it can respond to the distribution of capillary blood flow, the diffusion of CO begins to deteriorate and the mechanism of commitment is supported by multiple factors : 1. for progressive airway collapse and subsequent entrapment of gas in the alveolar units alveolar exchange 2. for anatomical loss of the exchange surface, as occurs in the conditions of emphysema 3. for an enlargement in terms of the diameter of the functional alveolar units which forces the gas to take a trip diffusive longer, as occurs in conditions of a progressive decrease of the force of elastic return; 4 . in the conditions of altered ratio VA / Q, especially in those conditions in which are established redistributions of blood flow with the formation of areas of hyperperfusion and low ratio. The ability to spread the CO, as measured as the ratio transfer is in respect of alveolar volume, discriminates the presence of alterations of the elastic return force much more than is done by the parameters of the pressure-volume (compliance) and a its reduction is considered to be an excellent predictor of the extent of pulmonary emphysema, investigated with high-resolution CT [31,32]. Its reduction it is correlated with a lower PaO_2 at rest, with a reduced level of exercise tolerance, and overall, is considered key measure in the evaluation of pathways to correct the severe hypoxemia in patients with COPD [33]. In chronic bronchitis, the test cannot be compromised and this figure has a certain utility in the differential diagnosis with other diseases. In fact the diffusing capacity for CO may be increased in asthma, thus allowing a sufficient discriminating power to differentiate asthma from emphysema, due to mechanisms inherent obstruction to airflow that appear to cause an increase in perfusion in poorly ventilated areas such as non-gravity dependent lung regions [34].

CARDIOPULMONARY TEST OF EXERCISE TOLERANCE

In the course of COPD, the anatomical changes that affect the airways and the pulmonary capillaries may show signs of their presence in the special conditions in which increased metabolic demands. In this sense, it is now accepted that the reduced exercise tolerance is a condition characteristic of patients with COPD [35] and as one of the major goals of bronchodilator therapy is to improve the quality of life, reducing the symptoms of difficulty of breathing [36]. The exercise tests, both incremental cycle ergometer or those at constant load, such as the 6-minute walk test, they tend to reveal not only ventilatory limits, but also constraints of reduced cardiac reserve, muscle deconditioning, alteration transport of O_2 and its use by the tissues, transport and disposal of CO_2, metabolic deficits of the musculoskeletal system. The parameters that can be measured more frequently are minute ventilation, tidal volume and respiratory rate, O_2 consumption and CO_2 production, their relationship with the ventilation (ventilatory equivalent), the pulse of O_2 (VO_2 / frequency rate), the ratio of physiologic dead space / tidal volume, thanks to automated systems that allow, breath by breath continuously at the mouth of the patient, rather accurate and fast measurements. In the course of COPD patients under exercise may exhibit any symptoms of fatigue, shortness of breath or fatigue and muscular exhaustion. The explanation of these symptoms is given by the inability of the heart - lung system to respond to increased demands for oxygen from the pheriphery, both mechanisms of altered production, and transport mechanisms in the periphery. Then, in the COPD patient the O_2 cost of ventilation can be increased as a result of airway obstruction that requires an increase in ventilation, the higher the more serious is the efforts of the disease. So you can attend to a reduced oxygen consumption at peak exercise, which is also reduced, even if their relationship can be kept within the limits of normality. The patient with COPD, in the exercise tends to increase ventilation by increasing tidal volume initially up to a limit where it appears a kind of self-restraint imposed by changes in lung volumes: the ventilatory demands are then supported by the increase in respiratory rate which, going hand in hand with an increase in functional residual capacity inevitably help to stop the test. The increase in functional residual capacity is considered an expression of the movement of tidal volume to higher lung volume, the point at which the airways are still patency (dynamic pulmonary hyperinflation). At this point the respiratory system is placed in the most unfavorable conditions from the standpoint of mechanics and function. In fact, if on one hand the minute ventilation increases to allow the supply of O_2, at a certain point the mechanism imposed by airflow limitation becomes critical because the changes appear on the side of oxygenation, as reflected by a ratio VA / Q unequal. In terms of CO_2 it can be said that the increase in ventilatory efforts around 50 % of maximal O_2 consumption value can be reduced as compensation metabolic acidosis that occurs during exercise, but also may increase when initiating the inequality ratio VA / Q, In these cases we see increases in the ratio of dead space tidal volume .

The cardio -pulmonary exercise test also provides important information to identify predictors of functional exercise tolerance, and more generally, of the quality of life in COPD patient, much more than they can do the spirometric indices of airway obstruction : in fact with the introduction of the flow-volume curves during exercise it has been possible to achieve this goal [37]. In this regard, more recently other authors have shown that some indices of hyperinflation and air trapping such as the ratio of inspiratory capacity, functional residual capacity and total lung capacity are highly correlated with the degree of dyspnea, with reduced exercise tolerance and indices of ineffective ventilation ($r = .81$, $p < 0.0001$) in patients with moderate-to- severe COPD [38].

STUDY OF VENTILATION-PERFUSION RELATIONSHIPS WITH NUCLEAR MEDICAL TECHNIQUES AND INERT GAS ELIMINATION-RETENTION TECHNIQUE

The physiological basis of abnormal gas exchange in COPD are characterized by clusters of variables hypoxemia and hypo or hypercapnia with incremental levels of severity. Among the mechanisms in support of one or the other factors as alveolar hypoventilation, the limitation of the diffusibility of respiratory gases, the presence of shunts of perfusion or ventilation, but, above all, the presence of inhomogeneities ratio VA / Q may have a role. The pathological substrates of such functional aspects range from progressive obstruction and / or distortion of the airway caliber resulting in ever smaller airflow limitation, loss of health excvhange surface, by the destruction of alveolar tissue, to that of the capillary network with a consequent reduction of the elastic properties of the lung. Therefore, the heterogeneous distribution of both the ventilation and the blood flow, which already in conditions of absence of pathological processes seems to reflect also the intrinsic properties of bronchi and vessels [39], it is still susceptible, under the action of inflammatory processes, to be preserved or even amplified by factors intrinsic to the system as a kind of reflex changes in the district .

The study of the ratio VA / Q in COPD can be addressed by using two techniques : the first of these is based on the combined use of ventilation and perfusion scintigraphy of the region, in particular the assessment of the regional deposition of aerosol or radioactive particles labeled with gamma-emitting isotopes [5,6]. The use of these two techniques allows to quantify the changes in intra-regional ratio VA / Q and, in particular, can highlight areas where prevails the parenchymal deposition of ventilation with respect to perfusion and vice versa (Figure 3). The areas of accumulation of tracer that is distributed in proportion to the intraregional ventilation allow to operate the measures of radioactive counting and be able to perform the

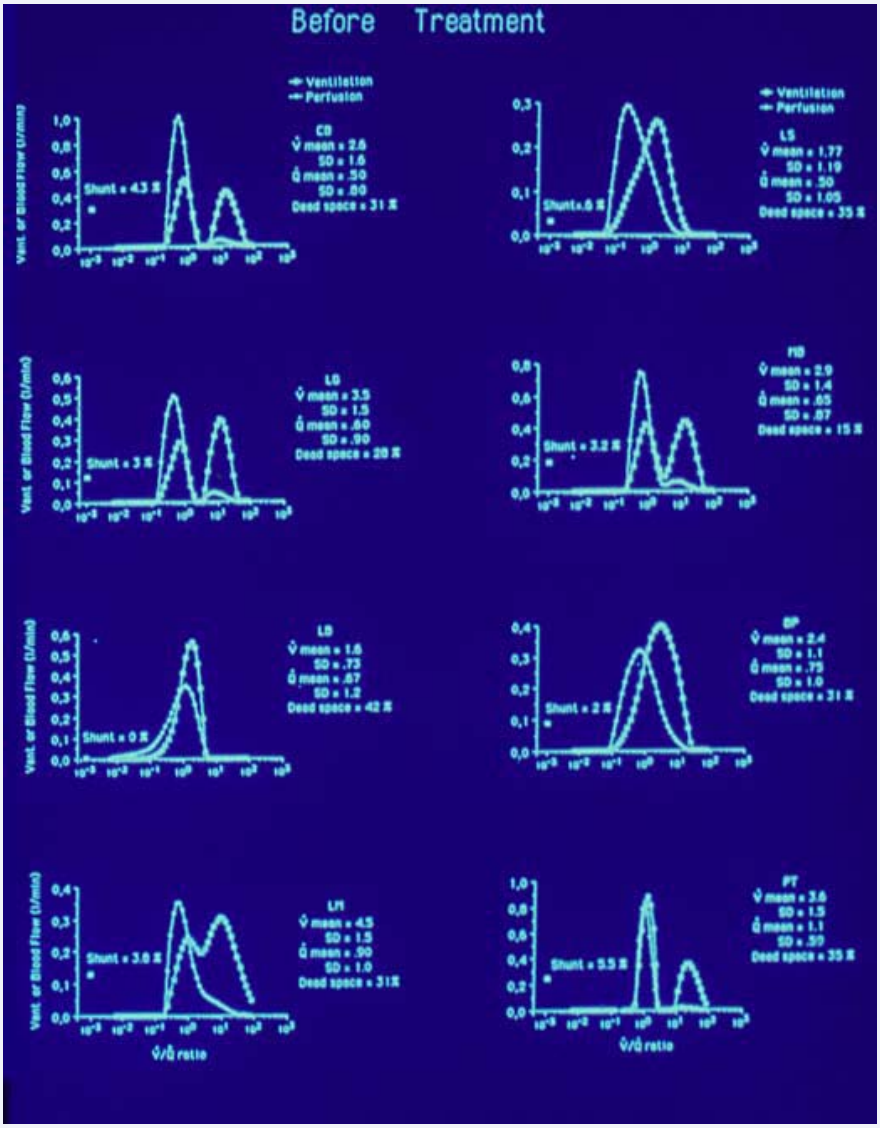

Figure 2 Representation of VA/Q distribuition by MIGET in COPD patients. Different patterns of VA/Q distributions are seen. These different distributions run either from bimodal or unimodal distribution of ventilation or from unimodal distribution of perfusion, to bimodal distribution of perfusion.

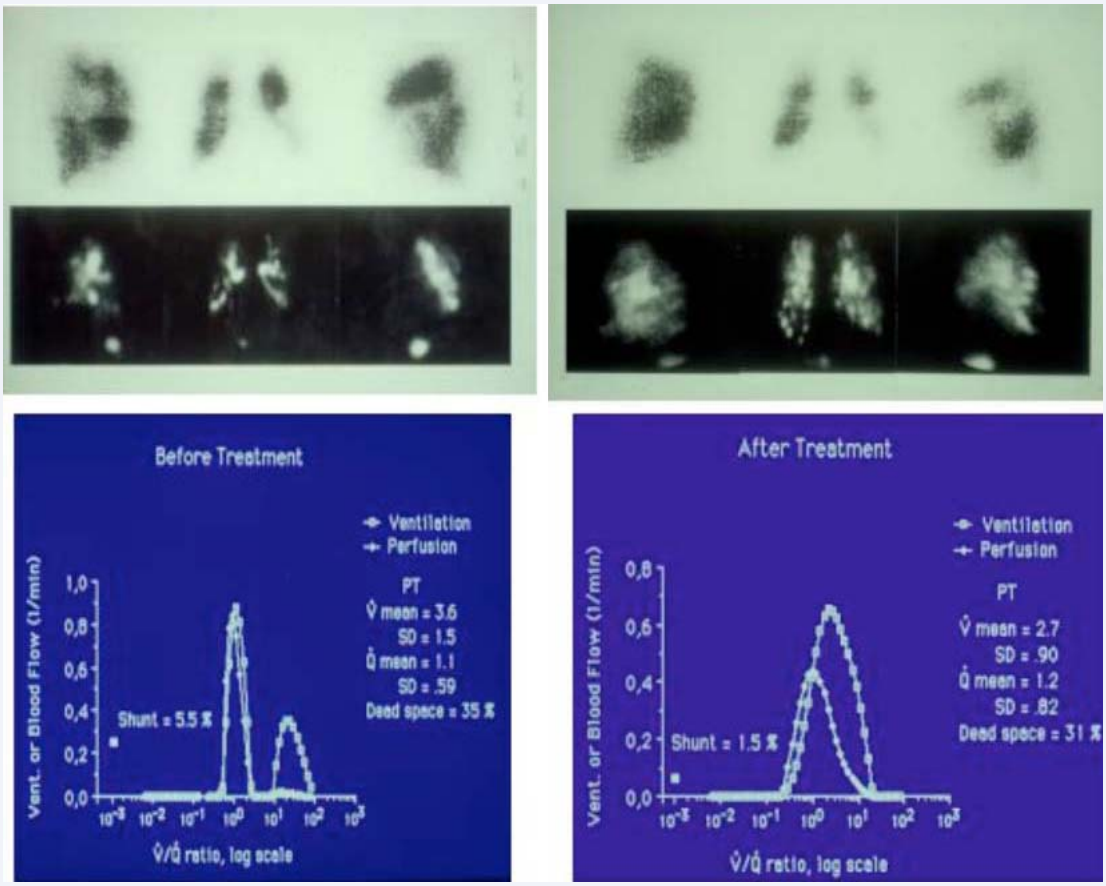

Figure 3 Top: regional distribution of perfusion (high) and ventilation (low) evaluated by radiosotopic techniques. Bottom: distribution of ventilation and blood flow according to MIGET in the same COPD patient in whom the nuclear distribution of convective ventilation and regional blood flow have been collected, before (left) and after treatment (right). As it is possible to observe a degree of improvement in the distribution of regional distribution of ventilation and perfusion is detectable with treatment. At the same time this improvement seems paralled by a better organization of the VA/Q mode where it is possible to observe a degree of redistrution toward a better VA/Q ratio, especially for the ventilation mode in a such vay that the bimodal distribution after treatment has disappeared.

calculations of ratio VA / Q on selected areas of the two lungs. The second of these techniques is based on the elimination of different inert gases (six) of different solubility coefficient and on the construction of retention curves and excretion of these gases and a lung model made up of 50 compartments (MIGET) (40), by mutuating the principle that the elimination or retention of a gas in the respiratory system depends both on VA/Q of that unit and on the partition coefficient of that gas, i.e. solubility coefficient air-liquid (blood). This technique, whichis not feasible for routine use, allows you to get information on the presence of true shunt perfusion (VA / Q = 0), ineffective ventilation (VA / Q = infinity) and the remaining 48 compartments where you can externalize the spectrum of functional ratio VA / Q of all corresponding to what happens for the phenotyping of the disease COPD. In fact, the technique, in the course of the last 30 years, has allowed us to characterize the most important alterations of VA / Q in COPD, having identified at least four typical patterns of distribution: an enlarged distribution of both perfusion and ventilation with the coexistence of regions of high and low ratio in about 45% of patients with COPD, a pattern characterized by a unimodal distribution of perfusion of regions with low and normal ratio VA / Q in 23% cases, a bimodal distribution of ventilation with regions of high and normal ratio in 18% of cases and finally a bimodal distribution of both the ventilation of both the perfusion in 14% of cases [17]. The bimodal pattern of flow distribution is typical of chronic bronchitis, in which prevails a large compartment well perfused but poorly ventilated in accordance with the abnormality of obstructive small airways and the consensual reduction of ventilation in those alveolar units subtended precisely by airway almost completely closed (development of regions of low ratio VA / Q). The bimodal pattern of ventilation is typical of emphysema where the destructive changes of the alveolar walls prevail, associated to the enlargement of the air spaces and the reduction in the capillary network (development of regions of high ratio VA / Q). Between these two extremes, the coexistence of other patterns indicates precisely the phenotypic variability of the disease. These patterns have no relation with the degree of airflow obstruction. More recently Rodriquez Roisin et al. [41] have evidenced how the gas exchange abnormalities in the course of COPD are related to FEV1 across the spectrum of severity, but still addressing how in the early phase of COPD, perfusion heterogeneity may predominateand it is greater than airflow limitation, thus suggesting that the disease involves the smallest airways in the early phase, then parenchyma and vessels, with

slight spirometric disturbances. Successively, the progression of VA/Q imbalance seems modest and it may reflect some tendency to equilibrium between the reduction of ventilation and blood flow in the same regions trough airway and alveolar diseases and capillary involvement. The alterations of ventilation and perfusion, even if they belong to the type of patterns indicative of irreversible destruction of the lung parenchyma, may show a certain level of reversibility or improvement after a period of medical therapy (Figure 3). This indicates that even in the context of regions of high ratio VA / Q we may have functional alterations for improvement and nuclear medicine techniques, described above, help us to do this in a such way that they are able to locate the regional office of this change [42].

CONCLUSIONS

From what has been said so far it can be concluded that for the study of gas exchange in COPD we have available simple techniques such as those that relate to the measurement of dissolved gases in the blood or the most elaborate and sophisticated techniques such as those designed to investigate the scenario of respiratory gases in the alveoli. Other techniques, some of which are very complex, allow us to accurately assess the pathophysiological mechanisms responsible for the alterations in gas exchange, because they have good resolution and are accurate in photographing the mechanisms of alteration of ventilation and perfusion. The young colleague in front of an altered results in the blood gas analysis, should think that he can employ different tests, as illustrated in this review, in order to explain the complex scenario of gas exchange impairment. Of course some techniques are more simple, others (MIGET) are more complex and their role in the clinical pratice is low and may be employed just for a research purpose.

Such an integrated approach, which, in my opinion, should be widespread and extended on a national and international level, surely may help to reveal the contribution of different factors in the progression of COPD and it can provide important control systems that help follow the evolution of the disease in addition to addressing a more precise therapeutic efforts in the last few years that are straining to cope with the disease also from the part of the circulatory system and not only from the ventilatory one.

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Conflict of Interest

No potential conflict of interest in the preparation of this manuscript has to be declared by the Author

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