CHEST

# Idiopathic Pulmonary Fibrosis and Hypothyroidism

## Cannot Forget Subclinical Disease and Difficult-to-Eliminate Corticosteroids

**To the Editor:**

We read with interest the original research entitled "Thyroid Disease is Prevalent and Predicts Survival in Patients With Idiopathic Pulmonary Fibrosis" in *CHEST* (September 2015).[1] In the study, the authors compared the prevalence of hypothyroidism among patients with idiopathic pulmonary fibrosis (IPF) and control subjects with COPD. They also compared survival among patients with IPF who did or did not have hypothyroidism. In the study, the authors recorded patients as having hypothyroid only when they reported the use of thyroid replacement therapy and did not report a history of thyroidectomy or radioactive iodine ablation. Hypothyroid status was not based on hormone levels. Consequently, some patients with subclinical hypothyroidism could have been missed. Subclinical hypothyroidism is much more prevalent than true hypothyroidism and the prevalence is still higher in the age group for IPF.[2] Although the condition is called subclinical hypothyroidism, frequently patients have nonspecific symptoms such as fatigue.[2] In case of coexisting IPF, such symptoms may be erroneously attributed to IPF and treatment may be denied.

In addition, the authors compared systemic steroids used by patients with IPF and those used by control subjects who had COPD to exclude the possibility of corticosteroids as a cause of hypothyroidism. However, the pattern of systemic steroid use in COPD and IPF is different. In COPD, systemic steroids are usually used for short durations in the setting of an acute exacerbation whereas in IPF, when steroids are used it is for a longer duration, resulting in a higher cumulative dose. Hypothyroidism associated with steroids has been seen to be dose dependent.[3] Thus, corticosteroid use may also be a contributing factor in the increased prevalence of hypothyroidism seen in the study.

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**FINANCIAL/NONFINANCIAL DISCLOSURES:** None declared.

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**DOI:** http://dx.doi.org/10.1016/j.chest.2015.10.076

## References

1. Oldham JM, Kumar D, Lee C, et al. Thyroid disease is prevalent and predicts survival in patients with idiopathic pulmonary fibrosis. *Chest*. 2015;148(3):692-700.
2. Cooper DS. Clinical practice: subclinical hypothyroidism. *N Engl J Med*. 2001. 26;345(4):260-265.
3. Brabant A, Brabant G, Schuermeyer T, et al. The role of glucocorticoids in the regulation of thyrotropin. *Acta Endocrinol (Copenh)*. 1989;121(1):95-100.

# Response

**To the Editor:**

Dr Dutt and colleagues aptly call attention to the high probability of undiagnosed subclinical hypothyroidism (HT) being present among patients included in our article recently published in *CHEST* (September 2015)[1] Because thyroid function tests (TFTs) were not performed for most patients with idiopathic pulmonary fibrosis (IPF), those who had subclinical HT, which is more prevalent than overt HT,[2] may have been missed. On review of patients with IPF without known HT, for whom TFTs were available (n = 65), elevated thyroid-stimulating hormone (TSH) was observed in six. Two were subsequently diagnosed with overt HT, one with non-thyroidal illness syndrome, and three with subclinical HT, which supports the observation of these authors.

Whether patients with undiagnosed subclinical HT were denied treatment with thyroid replacement therapy remains debatable, as TSH variability increases with age and treatment of a marginally elevated TSH level is of unproven benefit.[3] The prevalence and clinical consequences of subclinical HT in patients with IPF certainly deserve further investigation because of the

increased mortality risk associated with overt HT in this patient population. To facilitate such research and identify those with undiagnosed overt HT, we recommend systematic collection of TFTs in all patients with suspected IPF.

These authors also noted that treatment with systemic corticosteroids, which may lead to HT through TSH suppression,[4] is often of shorter duration and less cumulative dose in patients with COPD compared to those treated with historical IPF regimens. Whereas we agree with this statement in general, we adjusted only for chronic systemic corticosteroid use in our analysis. The high percentage of chronic systemic corticosteroid use among COPD control subjects in our study likely reflects a high severity of disease, as we are a major referral center for patients with advanced obstructive lung disease. Finally, if chronic systemic corticosteroid use were a major confounder in our analysis, we would expect to see more variability in the HT OR produced by our adjusted and unadjusted logistic regression models.

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**FINANCIAL/NONFINANCIAL DISCLOSURES:** The authors have reported to *CHEST* the following: M. E. S. has received institutional grants from the National Institutes of Health (NIH); Bristol-Myers Squibb; Gilead Sciences, Inc; Intermune; and MedImmune for the conduct of clinical trials in IPF. She has received honoraria for serving on a Data Monitoring Committee for Boehringer-Ingelheim GmbH and an advisory board for Intermune. I. N. has received honoraria for advisory boards with Boehringer-Ingelheim GmbH; Intermune; and Anthera Pharmaceuticals, Inc within the last 12 months related to IPF. He has also received speaking honoraria from GlaxoSmithKline and receives consulting fees from Immuneworks. He also has study contracts with the NIH, Stromedix, Sanofi SA, and Boehringer-Ingelheim GmbH for the conduct of clinical trials in IPF. None declared (J. M. O.).

**FUNDING/SUPPORT:** This investigation was supported by a National Institutes of Health T32 training grant [T32-HL007605].

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**DOI:** http://dx.doi.org/10.1016/j.chest.2015.11.014

## References

1. Oldham JM, Kumar D, Lee C, et al. Thyroid disease is prevalent and predicts survival in patients with idiopathic pulmonary fibrosis. *Chest*. 2015;148(3):692-700.
2. Canaris GJ, Manowitz NR, Mayor G, Ridgway EC. The Colorado thyroid disease prevalence study. *Arch Intern Med*. 2000;160(4):526-534.
3. Garber JR, Cobin RH, Gharib H, et al. Clinical practice guidelines for hypothyroidism in adults: cosponsored by the American Association of Clinical Endocrinologists and the American Thyroid Association. *Thyroid*. 2012;22(12):1200-1235.
4. Brabant A, Brabant G, Schuermeyer T, et al. The role of glucocorticoids in the regulation of thyrotropin. *Acta Endocrinol*. 1989;121(1):95-100.

# Noninvasive Ventilation and Risk of Leakage of Esophageal Anastomosis

## A Matter of "Transesophageal Pressure"?

**To the Editor:**

We read with interest the physiologic article by Raman and colleagues[1] in *CHEST* (February 2015). In the second in vivo experiment described in the article, five pigs were ventilated through a laryngeal mask airway and the pressure transmitted to the proximal esophagus was measured at increasing ventilatory pressures. The resulting pressure was negligible compared with that required to induce leakage at the anastomosis. The authors thus conclude that noninvasive ventilation (NIV) is a safe alternative to endotracheal intubation to treat respiratory distress after esophagectomy. However, this study has a relevant limitation.

The increase in esophageal pressure measured during mechanical ventilation does not reflect the stretch of the anastomosis. The distending force that stresses the wall of an organ depends on the differential pressure between inside and outside the organ. If the pressure is applied from outside, the organ will tend to collapse and no parietal strain develops. For example, as demonstrated by many articles on respiration, airway pressure far greater than pleural pressure (ie, high transpulmonary pressure) is required to induce lung injury.[2] On the contrary, when very high airway pressure is applied, pressure measured inside the esophagus reflects only a transmitted pressure and the esophagus is not dilated but is instead compressed from outside. For this reason, high intrathoracic pressures are not likely to stress the anastomosis. As Carron[3] highlighted in his letter to the Journal, swallowing air and the resulting gastric insufflation probably represent the main threat for anastomosis during NIV, as a positive transesophageal pressure may develop. The device used to provide ventilation in the current article was a laryngeal mask, which is less likely to induce gastric insufflation compared with face mask, the standard device for NIV.[4]