Original Research

Association of Hoover’s sign with Maximal Expiratory-to-Inspiratory Pressure Ratio in Patients with COPD

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Abbreviations:
BMI – body mass index
COPD - chronic obstructive pulmonary disease
GOLD - Global Initiative for Chronic Obstructive Lung Disease
IC – inspiratory capacity
MEP - maximal expiratory pressure
MIP- maximal inspiratory pressure
PFT - pulmonary function test
RV – residual volume
TLC – total lung capacity
VA - alveolar volume
Abstract

Purpose

In chronic obstructive pulmonary disease (COPD) some patients develop paradoxical inspiratory rib motion, which is termed Hoover’s sign. Our objective was to determine whether Hoover’s sign is associated with a difference in the maximal expiratory pressure (MEP), the maximal inspiratory pressure (MIP), the MEP/MIP ratio, and other features on PFTs.

Methods

This observational prospective single-center cohort study enrolled patients with an established diagnosis of COPD with GOLD stage III (severe) and IV (very severe) based on PFTs. Respiratory pressure measurements were also collected. Patients were examined for the presence or absence of Hoover’s sign on physical examination by two internal medicine resident physicians trained in examining for Hoover’s sign by a pulmonologist.

Results

A total of 71 patients were examined for the presence of Hoover’s sign. Hoover’s sign was present in 49.3% of patients. Observer agreement (κ statistic) was 0.8 for Hoover’s sign. Median MEP/MIP was significantly greater in patients with Hoover’s sign than those without Hoover’s sign (1.88 vs 1.16, p<0.001). Patients with Hoover’s sign also had a significantly lower MIP (39.0 vs 58.0, p<0.001) and higher residual volume to total lung capacity (RV/TLC%) ratio indicating a higher degree of air trapping (65 vs 59.5, p<0.014).

Conclusion

The presence of Hoover’s sign in patients with COPD is associated with a higher MEP/MIP ratio. This suggests respiratory pressure measurements can predict diaphragm dysfunction in
patients with stage III and IV COPD. Patients with Hoover’s sign were also found to have a lower MIP and more air trapping.

Introduction

Patients with COPD may have abnormalities of chest wall motion. One of the oldest described abnormalities of chest wall motion is Hoover’s sign, first described by Charles Franklin Hoover\(^1\), which is classically described as lung hyperinflation leading to a flattened diaphragm which causes the lower rib cage to move paradoxically during inhalation, in an inward direction rather than outward\(^2\). The sign is reported to have a sensitivity of 58\% and specificity of 86\% for detecting obstructive airway disease\(^3\) which may make it a useful sign in the diagnosis of COPD. Previous studies have shown a frequency of Hoover’s sign of 36\%, 43\%, and 76\% in Global Initiative for Chronic Obstructive Lung Disease (GOLD) moderate, severe, and very severe stages of COPD, respectively\(^4\).

In describing a phenotype of patients with Hoover’s sign, previous studies found that the presence of Hoover’s sign is associated with older age, higher BMI, and more severe airflow obstruction. Studies have not shown that Hoover’s sign is associated with a higher degree of hyperinflation\(^5\,^6\). The presence of Hoover’s sign in COPD may have important clinical implications because it is associated with higher exacerbation frequency\(^7\), higher dyspnea symptoms with exercise\(^8\), and an increased frequency of hospitalizations and emergency room visits\(^7\).
There are various tests to screen for respiratory diaphragm dysfunction including maximal inspiratory pressures with or without phrenic nerve stimulation, positional change in vital capacity from seated to supine, transdiaphragmatic pressure, electromyography, dynamic evaluation of diaphragmatic movement using fluoroscopy for unilateral diaphragm dysfunction, chest radiograph, and ultrasound\textsuperscript{9,10}. Many of these tests are invasive or require specially trained technicians to complete. The maximal expiratory pressure to maximal inspiratory pressure (MEP/MIP) ratio has been used as a screening test for diaphragm paralysis\textsuperscript{11}. Ultrasound has been validated in detecting diaphragm dysfunction in COPD\textsuperscript{10}, however this is an additional test requiring a specially trained technician patients with COPD must undergo to assess diaphragm function. Given that patients with COPD in our institution routinely undergo static pressure measurements during pulmonary function testing (PFT), our study aims to see if Hoover’s sign is associated with a change in the MEP/MIP ratio in patients with COPD. Since diaphragm dysfunction in Hoover sign could be described as incomplete paralysis, we hypothesized that there would be an observed increase in the MEP/MIP ratio in patients with COPD that had Hoover’s sign.

Methods
This observational prospective single-center cohort study was performed in an outpatient pulmonary clinic from October 2021 to May 2022. This study was approved by the Freeman Health System Institutional Review Board (approval number 2022001). Internal medicine resident physicians performed Hoover’s sign examinations and had previously attended clinic and were trained by a pulmonologist in detecting Hoover’s sign. No patients were previously known by the examiners. Inclusion criteria were the following: age >18 years old, known
diagnosis of COPD, had PFTs and respiratory pressures performed during the study period, had a FEV1/FVC ratio < 70%, had an FEV1 of < 50%, and had stable COPD without signs of acute exacerbation. Patients were excluded if they chose not to undergo examination. PFTs and respiratory pressure measurements were performed by trained respiratory therapy technicians who were blinded to any other data. Maximal static pressures were obtained in the seated position as per American Thoracic Society Guidelines. Subjects who met inclusion criteria based on data recovered from the medical registry were invited to return to the pulmonary clinic for Hoover’s sign examinations, Examiners were blinded to PFT and respiratory pressure data. Examinations for Hoover’s sign were performed by two internal medicine resident physicians while the patient was in the seated position.

The observer agreement of the findings was calculated with κ statistic and were interpreted as follows: 0-0.2, slight; 0.2-0.4, fair agreement; 0.4-0.6, moderate agreement; 0.6-0.8, substantial agreement; and 0.8-1.0, almost perfect agreement. The two comparison groups were those with the presence of Hoover’s sign and those with the absence of Hoover’s sign. Continuous variables and PFT variables were not normally distributed, therefore we report the median (range) as a measure of central tendency. Categorical variables were reported as the percentage of persons in each category. The Mann-Whitney U Test, a non-parametric method for comparing medians, and the χ² tests were used to determine statistical significance of the continuous, categorical, PFT, and respiratory pressure variables. A p value threshold of 0.05 was used to determine statistical significance. We expressed MEP/MIP and MIP as an absolute value to aid in clinical utility.
Results

A total of 71 patients who met inclusion criteria agreed to undergo Hoover’s sign examinations. There were 41 males (57.7%) and 30 females (42.3%) with a median age of 67.0 years (61.0-73.0 interquartile range, range 44-91). Thirty-five (49.2%) of the patients examined exhibited Hoover’s sign. Observer agreement as demonstrated by the \( \kappa \) was 0.8 indicating substantial to almost perfect agreement.

Between the two comparison groups age, sex, and BMI were not statistically different. Selected PFT and static pressure measurements are presented in Table 1. In patients with and without Hoover’s sign, the median FEV, median ventilation heterogeneity as measured by the alveolar volume to total lung capacity (VA/TLC) ratio, median degree of hyperinflation as measured by the inspiratory capacity to TLC (IC/TLC) ratio, and median MEP were not statically significant between the two groups. For subjects with Hoover’s sign, the median MEP/MIP ratio was significantly higher than those without Hoover’s sign (1.88 vs 1.16, \( p < 0.001 \)), which was driven by a statistically significant lower difference in MIP (39.0 vs 58.0, \( p < 0.001 \)). The difference in the median MEP/MIP ratio is displayed in Figure 1. The median degree of air trapping, as measured by the residual volume to TLC (RV/TLC) ratio, was higher among subjects with Hoover’s sign (65.0 vs 59.5, \( p < 0.014 \)), albeit not as strongly significant as the difference between the MEP/MIP and MIP.

Discussion

Our study showed that patients with COPD in our study population who had Hoover’s sign had a higher MEP/MIP ratio than those without Hoover’s sign. The presence of Hoover’s sign was also
associated with a higher MIP and RV/TLC ratio. Because of the \( \kappa \) value in our study, we demonstrated that Hoover’s sign can be detected with precision in trained examiners.

The MEP/MIP ratio in our study was lower than the reported value for those with unilateral diaphragm paralysis which was reported to be 2.1\(^{11}\). In addition, those in our study group without Hoover’s sign had a lower median MEP/MIP ratio than the median MEP/MIP ratio of 1.5 in the normal diaphragm function group in the Koo et al. study\(^{11}\). It is unclear why there was a difference between their normal diaphragm function group and ours, but it could be confounded by our study population who had advanced COPD whereas their study population had unexplained dyspnea with our assumption that COPD was ruled out in their study subjects. In addition, Hoover’s sign pathology results from diaphragm flattening leading to an increased radius of curvature, which increases muscle tension and causes the force vector on the lower aspects of the ribs to move inward rather than cephalad. This culminates in the lower rib cage motion directed inward on inspiration instead of outward\(^{15}\). With this physiology, Hoover’s sign can be described as incomplete diaphragm dysfunction rather than paralysis, so the MEP/MIP ratios between Hoover sign subjects and those with diaphragm paralysis cannot be directly compared. Therefore, since all of our study subjects had advanced COPD, and since Hoover’s sign is not synonymous with diaphragmatic paralysis, comparing any of our data and subject groups with the data and subject groups the Koo et al. should be done with caution since there may be significant confounders. Regardless, we show that the MEP/MIP ratio can accurately predict the presence of diaphragm dysfunction in patients with COPD manifesting as Hoover’s sign.
Although subjects with Hoover’s sign had a significantly lower MIP than those without Hoover sign, the values of MIP in both groups were heterogenous with wide ranges, making its utility in diagnosing diaphragm dysfunction less reliable. Therefore, we propose that the MEP/MIP ratio be used in place of MIP to determine whether patients with COPD have diaphragm dysfunction manifesting as Hoover’s sign. It is important to keep in mind that the Hoover’s sign examinations were performed in an outpatient pulmonary clinic in stable COPD patients. While we believe this has near universal value in the adult outpatient setting, we acknowledge validation needs to be confirmed in the primary care setting, emergency departments, and tertiary care centers before it universally used in these settings. In the primary care setting, its role may have limitations due to the technical challenges in obtaining respiratory pressure measurements, such as good lip seal and holding cheeks to minimize oropharyngeal influence.

In this study, we demonstrated that Hoover’s sign can be detected with precision in trained examiners and that respiratory pressures can be used as an adjunct to diagnose Hoover’s sign in patients with COPD. The agreement between observers in our study was similar or slightly higher than the $\kappa$ values previously reported. The prior training of the examiners and the characteristics of the patients included can probably explain the high degree of agreement in the series.

Compared to prior studies, our study did not show differences in baseline characteristics between those with and without Hoover’s sign. Specifically, we detected no difference in age or BMI between the two groups whereas prior studies showed those with Hoover sign to have higher BMI and older age. It is unclear whether this is population specific or due to other unforeseen
factors not considered in our study. Congruent with another study⁵, we found that Hoover’s sign was not associated with hyperinflation. We observed a novel finding of higher degree of air trapping in patients with Hoover’s sign than those without Hoover’s sign. This finding has not been previously reported. It is unclear whether this is an association in the disease process, or whether air trapping plays a role in the development of diaphragm dysfunction. Further studies would need to determine the role of air trapping in diaphragm function in patients with COPD.

Later in our study period, a small number of subjects disclosed that they had participated in pulmonary rehabilitation, which was not a question assessed in our study. Interestingly, none of these subjects had Hoover’s sign on exam. It is unknown whether patients might have had diaphragm dysfunction prior to rehabilitation. Pulmonary rehabilitation has been shown to partially revert diaphragmatic impairments as assessed by ultrasound¹⁶. Whether pulmonary rehabilitation would lead to resolution of Hoover sign on examination or air pressure measurements could be assessed in future studies.

In conclusion, we found that an increased MEP/MIP ratio is correlated with the presence of Hoover’s sign in patients with COPD with stage III and IV GOLD criteria disease and provides a simple alternative to assess for diaphragm dysfunction in this population.
Acknowledgements

TGM and PCS takes full responsibility for the article, including for the accuracy and appropriateness of the reference list. TGM and PCS conceived the study. TGM, PCS, and ZSA were involved in protocol development, researching literature, and gaining ethical approval. TGM and ZSA were involved in patient recruitment. TGM, ZSA, ABV, and ALM performed patient examinations. TGM, ZSA, ABV, ALM, and PCS contributed substantially to the study design, data analysis and interpretation, and the writing of the manuscript.

Declaration of Interest

There is no financial arrangement or other relationship to disclose that could construed as a conflict of interest.
References

1. Hoover CF. The diagnostic significance of inspiratory movements of the costal margins. 


Table 1. Baseline characteristics, pulmonary function test data, and maximal static pressure measurements of patients with COPD examined for Hoover sign

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Total (n=71)</th>
<th>Hoover Sign Absent (n=36)</th>
<th>Hoover Sign Present (n=35)</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>67.0 (61.0-73.0)</td>
<td>66.0 (60.0-72.0)</td>
<td>68.0 (62.0-75.0)</td>
<td>0.190</td>
</tr>
<tr>
<td>Male</td>
<td>41 (57.7)</td>
<td>23 (63.9)</td>
<td>18 (51.4)</td>
<td>0.288</td>
</tr>
<tr>
<td>BMI (kg/m²)</td>
<td>26.3 (22.2-30.4)</td>
<td>25.5 (21.9-31.2)</td>
<td>27.8 (22.2-29.8)</td>
<td>0.928</td>
</tr>
<tr>
<td>FEV1%</td>
<td>34.0 (26.0-40.0)</td>
<td>36.0 (28.0-42.5)</td>
<td>32.0 (24.0-40.0)</td>
<td>0.226</td>
</tr>
<tr>
<td>RV/TLC%</td>
<td>64.0 (56.0-69.0)</td>
<td>59.5 (51.0-67.5)</td>
<td>65.0 (61.0-69.0)</td>
<td>0.014</td>
</tr>
<tr>
<td>VA/TLC %</td>
<td>62.0 (55.0-74.0)</td>
<td>66.0 (55.2-80.5)</td>
<td>60.0 (52.0-71.0)</td>
<td>0.168</td>
</tr>
<tr>
<td>IC/TLC%</td>
<td>24.3 (17.8-29.9)</td>
<td>27.1 (19.0-31.4)</td>
<td>20.6 (16.4-27.9)</td>
<td>0.072</td>
</tr>
<tr>
<td>MEP</td>
<td>72.0 (53.0-91.0)</td>
<td>64.5 (52.2-86.8)</td>
<td>84.0 (59.0-99.0)</td>
<td>0.289</td>
</tr>
<tr>
<td>MIP</td>
<td>49.0 (38.0-64.0)</td>
<td>58.0 (45.5-78.0)</td>
<td>39.0 (34.0-51.0)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>MEP/MIP</td>
<td>1.49 (1.16-1.88)</td>
<td>1.16 (0.99-1.39)</td>
<td>1.88 (1.67-2.06)</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

Table 1. Continuous variables are reported as median (interquartile range). Categorical variables are reported as counts and percentages. Statistical significance across groups is determined by Mann-Whitney U test for continuous variables and \( \chi^2 \) test for categorical variables. Negative values were expressed as absolute values. BMI = body mass index. FEV1 = Forced expiratory volume in the first second; RV = residual volume; TLC = total lung capacity; VA = alveolar volume; IC = inspiratory capacity; MEP = maximal expiratory pressure; MIP = maximal inspiratory pressure.
Figure 1