

**Pulmonary Outcome Measures
in Duchenne Muscular
Dystrophy**

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Rationale

- Respiratory disease ~80% of mortality in DMD
- Preventable with preventive measures
- Any therapy that improves respiratory muscle strength will extend life expectancy
- If respiratory muscle strength improves, the therapy is a success, regardless of effect on other skeletal musculature

Measurable parameters

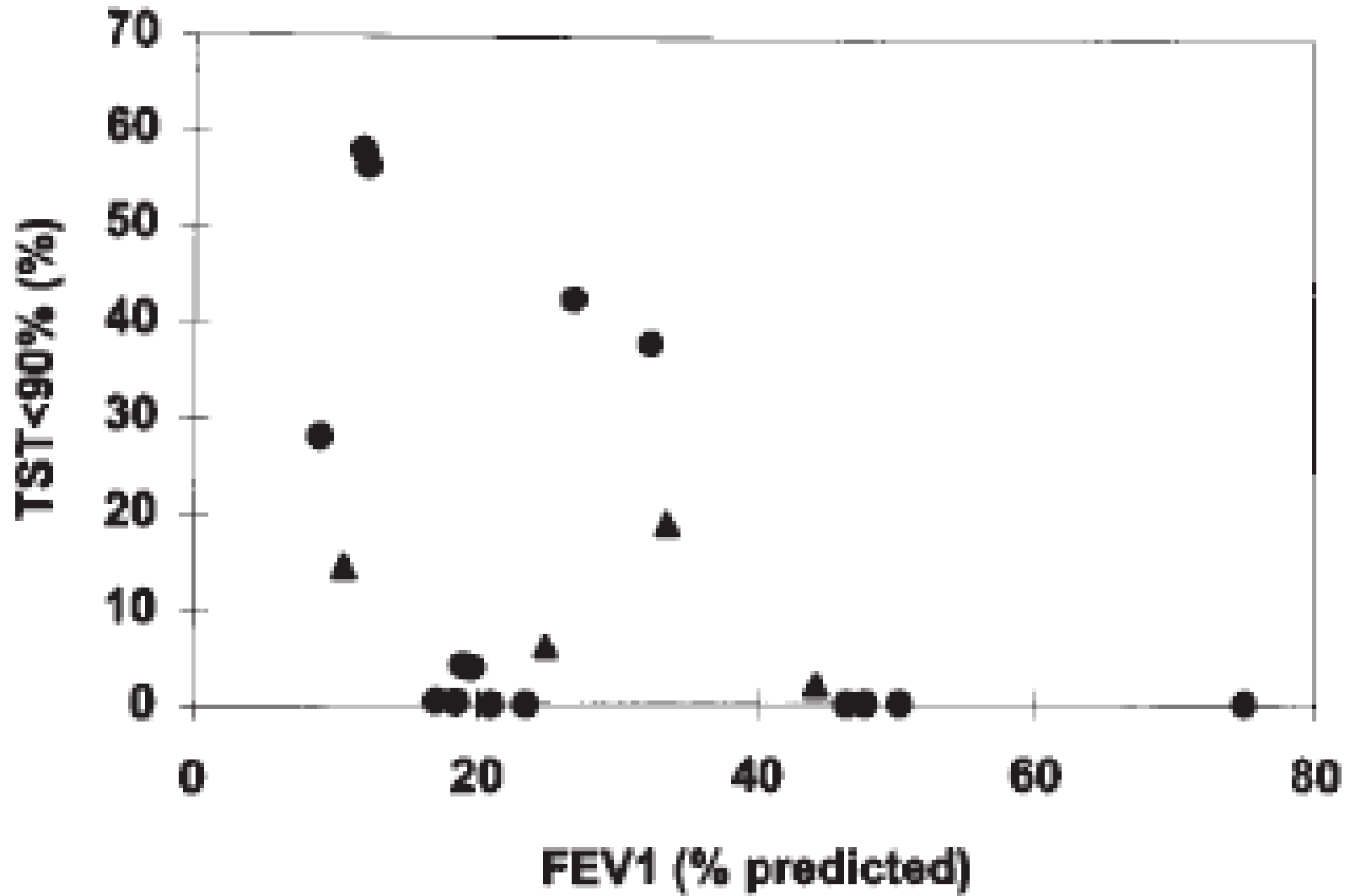
- Spirometry: FVC, FEV1, PEFr
- SaO₂ (awake v. asleep)
- End-tidal CO₂
- Peak inspiratory pressure, peak expiratory pressure (PIP/PEP)
- Rate of pneumonia, hospitalization, resp. failure

Forced Vital Capacity (FVC)

- Advantages: reproducible, accepted
- Disadvantages:
 - Effort-dependent, requires cooperative patient
 - Requires specialized equipment
 - Consistency requires similar equipment, predicted values
- Predictive value good:
 - FVC < 1 L median survival 3.1 y; 5 y survival 8%
 - Hukins, et al AJRCCM 2000 161:166
 - FEV1 <20% \Rightarrow CO₂ retention

Forced Expiratory Volume at 1 second (FEV1)

- Useful in measurement of obstructive diseases (asthma, CF, COPD)
- No more valuable than FVC in NMD
- Part of routine spirometry; follows FVC closely
- FEV1 <40% predicts nighttime hypoventilation/sleep hypoxemia
 - Hukins/Hillman, 2000
- Recommendation: yes



Note that OSA pts are triangles; non-OSA circles

Peak insp/exp pressure (PIP/PEP)

- <60 cm H₂O predicts ineffective cough
 - Szeinberg, et al: Chest, 1988;94:1232
- Predicted values for children published
 - Smyth, et al: Chest 1984;86;568. N=76
 - Wilson, et al: Thorax 1984;39;535. N=370
- Easy and inexpensive
- Fairly reproducible (10% variance)
- Recommendation: yes

Peak flow

- Peak flow (PEFR) is reported in spirometry
- Peak COUGH flow involves coughing into a Wright peak flow meter
- Disadvantage: effort dependent, vble
- Advantage: Bed side test, inexpensive
- Rough correlation with airway clearance (<160* predicts inadequate AW clearance)
- Recommendation: YES

*Bach, et al: Chest, 1996: 110;1566.

Hemoglobin Saturation (awake)

- Advantages: inexpensive, quick, reliable
- Disadvantages:
 - Poorly predictive of respiratory insufficiency
 - Influenced by airway disease
 - Daytime SaO₂ may not predict nighttime SaO₂
- Hukins & Hillman: FEV₁ and FVC significantly correspond to sleep desaturation
- Recommendation: Not useful as primary outcome measure

End-tidal CO₂?

- Corresponds to PaCO₂
- Non-invasive but not always available
- Poorly predictive:
 - Even with normal pCO₂ poor survivals seen
 - Phillips, et al: AJRCCM 1999; 160:198
- Hukins and Hillman: FEV₁<20% corresponds to elevated pCO₂
 - In other words, spirometry will suffice
 - Wakeful pCO₂ >45 predicts nighttime resp failure

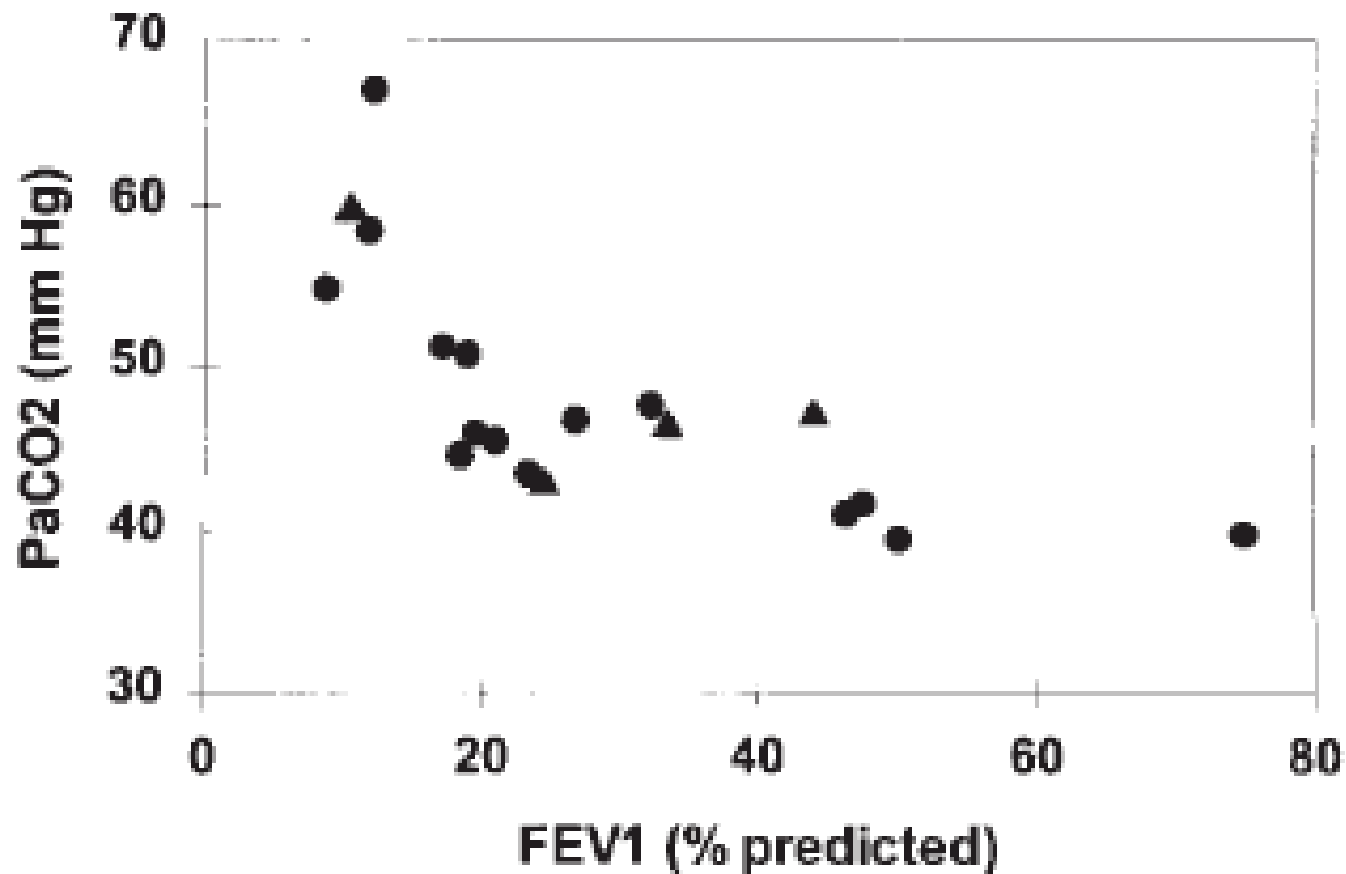


Figure 1. Relationship between wakeful Pa_{CO_2} and FEV_1 . Patients with obstructive apneas (more than four per hour) are indicated by *triangles*. All other subjects (*circles*) had less than one obstructive apnea per hour.

Sleep studies?

- Although sensitive and useful:
 - Very expensive
 - Very few pediatric sleep labs
 - Variability in interpretation lab to lab
 - Poor standards of normal in children

Conclusions

- Spirometry (FVC, FEV1, PEFr) useful
- PIP/PEP also recommended
- ET CO₂ as secondary measure to be considered - not as primary outcome
- SaO₂ not as useful but easily obtained
- Sleep studies are expensive, difficult to obtain, differ from lab to lab

