The role of the pulmonary function laboratory in the assessment of adults with neuromuscular disease

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BACKGROUND

Neuromuscular disease (NMD) can affect all respiratory muscle groups, and respiratory complications are the major cause of morbidity and mortality.[1] The duration of symptoms varies depending on the underlying diagnosis. NMD can be acute (e.g., Guillain-Barré syndrome; acute spinal cord or phrenic nerve trauma or infarction; epidural abscess; acute poisoning; drug-related NMD; metabolic disturbances; tetanus or other infections; and acute myasthenic crisis) or present slowly over months (e.g., amyotrophic lateral sclerosis, multiple sclerosis, spinal cord tumors, myasthenia gravis, syringomyelia, muscular dystrophy, and myotonic dystrophy). In the latter context, pulmonary function tests (PFTs) play a prominent role in objectively assessing respiratory muscle strength and potential consequences of weakness of the respiratory system (Figure 1).

OVERVIEW

A 55-year-old overweight man (BMI = 27 kg/m^2) with a history of heavy smoking (30 pack-years) was referred for a pulmonology consultation because of long-standing sporadic inclusion body myositis. He reported having experienced leg pain and weakness since he was in his 30s and 40s, respectively. Although there were no respiratory symptoms during wakefulness (with a modified Medical Research Council scale score of 1, with no cough or phlegm) or daytime somnolence (an Epworth Sleepiness Scale score of 6), the patient did report episodes of nocturnal choking and frequent rhonchi. Moderate left convex scoliosis was observed on physical examination. PFTs indicated a restrictive ventilatory defect (an FVC of 62% of the predicted value and a TLC of 68% of the predicted value) and respiratory muscle weakness (an MIP of 57% of the predicted value and an MEP of 69% of the predicted value). Of note, RV and the RV/TLC ratio were within and above the upper limit of normal, respectively. A proportional reduction in DL_{CO} (60% of the predicted value) and alveolar volume (V_A; 65% of the predicted value) corresponded to a carbon monoxide transfer coefficient (K_{CO}) within normal ranges (94% of the predicted value = a z-score of −0.30). Diffuse myocardial hypokinesis (a left ventricular ejection fraction of 49%) was observed on echocardiography. Mild obstructive respiratory disorder was observed during overnight polysomnography (an apnea-hypopnea index of 14.6 events/h), with significant CO_2 retention (mean partial pressure of end-tidal CO_2 = 39, with peaks of 51 mmHg).

Restriction is the typical finding in patients with respiratory muscle weakness. It is suggested by reduced FEV_1 and FVC with a preserved FEV_1/FVC ratio and confirmed by a reduced TLC. In cases of preserved FVC, a fall > 15% in FVC from the sitting position to the supine position supports a diagnosis of diaphragm weakness.[2] This threshold can be higher in the presence of concomitant ventilatory defects.[3] A high RV/TLC ratio was a consequence of a low TLC (rather than a high RV), in keeping with restriction. Nevertheless, when the expiratory muscles are involved, RV and RV/TLC may be increased, resulting in complex restriction (reduced FVC relative to TLC).[4] DL_{CO} is reduced in extraparenchymal restriction as a result of reduced V_A, which would lead to a supranormal K_{CO} (DL_{CO}/V_A). A "normal" K_{CO} with preserved V_A/TLC indicates some degree of concomitant intraparenchymal restriction.[5] In the current case, it was attributed to alveolar fibrosing sequelae from repeated episodes of pulmonary congestion caused by cardiomyopathy. Arterial blood gas analysis should be routinely obtained to determine whether daytime hypercapnia is present. Hypercapnia, however, may be evident during sleep only, when polysomnography with end-tidal or transcutaneous capnography is useful.

CLINICAL MESSAGE

PFTs are regularly recommended for patients with NMD who may exhibit varying rates of decline in lung function.[1] Objective testing is important because there is no correlation between respiratory muscle weakness and the degree of peripheral muscle weakness in several conditions.[6] Functional testing helps identify patients who need specific therapies, such as assisted cough, airway clearance, and ventilatory support.[1]

AUTHOR CONTRIBUTIONS

All authors contributed equally to this work.

CONFLICTS OF INTEREST

None declared.

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SPIROMETRY

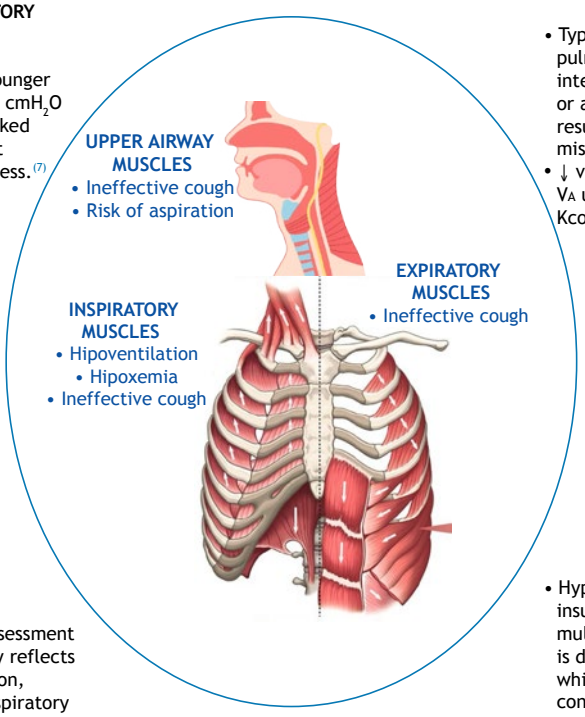
- ↓ FEV_1 and FVC with ↔ FEV_1/FVC ratio suggest restriction, the typical ventilatory defect in patients with respiratory muscle weakness.
- A fall in FVC > 15% from the sitting position to the supine position suggests diaphragmatic weakness.
- ↓ measured MVV in comparison with estimated MVV (= FEV_1 × 40) indicates ↓ respiratory muscle endurance.

BODY PLETHYSMOGRAPHY

- TLC < LLN is the gold standard for restriction.
- Patients with predominantly expiratory muscle weakness may demonstrate a ↓ expiratory reserve volume and an ↑ RV, leading to an ↑ RV/TLC ratio (complex restriction).

MAXIMAL INSPIRATORY PRESSURE

- Absolute values < -50-60 cmH_2O in younger individuals and < -40 cmH_2O in the elderly are linked with a higher pretest probability of weakness.[7]
- Severe bulbar dysfunction may cause difficulty performing the tests due to the lack of a tight seal of the lips around the mouthpiece. In these situations, the operator can assist by manually ensuring a tight seal for the patient.
- Alternatively, sniff nasal inspiratory pressure (SNIP) may be used to indicate respiratory muscle weakness.
- SNIP is a dynamic assessment that more accurately reflects diaphragm dysfunction, whereas maximal inspiratory pressure is more influenced by the recruitment of accessory inspiratory muscles.



DLco

- Typically preserved if no coexisting pulmonary parenchymal (e.g., interstitial lung disease, emphysema or atelectasis), or vascular disease resulting in ventilation/perfusion mismatch.
- ↓ values may occur due to reduced V_A usually resulting in supranormal Kco (DLco/V_A).

ARTERIAL BLOOD GAS ANALYSIS

- Hypercapnia is the hallmark of inadequate ventilation.
- Early in the course of chronic disease, ventilation may be adequate to maintain a normal $PaCO_2$. However, under stress (e.g., sleep, fever, infection) or with disease progression, ventilation cannot be sufficiently increased, and $PaCO_2$ rises.
- Hypoxemia frequently accompanies insufficient ventilation and is multifactorial. A small contribution is due to insufficient ventilation, while a more significant contribution is typically due to atelectasis-induced shunt from rapid, shallow breathing.

MAXIMAL EXPIRATORY PRESSURE

- Values < 60 cm H_2O suggest that the patient's cough is ineffective.
- A peak cough flow < 160 L/min identifies patients with an ineffective cough. Values between 160-270 L/min. indicate an increased risk for respiratory tract infections
- The absence of transient increases in peak cough expiratory flow (i.e., cough spikes) above the maximal flow-volume loop in spirometry indicates decreased cough effectiveness.

USE OF NONINVASIVE VENTILATION[1]

- The clinical indications for noninvasive ventilation can vary depending on NMD, age, and rate of disease progression.
- Any fall in FVC to < 80% of predicted with symptoms or FVC to < 50% of predicted without symptoms or SNIP /maximal inspiratory pressure to < -40 cmH_2O or hypercapnia would support initiation of noninvasive ventilation or further testing as clinically indicated for individual NMD.

RECOMMENDATIONS FOR LUNG VOLUME RECRUITMENT (BREATH STACKING) AND ASSISTED COUGH TECHNIQUES/DEVICES[1]

- For patients with NMD and hypoventilation, ↓ lung function or ↓ cough effectiveness.

Figure 1. Involvement of inspiratory, expiratory, and/or upper airway muscles in patients with neuromuscular disease (NMD) determines the predominating clinical presentation (in blue). Different pulmonary function tests (in black) can reveal functional impairments and support the indication of specific therapies (in red). MVV: maximal voluntary ventilation; LLN: lower limit of normal; ↓: decreased; ↑: increased; ↔: preserved; V_A: alveolar volume; and K_{CO}: carbon monoxide transfer coefficient.

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