Asthma Control Markers: Rationale & Interpretation

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Asthma Severity vs Asthma Control

Asthma severity is an inherit trait of the patient that reflects the intrinsic intensity of the disease process. Asthma control is the degree to which the manifestations are reduced. May fluctuate and can be assessed by clinical methods or biomarkers. It has 2 domains:

a) Current impairment: symptoms, activity limitation, and quality of life.


Asthma Control Markers

A. Clinical Markers

Methods using symptoms, activity limitations, exacerbations, need for rescuer medications, emergency department visits, hospitalizations, PFT. Most commonly known:

1. **ACQ**, Asthma Control Questionnaire
2. **ACT**, Asthma Control Test; c-ACT for 4-11 yr.
3. **NAEPP**, National Asthma Education and Prevention Program goals of therapy
4. **JTFPP**, Joint Task Force Practice Parameter on attaining optimal asthma control
5. **GINA**, Global Initiative for Asthma guidelines

They are easy to perform in clinical practice or research, and have been widely used particularly ACT, ACQ, and GINA.

Definition of asthma control according to each assessment tool

<table>
<thead>
<tr>
<th>Assessment Tool</th>
<th>Criteria</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>ACQ</strong></td>
<td>Mean score ≤ 1</td>
</tr>
<tr>
<td><strong>ACT</strong></td>
<td>Score ≥ 20</td>
</tr>
</tbody>
</table>
| **NAEPP**       | SABA use ≤ 2 times/ week in previous 2 weeks  
Nocturnal symptoms ≤ 2 times in previous month  
No activity limitations  
No recent ED visits or hospitalizations for asthma  
FEV1 ≥ 80% of predicted |
### JTFPP
- SABA use ≤ 2 times/week
- Asthma symptoms ≤ 2 times/week
- No nocturnal symptoms
- No activity limitations
- Patient self-assessment that asthma is controlled
- Physician global assessment that asthma is controlled
- FEV1 ≥ 80% of predicted

### GINA
- SABA use ≤ 2 times/week
- Daytime symptoms ≤ 2 times/week
- No nocturnal symptoms
- No activity limitations
- No exacerbations
- FEV1 ≥ 80% of predicted

<table>
<thead>
<tr>
<th>Domain</th>
<th>ACQ</th>
<th>ACT</th>
<th>NAEPP</th>
<th>JTFPP</th>
<th>GINA</th>
</tr>
</thead>
<tbody>
<tr>
<td>Daytime symptoms</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
</tr>
<tr>
<td>Nighttime symptoms</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
</tr>
<tr>
<td>Activity limitation</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
</tr>
<tr>
<td>Short-acting β-agonist use</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
</tr>
<tr>
<td>Exacerbations</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>X</td>
</tr>
<tr>
<td>ED visits/hospitalizations</td>
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<td></td>
<td></td>
<td></td>
<td>X</td>
</tr>
<tr>
<td>Patient self-assessment</td>
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<td></td>
<td></td>
<td></td>
<td>X</td>
</tr>
<tr>
<td>Physician assessment</td>
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<td></td>
<td>X</td>
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<tr>
<td>FEV1 % predicted</td>
<td>X</td>
<td>X</td>
<td>X</td>
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<td>X</td>
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</tbody>
</table>
B. Biomarkers (primarily for research)

1. **Exhaled nitric oxide level**: compliment clinical markers. Has multiple limitations (see below).
2. **Eosinophils or ECP in induced sputum or BAL**: Reflect eosinophilic inflammation and usually predict response to corticosteroids. Elaborate procedure and requires experience.
3. **Exhaled breath condensate**: poor control is associated with low pH and increased IL4, RANTES, and cyst-LTs. Time consuming, costly, and requires experience.
4. **Urinary LTE4**: increased during asthma exacerbation. Predicts response to LT antagonists.
5. **Serum periostin**: seems to be a very sensitive marker for eosinophilic inflammation, but of low specificity.

**Factors that increase FeNO**
- In healthy children levels increase with age
- Males have levels 20-30% higher than in females
- During menstruation
- Intake of nitrate-rich diet
- Asthma
- Atopic disease, particularly allergic rhinosinusitis
- Resp infections that promote Th2 (e.g., rhinovirus, tuberculosis)
- Ethnicity; Chinese > Blacks > Caucasians

**Factors that reduce FeNO**
- Tobacco smoking. Passive smoking causes transient reduction (for only about 30 min)
- Alcohol consumption
- Inflammatory lung diseases other than asthma, e.g., COPD, BPD, CF, pulmonary hypertension, pneumonia, influenza.
- Ciliary dyskinesia
- ICS therapy
- Spirometric maneuver
- Exercise

**2011 ATS Clinical Practice Guidelines: Recommendations for FeNO:**
1. Diagnosis of eosinophilic inflammation
2. Monitoring airway inflammation in asthma
3. Use in accounting for persistent or high allergen exposure
4. Use to determine likelihood of steroid responsiveness:
   - If FeNO <25 ppb (<20 ppb in children): Unlikely
   - If FeNO >50 ppb ( >35 ppb in children): Likely
   - If FeNO 25-50 ppb (20-35 ppb children) interpret cautiously
5. Recognize poor compliance with ICS intake

**Limitations of FeNO measurement**
- Expensive equipment, calibration & supplies
- Requires patient cooperation for optimal performance
- Many factors influence eNO level; up & down
- Limited effect on improving asthma control when added to guidelines approach
- Normal ranges are not settled; vary by age, gender, race, habits (diet, alcohol, smoking), etc.
References