



MGC DIAGNOSTICS®

NEWSLETTER
Volume #2

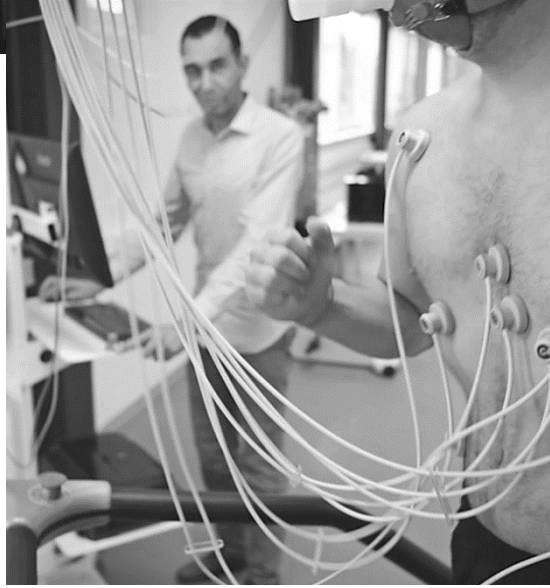


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WHAT'S NEW IN RESPIRATORY MUSCLE ASSESSMENT?

Assessing respiratory muscle function is crucial for clinicians, physiologists and researchers. Several developments have increased our understanding in the field.

> CONTINUE READING ON PG. 4



WELCOME

Introducing the second volume of the MGC Diagnostic Newsletter! We hope that this bulletin will be a helpful and informative resource regarding some hot topics in the cardiorespiratory field.

Also This Issue:

- > Overview of Different Muscular Investigation Methods (PG. 12)
- > Clinical Implication of Respiratory Muscles Testing (PG. 15)



RESPIRATORY MUSCLES IMPAIRMENT: ROLES

The 2019 ERS/ATS Task Force provides an opportunity to review the study of the respiratory muscles function and to situate its importance in the clinical practice of pulmonologists.

> CONTINUE READING ON PG. 7

COMMON TESTS OF RESPIRATORY MUSCLES TESTING

In 2019 ERS published a new statement on respiratory muscles testing. Let's take a look at the most common tests.

CONTINUE READING ON PG. 10





THE FUTURE

OF DIAGNOSTICS

EDITORIAL

Happy New Year from your MGC Diagnostics Family.

In this issue we will highlight Respiratory Mechanics and many of the associated diagnostic testing techniques, but first, let me update you on important developments at MGC Diagnostics since our last newsletter.

We have expanded our global footprint with the acquisitions of two strategically located business partners. The first in France, with the acquisition of MSE Medical, followed by the acquisition of Ascencia Healthcare Facilitators in Australia, creating two new direct markets

– MGC Diagnostics France and MGC Diagnostics Australia. Lastly, and of great importance, is the newly formed partnership with Shanghai Honghang Medical as our exclusive business partner in China.

In addition to expanding our MGCD Family with the addition of more than 20 Cardiorespiratory Sales, Service and Marketing Specialists throughout these territories, we have recruited globally recognized experts to lead our international expansion plan – please check out our Twitter and LinkedIn for further details.

The science and physiology of Respiratory Mechanics is today often overlooked, but remain the fundamental first principles every respiratory scientist/technician uses when conducting pulmonary function tests, especially when measuring lung mechanics. Many of us were very fortunate to learn from the giants in this field where these physiologic fundamentals of pressure, volume and airflow were deeply instilled – names like West, Macklem, Mead, Hyatt, Rodarte, Pride, Permutt, Goldman, Agostoni, Konno, Decramer, Pedotti, Woolcock, DuBois, Comroe, Milic-Emili, Hughes – and many, many more responsible for defining the science of gas exchange and diffusion.



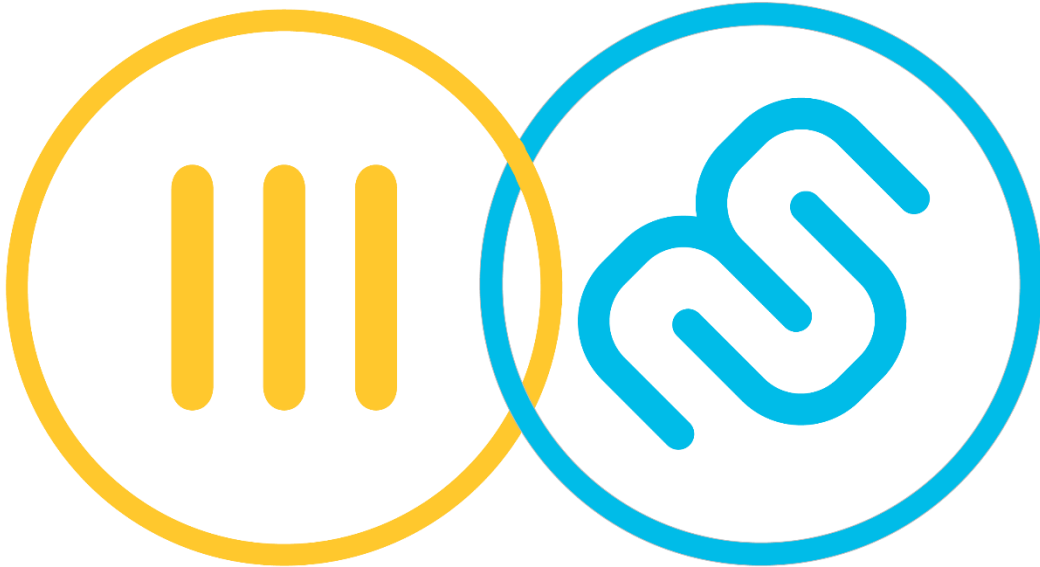
What follows is a brief summary of today's efforts to standardize respiratory muscle testing as reflected in the American Thoracic and European Respiratory Society's Statements. As you read this edition of MGC Diagnostics Newsletter, I encourage everyone to return to the early works of our mentors mentioned above and refresh your basic respiratory physiology skills – a strong understanding of the principles of respiratory mechanics provides an invaluable 'toolbox' to use in your daily diagnostic testing of patients – whether that be coaching, interpretation, research and trouble-shooting. Better still, please share that 'spark' which created your passion for respiratory physiology and pulmonary function testing with the current and next generation of Respiratory Technicians/Scientists.

Sincerely,

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Introduction to What's New in Respiratory Muscle Assessment

Pr. P. LAVENEZIANA

First author of the '2019 ERS statement on respiratory muscle testing at rest and during exercise'

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Assessing respiratory muscle function is crucial for clinicians, physiologists and researchers. Several methodological developments over the past twenty years have increased our understanding of respiratory muscle function and responses to interventions in health and disease. Substantial research has been done over the past two decades, since the publication of the 2002 American Thoracic Society (ATS)/European Respiratory Society (ERS) statement on respiratory muscle testing, in the field of breathing mechanics, respiratory muscle neurophysiology and imaging, in adults, in children and critically ill patients in the intensive care unit (ICU).

Remarkable advances in respiratory muscle and lung mechanics assessment have come up in the past few decades.



A recently published ERS task force statement assessed the field of respiratory muscle testing in health and disease. This statement critically evaluated the most recent scientific and methodological developments regarding respiratory mechanics and muscle assessment. An original and novel approach was applied which allowed to address several characteristics of various methods: 1° the validity (i.e. the extent to which a test or variable is related to the function of a physiological system or to patient-meaningful variables, such as symptoms or exercise); 2° precision; 3° reproducibility; 4° prognostic information (i.e. relationship with the



natural history of the disease); 5° discrimination (i.e. whether a variable can differentiate the severity of the disease as conventionally measured); 6° clinically meaningful difference (i.e. the minimal difference in a tested variable that is considered to be functionally worthwhile or clinically important) and; 7° responsiveness to interventions. A particular emphasis was given to evaluation during exercise, which is a useful condition to stress the respiratory system.

This introduction aims at spreading out this statement with the purpose of stressing the relevance, and promoting the culture of respiratory muscle function assessment in respiratory disease. In this regard, diverse methods are now available for

the assessment of the respiratory muscles; however it should be born in mind that the technique used should be tailored to the question raised, as they are especially useful in diagnosing, phenotyping and evaluating treatment efficacy in patients with respiratory symptoms and neuromuscular diseases (NMDs). This could be a major problem: having requested the specific test, the clinician has then to decide what to do with the result, and here the process becomes much more difficult. Several reasons may be recalled here: 1° the difficulty for some patients to perform the test; this requires good technique from both the physiologist and the patient, and also applies for tests considered as routine evaluations such as maximal static inspiratory and expiratory mouth pressure (MIP and MEP, respectively); 2° the obtained values can be affected by factors such age, comorbid disease, ethnic differences and so on; 3° the normal range could be quite wide, and sometimes several normal ranges have been reported; 4° the technique of performing the tests may vary from laboratory to laboratory. This statement responds to each and every question raised before, and attempts to answer each one in a coherent and logical manner, by stressing the importance of the Lower Limit of Normal (LLN) because in medical practice mean normal population values are of very little interest, the relevance of the technique being used, and last but not least the specific clinical question posed by the clinician.

In this ERS statement, remarkable advances in respiratory muscle and lung mechanics assessment in the past few decades have come up, and three of them merit to be highlighted here.

First, the noninvasive and readily available measurements of upright and supine vital capacity (VC) in the evaluation of respiratory muscle function, especially the diaphragm. The novelty is that a 15%

decrease in the supine position (15% represents twice the coefficient of variation of the measure and could be considered the LLN) may orient towards a unilateral diaphragm weakness, which is usually associated with a modest decrease in VC, to approximately 75% of predicted, while FRC and TLC are usually preserved.

Second, indices of respiratory muscle effort during exercise such as the esophageal pressure tidal swings (Poes,tid) can serve as an index of global respiratory muscle effort during exercise, and can identify differences in disease severity in patients with COPD (i.e. by Global Initiative for Chronic Obstructive Lung Disease stages). Those indices are sensitive to changes over time and to interventions, and are related to the perception of dyspnoea during exercise.

Third, the increasing availability of new and novel respiratory muscle imaging techniques such as the ultrasound to assess diaphragm dimensions and activity, in terms of static measurement of end-expiratory diaphragm thickness, dynamic evaluation of the ratio of inspiratory to expiratory diaphragm thickness, reported as thickening ratio, and diaphragmatic excursion. Other imaging tools such as optoelectronic plethysmography (OEP) and structured light plethysmography (SLP) can be considered as emerging, non-contact, noninvasive methods to assess breathing pattern and diaphragm (dys)function either in healthy or in patients with respiratory diseases.



This ERS statement is meant to launch new attitudes for clinicians, physiologists and researchers and encourages them to apply and fully translate it to the clinical care of individual patients. This requires a huge effort especially in this era in which less and less time is dedicated to training in the practical realization and interpretation of the more advanced tests of respiratory muscle function worldwide. A great effort is required to dedicate, learn, practice, interpret, decide, and apply actions in response to the results obtained. There is no time for all this, because of the

hectic daily work, the insufficient time dedicated to learning, the scant possibilities of acting accordingly once the results of these tests are obtained and other higher priorities. This contributes to a vicious circle in which only a bunch of pulmonologists know and perfectly handle these tests that are available only in specialized centers. How to fight this disappointing and unfortunate situation? It is critical that new generations of pulmonologists must be intensively exposed to clinical physiology concepts and practices.

“ It is critical that new generations of pulmonologists must be intensively exposed to clinical physiology concepts and practices. ”

- Pr. P. LAVENEZIANA





ADVANCES IN THE ASSESSMENT OF RESPIRATORY MUSCLES

Aetiology of Respiratory Muscles Impairment: THE ROLE OF THE RESPIRATORY PHYSIOLOGIST AND THE PULMONOLOGIST

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The 2019 European news (ERS/ATS task force) provides an important opportunity to review the study of the respiratory muscles function and to situate its importance in the clinical practice of pulmonologists. Before talking about advances in the assessment of the function of respiratory muscles accessible to clinicians, it is worth noting the frequency and diversity of clinical situations in which we have to assess function or dysfunction of these muscles and to evaluate possible progress in response to targeted therapeutic interventions such as selective training of respiratory muscles, with the search of reliable, reproducible, sensitive, and minimally invasive methods possible.

The circumstances in which pulmonologists are led to consider respiratory muscle dysfunction are frequent

and above all extremely diverse. The very classic, once almost mundane, unilateral or bilateral *elevation of diaphragmatic domes* (visible on the X-ray and/or radiography) has today succeeded the much more complex analysis of *'disproportionate dyspnea'* (the symptom is frequent and disabling, while ventilatory function is not severely affected). The symptomatology can be that of *'abnormal fatigue'*, which is actually an excessive daytime drowsiness, leading to the question of diaphragm dysfunction in front of polysomnography's that are not those typical of a syndrome sleep apnea (with its hypoxia-reoxygenation sequences) but rather more prolonged episodes of hypoventilation, occurring preferentially during certain stages of sleep (particularly in REM –

Rapid Eye Movement – sleep). Clinician’s warned of the symptoms associated with respiratory muscle dysfunction will, therefore, need to confirm the diagnosis of respiratory muscle impairment, which are adapted either on functional tests specific explorations, either on static or dynamic imaging methods.

The etiological circumstances that lead to suspicion of diaphragm paralysis have also evolved considerably over time, and to the classic forms of mediastinal phrenic impairment of lung cancers, has succeeded other etiological circumstances, better recognized today. Old iatrogenic paralysis (cooling of left phrenic nerve during extra-body circulation, hematoma in contact with the phrenic nerve during the placement of a jugular catheter in intensive care) give way to recent circumstances relatively frequent (cryoablation of ectopic focus of pulmonary veins in the treatment of anti-a-rhythmic-resistant atrial fibrillation or upper right pulmonary vein crossing the trunk of the phrenic nerve), or exceptional (osteopathic maneuver on an

arthrosis spine). Other circumstances are also better recognized: central paralysis (multiple sclerosis, post-stroke, ...), diabetic mono or polyneuritis, cervical lesions (main phrenic root – C4) of degenerative (osteoarthritis) or post-traumatic origins (cervical sprain, 'whiplash'). The involvement of a respiratory muscle injury occurs very differently in other respiratory impairment situations. In chronic respiratory diseases such as COPD, asthma, idiopathic pulmonary fibrosis and cystic fibrosis, it is a matter of identifying specific phenotypic characteristics of subjects with a more or less significant respiratory muscle damage. In this situation, it involves identifying it in a frame containing other signs of sarcopenia (muscle mass of the quadriceps clearly decreased, in COPD or cystic fibrosis, for example), with a table of dyspnea associated with these diseases that can lead to specific management in rehabilitation.

Table 1 summarizes the main causes of unilateral and bilateral diaphragm impairments.

	Causes
Central Nervous System	Post-stroke, multiple sclerosis, amyotrophic lateral sclerosis
Pons	Chiari malformation, syringomyela with anterior horn compression
Cervical roots of the phrenic nerve	Trauma, arthrosis, hyperflexion accident (whiplash syndrome)
Brachial plexus	Elongation by upper arm and shoulder trauma
Nerve compression	Hematom after jugular puncture, mediastinal compression, cryotherapy of pulmonary veins for atrial fibrillation
Phrenic neuropathy	Diabetes, Personnage and Turner
Neuromuscular disease	Pompe disease, facioscapulohumeral-muscular-dystrophy (FSHD), titine mutation

Table 1: Examples of causes of diaphragmatic dysfunctions – Dr. B Wuyam.

Finally, the damage to the respiratory muscles also involves the evaluation of the impact of the respiratory muscles on the global function in neuromuscular diseases and amyotrophic lateral sclerosis. While these are rare diseases, often followed in reference and/or specialized centres, the diagnostic role for the pneumologist is of prime importance in the recognition of some of these conditions in adulthood. We all have examples of clinical cases where preferential involvement of the respiratory muscles has allowed for the first diagnostic suspicion of neuromuscular impairment at an early stage of stress intolerance. However, it is worth noting that the relative frequency of myasthenia, particularly in the form of acute respiratory failure without apparent cause, and for which the presence of a previously unnoticed diplopia or EMG signs with decrement is of the utmost importance in the diagnostic recognition.

Last point for pulmonologists interested in exercise and rehabilitation, new concepts such as the fatigue of respiratory muscles are emerging in the evaluation of respiratory muscles, and make their assessment useful not only at rest, but immediately during an exercise test (with the need to define couples of intensity/exercise duration relevant to this type of concept). In addition, selective training methods of respiratory muscles also find their place in the implementation of respiratory rehabilitation programs. Depending on the context and experience, specific management by selective training (strength or endurance) of the respiratory muscles should be evaluated, and the effectiveness and the need to monitor it is currently debated (but probably recommendable) in the broad community of respiratory pulmonologists and caregivers such as physiotherapists practicing respiratory rehabilitation.

2019 ERS Respiratory Muscles Testing:

LET'S TAKE A LOOK AT THE MOST COMMON TESTS

R. COOK

Global Group Product Director

In 2001 the ATS and ERS published a joint statement on respiratory muscle testing. Within these guidelines were recommendations on MIP/MEP testing, SNIP and Vital Capacity in the upright and supine positions, as well as several other modalities. The ERS published a new statement in 2019 after reviewing the data obtained since the previous joint ATS/ERS statement was published. While a majority of the guidelines did not change, this article will focus on the main respiratory muscle tests in clinical situation, and note the changes to the testing procedures.

Maximal Inspiratory Pressure/Maximal Expiratory Pressure (MIP/MEP)

Standard testing for MIP/MEP, also called P_{Imax} and P_{Emax} is relatively straight forward and most subjects can easily tolerate the test without difficulty. MIP efforts are usually measured near the subject's Residual Volume (RV). MEP efforts are usually performed near the subject's Total Lung Capacity (TLC). Generally, a single session measuring MIP/MEP values may be used as a screening instrument; however, when serial measurements over time (days/weeks) are performed, a better understanding of the patient's progress or regression can be examined.

The test is performed with a pressure manometer attached to a mouthpiece that can be occluded. The system should have a small leak (approximately 2 mm internal diameter and 20-30 mm in length) to "prevent glottic closure during P_{Imax} and reduce the use of buccal muscles during P_{Emax}".

When the subject is at either RV or TLC, the mouthpiece is occluded and the subject is asked to maximally inhale or exhale, depending on the effort performed. Ideally the pressures should be maintained for at least 1.5 seconds so that the maximum pressure sustained for 1 second can be recorded. The performance can be improved after an initial warm-up of the respiratory muscles.

Training and learning effects should be taken into account and at least five efforts should be performed for good reliability. It also states: "Once the operator is satisfied, the maximum value of three inspiratory manoeuvres or three expiratory manoeuvres that vary by less than 10% are recorded." This is a change and a tighter specification from the 2001 guidelines that looked at efforts that varied by less than 20%.

In the previous guidelines, a MIP value of -80 cmH₂O generally excluded significant inspiratory muscle weakness. The revised statement suggests that looking at the Lower Limit of Normal (LLN) for MIP can be used to determine muscle weakness; however, the LLNs are dependent on the equations being used.



While the new guidelines make comments on testing with pediatrics, the measurements obtained seem to have limited value and they recommend using the peak values instead of values sustained for 1 second in order to keep the test simple.

Sniff Nasal Inspiratory Pressure (SNIP)

SNIP test is not specific of diaphragm contraction, but results from the coordinated action of several inspiratory muscles. It's a complementary test to MIP, but should not be considered interchangeable with MIP. SNIP measurements require the subject to perform a maximal inspiratory maneuver through one nostril to obtain the most negative pressure achievable. However, rather than starting at near RV, the subject is instructed to begin the maneuver at relaxed end exhalation.

...when serial measurements over time are performed a better understanding of the patient's progress or regression can be examined.



The actual effort is performed by wedging a catheter that is connected to a pressure transducer into one of the subject's nostrils. At the end of a resting exhalation, the subject is asked to "sniffs" quickly and deeply while the other nostril is kept open. The pressure does not have to be maintained, and the duration of the effort should be less than 500 msec. Several efforts from each nostril may be performed (usually 10 tests, but more might be necessary) and the highest pressure reading is reported.

Static Lung Volumes – Vital Capacity (VC)

The most common measurement of lung volumes is the Vital Capacity (VC). This is the maximum volume of air that can be moved in the lungs (from RV to TLC or vice-versa). The measurement can be performed

slowly or as a forced maneuver. In the context of looking at muscle weakness, the VC is measured without force or rapid effort. Vital Capacity measurements are easy to perform using equipment as simple as a handheld spirometer. They also have the advantage in that they are very repeatable from effort to effort; however, the VC has poor specificity for the diagnosis of respiratory muscle weakness. The VC can be considered significant in that it can be dramatically affected by diaphragmatic paralysis and neuromuscular weakness (VC value less than 80% predicted in case of unilateral affection, and less of 50% in case of bilateral affection).

VC can also be used to characterize the effect that body position has with subjects who have neuromuscular disease. Normally subjects are tested in a supine and upright position, and testing in a supine position can decrease the VC, sometimes as much as 50%. According to Ruppel's Manual of Pulmonary Function Testing, a normal subject may see a decrease in VC of 3 to 8%, while subjects with neuromuscular disease will have a decrease greater than 10%. According to the ATS/ERS, fall greater than 15% is considered the Lower Limit of Normal (LLN), while 30% or more is generally associated with severe diaphragmatic weakness. After performing acceptable and repeatable VC maneuvers in a sitting position, the subject is asked to repeat the efforts while in a supine position. The VCs are then compared, looking for a significant decrease between the first and second session of testing. Depending on the amount of decrease, if any, the clinician can then determine the subject's status and if further tests need to be performed and evaluated.

The 2019 ERS statement on respiratory muscle testing relies on previous documentation on spirometry to cover the methodology of test performance.

Overview of Different Muscular Investigation Methods

BEYOND CONVENTIONAL MUSCULAR TESTING

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Diaphragm muscle is the main inspiratory muscle, so its correct functioning is essential. A diaphragmatic dysfunction is usually reflected in a restrictive functional profile, i.e. a decrease in available lung volumes. The appearance of a restrictive syndrome is confirmed with a lung volumes measurement where the TLC is inferior of the Lower Limit of Normal (LLN), or may be suspected if TLC is decreasing over time. The evaluation of Vital Capacity (VC) is not a good indicator for highlighting a restrictive syndrome, since an advanced obstructive pathology will also

show a decreased VC. However, the evaluation of the VC changes from upright to supine position is a relevant criterion to attest a dysfunction of the diaphragmatic activity. From this observation, experts have set up a decisional tree (figure 1) outlining the steps in management of diaphragmatic impairment diagnosis.

A normal VC while lying down excludes a clinically significant disease. If doubt remains, muscular pressures measured at the mouth and SNIP may provide additional information.

In addition to the most commonly used maneuvers for diagnosis of respiratory muscle such as MIP/MEP, SNIP or Peak Cough Flow (PCF), other methods based on imaging or neural stimulation could make a diagnosis more accurate.

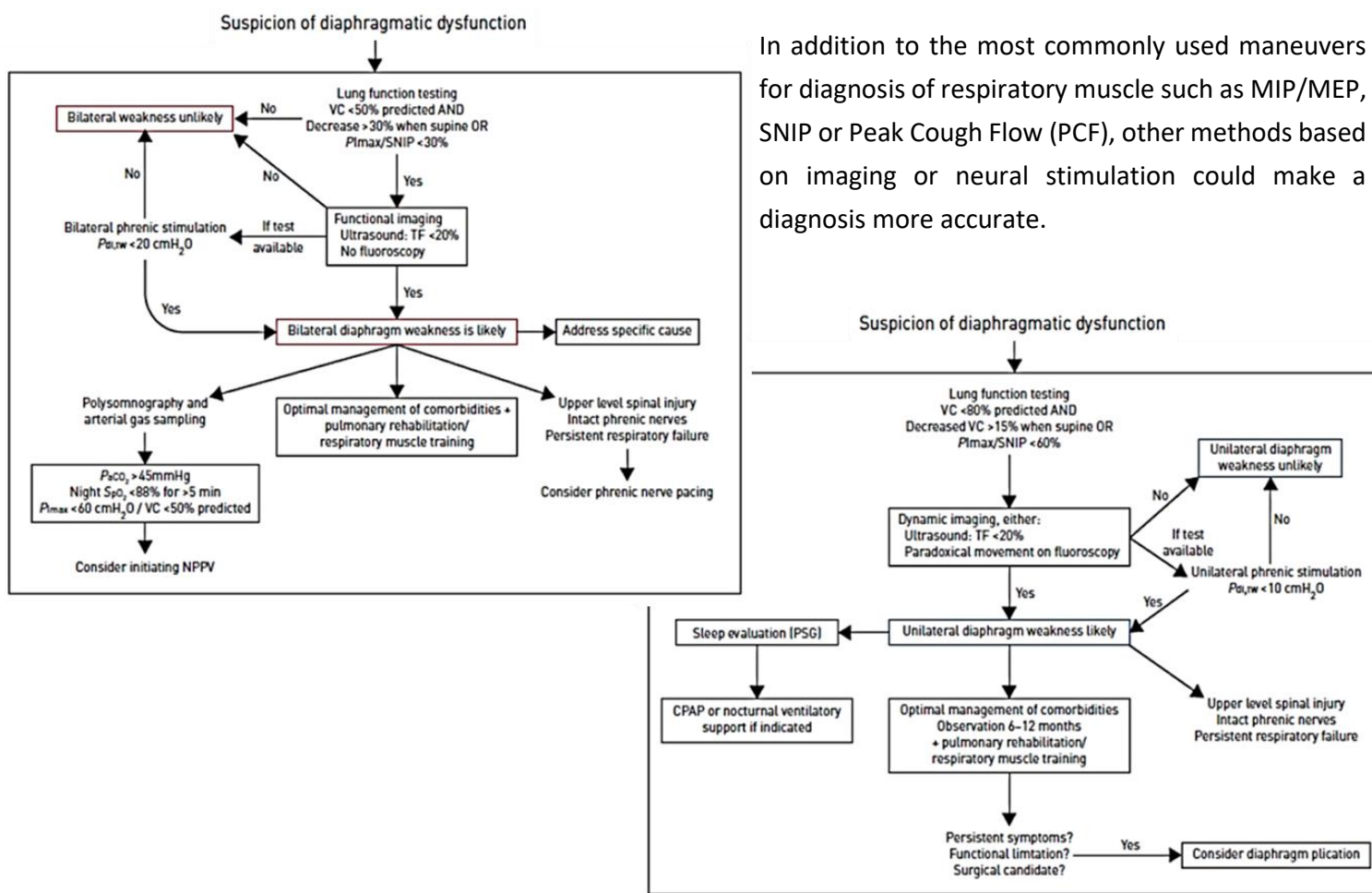


Figure 1: Expert opinion on the suspicion of diaphragmatic dysfunction – 2019 ERS Guidelines.

Non-invasive imaging, such as Ultrasound imaging (and/or chest fluoroscopy in more severe cases to identify paradoxical diaphragm motion) are primarily used to provide additional information. Ultrasound imaging (figure 2) provides information on the thickness of the diaphragm through three variables: 1° Static measurement of end-expiratory diaphragm thickness (Tdi), 2° the ratio between the inspiratory and expiratory diaphragmatic thickness during dynamic evaluation (TF) and 3° the diaphragmatic excursion that evaluates the movement of the diaphragm during breathing. Similar values in Tdi were recorded for healthy patients or patients suffering from diaphragm weakness, so that Tdi value is lacking to identify diaphragmatic dysfunction, but rather used for monitoring the evolution of diaphragm weakness. Diaphragmatic dynamic contractions (TF) produce shortening and thickening of the inspiratory muscle. However, the correlation between thickening and stress of the diaphragm is tenuous since only a maximum of one third of the variability in inspiratory effort is explained by ultrasound measurements of diaphragm thickening. Diaphragmatic excursion is more sensitive to changes in the respiratory pattern. Therefore, it is usually used to identify weakness of the diaphragm in the context of COPD, acute stroke or after abdominal surgery.

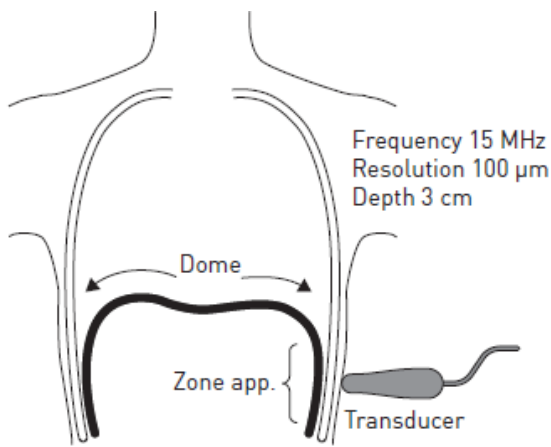


Figure 2: Diaphragm thickness and thickening fraction measurement – 2019 ERS Guidelines.

Some other non-invasive imaging techniques consist of Optoelectronic Plethysmography (OEP) and Magnetic Resonance Imaging (MRI). OEP is a recognized technique for measuring volume variations of the chest wall and its different compartments (figure 3). Cameras and reflective markers allow for very precise measurements both in static and dynamic ways. As an example, it was reported with this technique that patients with more severe COPD experienced dynamic hyperinflation consistently during exercise. Additionally, this method allows to distinguish different patterns of breathing from chest wall volume displacement in patients to cope with respiratory failure. This non-invasive method also assesses the effects of surgical techniques, such as laparoscopic surgery, on chest wall kinematics and inspiring muscles activity.

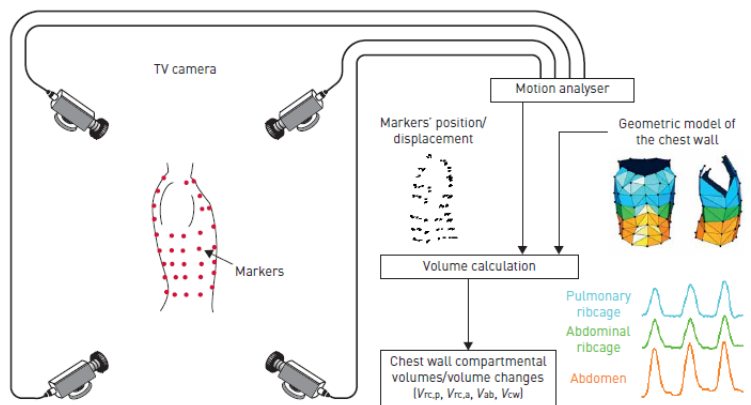


Figure 3: Optoelectronic plethysmography – 2019 ERS Guidelines.

Two and three-dimensional Magnetic Resonance Imaging (MRI) is increasingly used to assess diaphragm size, structure and functions. Two-dimensional MRI can qualitatively evaluate muscle atrophy in axial and coronal images, and measure cranio-caudal move. Dynamic MRI provides information about chest wall and diaphragm movement. Few publications about this technique have been written, making conclusions difficult. Further studies are needed to assess validity, reproducibility and accuracy of this tool.

Other methods based on neuromuscular function provide indications about respiratory muscle conditions. There are two main types of electrophysiological explorations: 1° the recording of signals of muscle origin (electromyography – EMG) or neuronal (electroencephalography – EEG), and 2° the study of the response to stimulation.

Electromyogram (EMG) is a technique for studying the activity of nerves and muscles. Applied to respiratory muscles, the EMG allows for the study of the patient profile and their level of activation in order to detect and identify neuromuscular pathologies. Combined with explorations of the mechanical function of these muscles, it can assess the quality of electromechanical coupling. The EMG signal can be recorded using surface electrodes, intramuscular electrodes or with an esophageal catheter during volitional contraction of the respiratory muscles; inspiratory with Sniff manoeuvre or expiratory by coughing. Electroencephalography (EEG) is an examination which records the electrical activity produced by neurons in the brain, particularly motor and pre-motor areas. It is measured using electrodes placed on the scalp or with transcranial electrodes

Stimulation tests measure the quality of nerve and neuromuscular transmission. These stimulations can be electrical or magnetic. For example, phrenic stimulation, also known as "Twitch Pdi," measures the difference between gastric and esophageal pressure using a catheter, by sending an electrical or magnetic stimulus. Since the diaphragm is exclusively innervated by the phrenic nerve, its stimulation makes it possible to specifically study this muscle independently of other respiratory muscles. This technique is a "Gold Standard" for measuring the strength of the respiratory muscles and is useful in complex situations, such as connective tissue diseases.

Another type of stimulation, The Transcranial Stimulation (TMS), is most often performed using a magnetic stimulator and allows the measurement of the central conduction time of the limb muscles and diaphragm. For example, an extension of the central conduction time may occur with multiple sclerosis.

Other tests such as polysomnography (sleep study) or blood gas analysis can also give us indications on the state of respiratory muscle function.

To conclude, the evaluation of respiratory muscle is more accurate when combining several tests. Easy-to-perform methods are used for an initial evaluation such as VC, SNIP, MIP or MEP and the diagnosis might be completed by more specific technology. Considerable research has been undertaken over the past 17 years, and key advances have been made in the field of mechanics of breathing, respiratory muscle neurophysiology (electromyography, electroencephalography and transcranial magnetic stimulation) and imaging (ultrasound, optoelectronic plethysmography and structured light plethysmography) which make those technologies more understandable and efficient.



USING MIP AND SNIP TO IMPROVE INTERPRETION OF RESPIRATORY MUSCLES TESTS

Clinical Implication of Respiratory Muscles Testing

WHAT INFORMATION ARE BEHIND THESE TESTS?

S. GIOT

Clinical Application Specialist International

In healthy subjects, breathing is easy. In normal situations, we are not aware of our respiration, but we know it's allowed by the good synchronization of several muscles and governed by complex mechanics. Inhalation is an active process; central neuronal drive of respiration sends inputs for expansion of the chest cage by contraction of intercostal muscles and the diaphragm. On the contrary, during quiet respiration exhalation is passive; inspiratory muscles relax and respiratory system returns to resting level thanks to elastic recoil of the lung tissue. During vigorous expiration and cough, the mechanism becomes active with the contribution of the abdominal muscles which force the diaphragm upwards to increase the rate of expiratory flow.

In some pathological situations, respiratory mechanics

may be altered, which results in symptoms such as dyspnoea, difficulties for coughing or sleep-disorders. Dyspnoea is caused by the inability to inhale efficiently in the case of advanced Neuro-Muscular Disease (NMD) or, to a smaller extent, an inhalation requiring extra effort leading to respiratory fatigue or exhaustion. This latter situation may be encountered in early NMDs, in Interstitial Lung Diseases (ILD) where the stiffening of the lung tissue diminishes compliance, or in COPD at an advanced stage where hyperinflation alters the respiratory mechanics, all causing insufficient inspiration.

Difficulties of exhalation due to respiratory muscle impairment may lead to adverse clinical consequences, mainly when subjects need strength for coughing. One of the many common complications

of respiratory muscle weakness is the risk of bronchial and/or pulmonary infections and hypoventilation. These two pathological situations may lead to a mucous congestion of the respiratory tract, and an inefficient cough will inevitably worsen the clinical situation. The removal of the mucous must then be facilitated by physiotherapeutic or mechanic aids.

MIP (P_Imax) and MEP (P_Emax) are the most common tests in PFT labs for screening respiratory strength and give a good baseline information. A strong correlation exists between P_Imax and exertional dyspnoea, regardless of the FEV₁ of the subject. Accordingly, P_Imax evaluation gives relevant clinical information, which was highlighted in a 550 subject study during cycle ergometry exercise (Figure 4).

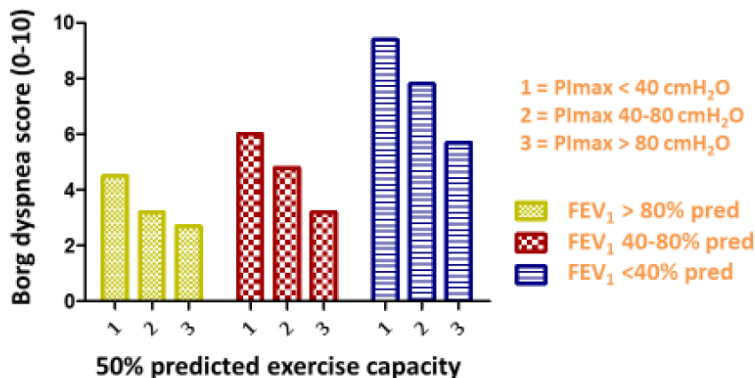


Figure 4: Dyspnoea score perceived during cycling according to P_Imax and FEV₁ (Killian KL et al., Clin Chest Med 1988;9:237-248).

However, we have to remain aware that these volitional tests may present low values due to poor technique or insufficient effort rather than muscle weakness. MIP/MEP may also be compromised in some conditions where impairment of the central neural drive is the cause of the inability to generate the necessary effort. Assessment of respiratory muscle function in such situations will require various non-volitional techniques of electrical or magnetic stimulation.

Respiratory muscles tests are therefore difficult to interpret alone with confidence. Therefore, additional

tests may be required, which can be more complex and invasive (e.g.: neuronal magnetic stimulation, placement of an esophageal catheter to measure respiratory pressures, or study of electrical activities). However, by combining for example both non-invasive MIP and Sniff test (SNIP), the probability to diagnose an inspiratory muscles weakness is already improved by an additional rule-out of about 20% compared with either test alone. In addition, if these two tests are combining with Sniff test with invasive pressure measurement (esophageal and gastric pressures for diaphragmatic pressure measurement), the diagnostic precision is not significantly improved compared with only MIP and SNIP. Which means that in common clinical situations, if the subject does not present nasal or airways obstruction, the combination of the two non-invasive tests (SNIP and MIP) is almost as precise as when the invasive Sniff test is added to the assessment.

In the previous ATS/ERS statement, a cut-off of -80 cmH₂O was proposed as a practical threshold to exclude clinically important inspiratory muscle weakness. New ERS Guidelines summarizes predictive equations recommended to be used (predicted values and LLN). Selection of the right equation is capital since the presence or absence of respiratory muscle weakness is critically dependent upon the specific equation being used. Rodrigues et al. (2017) reported the prevalence of respiratory weakness ranged from 33,4 to 66,9% according to the choice of the reference equation on more than 1500 subjects.

While in inspiratory muscle strength evaluation MIP is the preferred method, SNIP is less used as it is complementary to MIP and not directly interchangeable; SNIP leading to less reliable outcomes in subjects with severe weakness and dyspnoea. Furthermore, SNIP shows a prognostic role uncertain in respiratory disease due to the lack of

studies. However, in some situations, SNIP is useful because of its simplicity and is less prone to learning effects. SNIP can also give relevant clinical information; for example in Duchenne muscular dystrophy, SNIP declines earlier than PEF, allowing an early therapeutic management. In addition, SNIP values lower than -40 cmH₂O were significantly associated with desaturation during sleep in Amyotrophy Lateral Sclerosis (ALS) patients. As a consequence, SNIP should be part of the routine evaluation of muscle strength in NMDs.

In agreement with previous ATS/ERS guidelines, SNIP Lower Limit of Normal (LLN) is around -70 cmH₂O for males and -60 cmH₂O in females, keeping in mind that there is a positive correlation with age.

In expiratory muscle assessment, the combination of different tests is also relevant, but implies the use of invasive tests. MEP and invasive gastric pressure measurement during cough (cough P_{gas}) results a similar diagnostic outcome, but the combination of these two tests, and more with a third invasive one (Twitch T10: magnetic stimulation of the thoracic nerve roots) will increase the specificity of the diagnosis; which is not easy to perform in routine in every lab.

In Table 2, ERS Guidelines summarizes the main clinical characteristics of MIP, MEP and SNIP tests.

Another easy-to-perform test for a respiratory muscle evaluation consists of measuring the decline of the Vital Capacity (VC) from upright to supine position. According to the 2019 Guidelines, a 15% fall in supine VC could be considered as the LLN. Since a significant reduction of the VC in supine position in patients with diaphragm weakness is well correlated with the reduction in Sniff-P_{di} (invasive measurement of diaphragmatic pressure during sniffing), this test specifically emphasizes the diaphragm activation. Additionally, a significant fall in VC in supine position may be the key to initiate further muscle investigations. In many NMDs, ALS in particular, a significant reduction of VC as well as its rate of decline over time are recognised as criteria for initiating non-invasive ventilation. Reduction in VC in the supine position is also a very sensitive criteria (80-95%) of sleep disordered breathing, respiratory failure, worse prognosis and, in a lesser extent, response to treatment.

In conclusion, the outcomes of an inspiratory or expiratory strength test is quite similar to that of any other test, but what will enhance the power of diagnosis is the combination of these tests. Compared to expiratory tests, evaluation of inspiratory muscles is clinically more relevant, and good performance of the combination of non-invasive MIP and SNIP tests should be kept in mind.

Main variables	Repeatability/reliability/validity	Cautions	Setting (expert centres, general clinical use, research, etc.)
P_{max}	Sufficiently repeatable and reliable measurements in untrained subjects (<10% variability between efforts) can usually be obtained within 5 efforts [297]. Peak values are typically reached after 9 attempts [298].	Standardisation of lung volumes, mouthpiece and recorded pressure (peak versus plateau) required.	SNIP and mouth pressures can be used in clinical practice after thorough training of the procedures.
P_{Emax}	Reliable peak values usually achieved after 5–6 efforts. Within subject between occasion coefficient of variation around 10% [21].	Standardisation of lung volumes, mouthpiece and recorded pressure (peak versus plateau) required.	
SNIP	Yes. Possibly fewer efforts needed for acceptably reliable measurements in comparison to P_{max} in untrained subjects [12, 13, 20, 299, 300].	Cautions in subjects with severe nasal congestion. Although SNIP and P_{max} has a good correlation, the agreement between these two methods is variable. Thus, they are complementary and not interchangeable in the evaluation of inspiratory weakness	SNIP in association with P_{max} reduces the false-positive diagnosis of inspiratory weakness by nearly 20% [5].

Table 2: Characteristics of the main routine voluntary manoeuvres to assess respiratory muscle strength – 2019 ERS Guidelines.

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