Hiatus hernia and interstitial lung abnormalities

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Hiatus hernia and interstitial lung abnormalities

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Summary

Hiatus hernia (HH) is not associated with ILA or its progression but is almost twice as prevalent in the UIP subtype. Moderate to large HH was associated with more deaths in those with UIP as well as increased mortality across the 4885 participants overall.
The prevalence of hiatus hernia (HH) in patients with idiopathic pulmonary fibrosis (IPF) is approximately 40%,\(^1\)-\(^3\) greater than the prevalence of HH in other chronic lung diseases. While the role of gastroesophageal reflux disease (GORD) and its treatment remain an area of controversy in IPF,\(^4\),\(^5\) HH is associated with reduced survival\(^2\),\(^3\) and more rapid lung function decline.\(^3\) The cause for the increased prevalence of HH in IPF remains unknown. It is possible that the increased rate of GORD associated with hiatus hernia leads to frequent chronic micro-aspiration events\(^1\), which could contribute to the development of pulmonary fibrosis. Alternatively, it is plausible that as IPF progresses, the biomechanics of the fibrotic lung result in progressively more negative intrathoracic pressure causing cranial migration of the oesophagogastric junction (GOJ) and stomach into the thorax. The association between hiatus hernia and early stages of pulmonary fibrosis has not been previously assessed.

Interstitial lung abnormalities (ILA) are patterns of density seen on thoracic CT scans identified incidentally in those without a pre-existing diagnosis of interstitial lung disease (ILD).\(^6\) These likely represent a broader range of disorders than IPF alone,\(^7\) and there is evidence that early developing stages of pulmonary fibrosis are present in some individuals identified with ILA.\(^8\)-\(^10\) To explore the role of HH in the early development of pulmonary fibrosis, we sought to evaluate the association with hiatus hernia and ILA. We additionally sought to determine the associations between HH and ILA progression and mortality.

Protocols for participant enrolment in the Age Gene/Environment Susceptibility (AGES)-Reykjavik study have been described previously.\(^11\) HH status was characterized in 4885 (92\%) of the 5320 participants recruited between 2002 and 2006, who had both chest CT and mortality data as of 2016. The methods for thoracic CT characterization of ILA and ILA progression in the AGES-Reykjavik cohort have been previously described.\(^10\),\(^12\),\(^13\) The presence of HH was evaluated on thoracic CT scans by a single reader. Two radiologists additionally graded all cases of HH on a previously described four point scale.\(^14\) Briefly, a grade 1 HH is a “sliding” hernia with the GOJ above the level of the diaphragm, a grade 2 HH is a “rolling” hernia with a portion of the gastric fundus above the diaphragm with a normal position of the GOJ, a grade 3 HH is a mix of the previous two with both an abnormal placement of the gastric fundus and the GOJ, and a grade 4 HH includes additional elements of the abdominal viscera in the hernia sac (Figure 1). Written informed consent was obtained from all participants and the Icelandic Bioethics Committee (VSN: 00-063) and the institutional review board of the Brigham and Women's Hospital approved this study.

Analyses evaluating the association between HH and ILA, ILA subtypes, and ILA progression were performed using logistic regression. Multivariable analyses were adjusted for age, sex, body-mass index (BMI), pack-years smoking, and current smoking status. Cox models were used to evaluate associations between HH and mortality. Reported p-values were two-sided with those less than 0.05 considered statistically significant.

The prevalence of HH in research participants with ILA (21\%) was similar to the prevalence of HH in the entire cohort (23\%). Regardless of size, the presence of a HH was not associated with ILA. Similarly, there was no association between HH and ILA (odds ratio (OR), 1.01; 95\% confidence interval (CI), 0.76 – 1.35; p=0.94) when adjusting for covariates. Moderate to large HH (grade II –IV) were similarly not associated with the presence of ILA (OR, 1.26; 95\% CI 0.73-2.19; p=0.41), after adjusting for covariates. The presence of HH, regardless of size was not associated with an increased
risk of ILA progression (OR 1.50, 95% CI 0.75-2.97, p=0.25). Furthermore, the presence of a HH was not associated with development of an ILA when serial imaging was analyzed (OR=1.05, 95% CI 0.81, 1.37, p=0.71)

The prevalence of hiatus hernia was 37% (7/19) in those with ILA limited to a usual interstitial pneumonia (UIP) pattern. Although there was a >2-fold increase in the odds of a HH in those with a UIP pattern compared to those without ILA, after adjusting for covariates, this finding was not statistically significant (OR, 2.34; 95% CI 0.89-6.17; p=0.09).

In the overall cohort, while the presence of HH was not associated with mortality (hazard ratio [HR] 0.92, 95% CI 0.77 - 1.10, p=0.35), after adjusting for covariates there was an increased risk of death in participants with a moderate to large (grade II – IV) HH (HR, 1.65; 95% CI 1.24 – 2.18, p=0.0005). The median follow-up time was 5.4 years. By the second year of follow up, 14/222 (6.3%) of those with a moderate to large HH (grade II – IV) had died compared with 80/4663 (1.7%) of those without a HH or with a small hiatus hernia (grade 0-I). By the fourth year 37/222 (17%) of those with a grade II – IV HH had died compared with 458/4663 (9.8%) of those with a grade 0 – I HH.

Amongst those with ILA, the presence of HH of any size and specifically a moderate to large HH was not associated with mortality (HR 1.36, 95% CI 0.85-2.16, p=0.20), and (HR 1.71, 95% CI 0.68-4.31, p=0.26) respectively. During the follow up period, 63% (12/19) with ILA and a UIP pattern had died; 58% (7/12) of those with UIP and no HH died, 71% (5/7) of those with UIP and a hiatus hernia died, and both participants with a moderate to severe HH (2/2) died.

There was a positive association between prescription of antacid therapy (both proton pump inhibitors (PPIs) and H2 blockers) and the presence of HH (OR 1.88, 95% CI 1.59-2.23, P<0.0001). There was no evidence for an association between antacid therapy and ILA (OR 1.25 95% CI 0.94-1.66, p=0.13) or risk of ILA progression (OR 1.48, 95% CI 0.73-2.99, p=0.27).

This is the first study to utilize thoracic CT scans to systematically evaluate the prevalence of HH in a general population sample and to explore the potential impact of HH on the development of early stages of ILD. We report that the prevalence of HH in ILA is similar to that of the general population and that the presence of HH is not associated with an increased risk of ILA or ILA progression. These data do not support the view that GORD is a major contributor to the early stages of ILD although it is conceivable that GORD and micro-aspiration become more relevant in susceptible individuals as disease progresses and the lung becomes primed for fibrogenesis.

This data is consistent with prior studies in IPF patients\(^1-3\) that demonstrate that the prevalence of HH is twice that of the general population at almost 40%. Furthermore, our data demonstrate that in those with UIP, the presence of a HH was associated with an increased risk of death, although this analysis is limited by a small sample size. The increased prevalence of HH in UIP and observed mortality signal could be the consequence of accelerated progression of fibrotic lung disease mediated by repeated micro-aspiration events among those with UIP and a HH. Alternatively, it is possible that a HH may serve as a marker of a group of patients with more advanced fibrotic lung disease whose progressive negative intrathoracic pressure results in a retraction of the stomach into the thoracic cavity. Definitively addressing this question will require longitudinal gastrointestinal physiology studies in patients with pulmonary fibrosis.
This analysis has a number of limitations. Lung function data was not available which limits our ability to determine if the extent of restrictive deficits could contribute to the prevalence of HH among those with ILA. The analysis of participants with UIP was limited by small numbers and so it is not possible to establish whether the presence of HH in those with UIP was associated with ILA progression or development of clinically relevant ILD. Thoracic CT is not the gold standard test for the diagnosis of HH and is likely to underestimate its prevalence. However, the positive association between hiatus hernia and prescription of antacid therapy in this study suggests that participants with a HH were sufficiently symptomatic of GORD to require pharmacological therapy and that thoracic CT is a pragmatic and effective tool for identification of clinically relevant HH.

In summary, our study does not demonstrate an association between hiatus hernia and ILA and in those with an ILA, the prevalence of hiatus hernia is similar to that of the general population suggesting that GORD is not a driver for the early stages of ILD. We report that those with a UIP pattern have a two-fold increase in the prevalence of hiatus hernia, a rate similar to the 40% reported in IPF cohorts. In participants with UIP and a moderate to large hiatus hernia there was a suggested increased risk of mortality and although this analysis was limited by small numbers, this group of individuals should undergo close surveillance and may be at higher risk of worse outcomes. The finding that moderate to large hiatus hernia is associated with an increased risk of death across the whole cohort is potentially important and requires further study.

Figure Legend:

Figure 1: Hiatus hernia and ILA classification

Graphical representation of normal thoracoabdominal anatomy (no hiatus hernia) (a), Grade I hiatus hernia (b) and Grades II – IV hiatus hernia (c). Mediastinal and lung windows from axial chest computed tomography scans demonstrate hiatus hernia anatomy and parenchymal involvement respectively for participants with and without interstitial lung abnormality (ILA) (A1 – F2). Participant A has no hiatus hernia and no ILA (A1 & A2). Participant B has no hiatus hernia and subpleural ILA with fibrosis (B1 & B2). Participant C has a Grade I hiatus hernia and no ILA (C1 & C2). Participant D has a Grade I hiatus hernia and subpleural ILA without fibrosis (D1 & D2). Participant E has a Grade II – IV hiatus hernia and no ILA (E1 & E2). Participant F has a grade II – IV hiatus hernia and subpleural ILA with fibrosis (F1 & F2).

References


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Notes: ![A1](image1) and ![A2](image2) represent images for No Interstitial Lung Abnormalities with Medial Windows and Lung Windows, respectively. Similarly, ![E1](image3) and ![E2](image4) represent images for Interstitial Lung Abnormalities with Medial Windows and Lung Windows, respectively.