Lack of Correlation of Sinonasal and Otologic Reported Symptoms With Objective Measurements Among Patients With Primary Ciliary Dyskinesia: An International Study

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Sinonasal and otologic symptoms are common among patients with primary ciliary dyskinesia (PCD) of all ages [1-3]. Since most PCD symptoms are nonspecific, patients with PCD may learn to live with their symptoms or perceive them as unbothersome; thus, they underreport symptoms during clinical visits. Yet, objective tests possibly fail to capture the true burden of sinonasal and otologic disease in daily life. To inform decision-making during ENT specialist clinical follow-up, we assessed correlations between patient- and parent-reported ENT symptoms and objective measurements of ENT disease among patients with PCD.

We assessed agreement between patient- or parent-reported ENT symptoms and ENT consultation outcomes, indicating disease (agreement yes); no disease (agreement no); and disagreement (reference category). Agreement for no disease between reported ear pain and acute otitis media (AOM) or otitis media with effusion (OME) on examination; (5) reported ear discharge and ear discharge on examination; (2) reported blocked nose and nasal polyps or hypertrophic turbinates; (3) reported headache while bending down and facial pain at examination; (4) reported ear pain and acute otitis media (AOM) or otitis media with effusion (OME) on examination; (5) reported ear discharge and ear discharge on examination; (6) reported hearing problems and impairment on audiometry. We studied whether age, sex, and center were associated with agreement using multinomial logistic regression. The models provided three possible patient and examination outcomes, indicating disease (agreement yes); no disease (agreement no); and disagreement (reference category).

We included 404 participants from 12 centers (Table 1) with a median age of 15 years (interquartile range [IQR], 9–22 years; female, n=187 [46%]) and a median age at diagnosis of 9 years (IQR, 3–17 years). Table 1 shows the prevalence of patient-reported symptoms and clinical examination findings. Audiometry results were available for 280 participants.

We found no correlations for most patient-reported symptom and examination combinations we tested (Fig. 1). Underreporting varied by symptom and was higher for blocked (23%) or runny (25%) nose. Reported ear discharge correlated poorly with ear discharge at examination (kappa 0.28; 95% confidence interval [CI], 0.18–0.37). From the tested combinations, reported hearing problems correlated best with audiometry results; however, the correlation remained weak (kappa 0.41; 95% CI, 0.30–0.52). We performed sensitivity analyses assessing examination findings with frequent (reported daily or often) instead of prevalent symptoms; no improvement in the correlations was found (data available from authors).

We assessed age, sex, and center as possible determinants of agreement. Agreement for no disease between reported ear pain and AOM or OME (relative risk ratio [RRR], 1.0; 95% CI, 0.9–1.0 for each year increase) increased with age and was higher among participants in Cyprus and Istanbul. Age did not play a role in agreement for other reported symptoms and examination findings. Agreement regarding no hearing impairment from a comparison of reported hearing problems and audiometry results was higher among participants in Istanbul (RRR, 9.8; 95% CI, 3.1–31.2) compared with the Netherlands (reference category); agreement about hearing impairment was higher among participants from the United Kingdom (RRR, 8.8; 95% CI, 1.9–41.0). Sex did not appear to play a role in agreement. We found
no correlation between patient-reported sinonasal symptoms and relevant clinical examination findings. Otolologic symptoms correlated poorly or weakly with otoscopy and audiometry findings. Nonetheless, we identified age and center as agreement determinants.

Our study is the first to assess potential correlations between patient- and parent-reported symptoms with objective measurements among patients with PCD. Previous clinical studies related to ENT disease among patients with PCD included non-standardized symptom information extracted from medical charts, precluding direct comparisons [3,11,12]. A prospective study in the United States found that nasal congestion and runny nose reported by adults with postsurgical chronic rhinosinusitis (CRS) correlated with nasal endoscopy scores [13]. A large Korean study among adults found an association between reported hyposmia or anosmia and nasal endoscopy findings indicative of CRS (mainly nasal polyps and mucopurulent discharge in middle meatus) and symptom combinations with stronger associations compared with individual symptoms [14]. Correlation from using composite outcomes [10] or endoscopy scores [11] or studying different participant age ranges possibly explains the variation in findings [15,16]. Follow-up and examination techniques or the cultural acceptance of some symptoms also possibly account for differences among centers.

The reporting of standardized symptom and examination findings and the large number of participants for a rare disease strengthened our study. Despite PCD symptom chronicity, a limitation of this study is that it analyzed patient-reported symptoms from the previous 3 months—not just the examination day—which may be linked to weaker correlations. Otolologic symptoms among children are difficult for parents to evaluate, which possibly explains the role of age as an agreement determinant [17,18]. Although patients with longer follow-up might evaluate their symptoms more accurately, we did not collect such information.

Many participants appeared to underestimate and underreport their symptoms, to which they grew accustomed over time, while

### Table 1. Characteristics of EPIC-PCD participants, overall and by age group (n=404)

<table>
<thead>
<tr>
<th>Variable</th>
<th>Total</th>
<th>Age 0–6 yr</th>
<th>Age 7–14 yr</th>
<th>Age 15–30 yr</th>
<th>Age 31–50 yr</th>
<th>Age &gt;50 yr</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of participants</td>
<td>404 (100)</td>
<td>45 (100)</td>
<td>131 (100)</td>
<td>163 (100)</td>
<td>42 (100)</td>
<td>23 (100)</td>
</tr>
<tr>
<td>Age (yr)</td>
<td>15 (9–22)</td>
<td>4 (2–5)</td>
<td>10 (8–12)</td>
<td>18 (16–22)</td>
<td>37 (34–42)</td>
<td>57 (56–62)</td>
</tr>
<tr>
<td>Female sex</td>
<td>187 (46)</td>
<td>21 (47)</td>
<td>59 (45)</td>
<td>77 (47)</td>
<td>18 (43)</td>
<td>12 (52)</td>
</tr>
<tr>
<td>Age at PCD diagnosis (yr)</td>
<td>9 (3–17)</td>
<td>1 (0–2)</td>
<td>6 (1–8)</td>
<td>13 (8–17)</td>
<td>34 (29–36)</td>
<td>51 (43–55)</td>
</tr>
</tbody>
</table>

### Cardiovascular malformation

<table>
<thead>
<tr>
<th>Variable</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Yes</td>
<td>35 (9)</td>
</tr>
<tr>
<td>No</td>
<td>303 (75)</td>
</tr>
<tr>
<td>Not reported</td>
<td>66 (16)</td>
</tr>
</tbody>
</table>

### Patient-/parent-reported symptom^a^b^c^d^e^

<table>
<thead>
<tr>
<th>Symptom</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Runny nose</td>
<td>248 (61)</td>
</tr>
<tr>
<td>Blocked nose</td>
<td>242 (60)</td>
</tr>
<tr>
<td>Headache while bending down</td>
<td>44 (11)</td>
</tr>
<tr>
<td>Ear pain</td>
<td>207 (51)</td>
</tr>
<tr>
<td>Ear discharge</td>
<td>109 (27)</td>
</tr>
<tr>
<td>Hearing problems (n=280)^f^</td>
<td>133 (48)</td>
</tr>
</tbody>
</table>

### Examination findings

<table>
<thead>
<tr>
<th>Symptom</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nasal discharge</td>
<td>300 (74)</td>
</tr>
<tr>
<td>Nasal polyps^c^</td>
<td>55 (14)</td>
</tr>
<tr>
<td>Hypertrophic turbinates^c^</td>
<td>222 (55)</td>
</tr>
<tr>
<td>Facial pain</td>
<td>53 (13)</td>
</tr>
<tr>
<td>Acute otitis media</td>
<td>6 (1)</td>
</tr>
<tr>
<td>Otitis media with effusion</td>
<td>122 (30)</td>
</tr>
<tr>
<td>Ear discharge</td>
<td>36 (9)</td>
</tr>
<tr>
<td>Hearing loss measured at audiometry (n=280)^g^</td>
<td>119 (43)</td>
</tr>
</tbody>
</table>

Values are presented as number (%) or median (interquartile range).

**EPIC-PCD, ENT Prospective International Cohort of Patients with Primary Ciliary Dyskinesia.**

^a^Ever reported at any frequency during the past 3 months. ^b^All % refer to 280 participants with available audiometry results. ^c^Bilateral or unilateral.

^d^Hearing loss measured at audiometry ranging from mild to profound based on the World Health Organization grade—could be bilateral or unilateral.

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others showed increased perception, noticing their impaired quality of life and reported symptoms in more detail. For these reasons, our findings necessitate regular ENT consultations for all people with PCD. This approach possesses possible therapeutic implications, especially for hearing impairment and nasal polyp diagnoses, both with highly underreported symptoms. Patient-reported measures complement objective measures since findings from clinical examinations vary with time. Symptom combinations or quality-of-life measures might be more closely associated with examination findings.

CONFLICT OF INTEREST

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**REFERENCES**


