Editorial

# Idiopathic tracheal stenosis and hormone receptors

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We read with intrigue "The Role of Local Expression of Hormone Receptors in the Genesis of Idiopathic Tracheal Stenosis" by Schweipert *et al.* (1). There are many etiologies of tracheal stenosis; these include malignancy, inflammatory, post-traumatic and idiopathic. While neither malignancy nor post-traumatic tracheal stenosis (PTTS) have shown preference for female *vs.* male sex; historically idiopathic tracheal stenosis (ITS) has been shown to occur in females. ITS has also been shown to be mainly subglottic and to occur in the proximal trachea (2). This manuscript sought to examine the hormone receptor status of progesterone and estrogen receptors in tissue samples from those who developed tracheal stenosis warranting resection.

The authors performed a retrospective single center analysis which analyzed the immunohistochemical staining of all tracheal specimens from 27 patients greater than 16 years of age who received tracheal resection between 2008–2019. Tracheal resection was performed for either idiopathic or PTTS. The PTTS subgroup was the control group. Progesterone and estrogen receptor staining of specimens were performed; due to retrospective nature of study blood or local hormone receptor expression in initial biopsies were not examined.

There were 11 patients in the ITS group and 16 in the PTTS group. There was a significant difference in both gender and age distribution between each subgroup with patients who developed ITS all being female with a median age approximately 10 years younger than those with PTTS. Although stenosis in the ITS group was found to more often occur closer to the vocal cords with shorter segment; there was no statistical significant difference in location of stenosis between groups. However, resection procedures differed between groups with those with ITS receiving cricotracheal resection with laryngotracheal end-to-end anastomoses more often than that of the PTTS group. On histopathology the ITS specimens were found to have expression of both estrogen and progesterone receptors. One hundred percent of the specimens in the ITS group showed strong expression of estrogen receptors in the fibroblasts with 72.7% showing progesterone receptors. In the PTTS group 37.5% showed slight staining for estrogen and 18.8% for progesterone. Although analysis of oral contraceptive use or hormone substitution between ITS and PTTS was performed, there was no further data analysis (40.7% of patients used these compounds, 63.6% in the ITS group and 25% in the PTTS group).

Past studies (3,4) analyzing patients who developed ITS showed that most patients who developed ITS were female. It is hypothesized that the pathophysiology contributing to the development of ITS is most likely due to fibrosis from hyperactive fibroblasts. It has been noted that there is increased expression of female hormone receptors in fibroblasts in patients with ITS. This study reaffirms this belief by also noting that there is significantly greater expression of female hormone receptors in comparison to those with PTTS.

While the study reaffirms that there are excessive fibroblasts with strong hormone expression in the areas of

scar tissue it has a few limitations. The retrospective nature of the study does not allow for concomitant blood levels of hormones to be analyzed. Additionally, the role of prior or ongoing oral contraceptive use or hormone substitution is unclear as the use in the 2 groups is mixed and no conclusions can be drawn from them. While the study sheds some light onto the etiology of ITS, it does not explain the pathogenesis of this disease. Additionally, one cannot make any therapeutic decisions based on the knowledge from this study. Since patients have already developed ITS, it's too late to perform any local or systemic manipulation to decrease its incidence. There also does not seem to be any role for post-operative hormonal manipulation as the post-operative course and results are exceptional. As highlighted in the discussion of this manuscript there may be additional factors (molecular, immunological, environmental) that may additionally play a role in the pathogenesis of this rare disease (5,6).

We commend the authors on their dedication to investigating the pathophysiology of ITS. Further studies to elucidate the molecular mechanisms of disease development are required. This would help identify the cohort of your female patients predisposed to this disease and could help prevent requiring surgical resections by allowing earlier hormonal manipulation.

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*Ethical Statement:* The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.



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