Association of Idiopathic Subglottic Stenosis and Body Mass Index

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Abstract

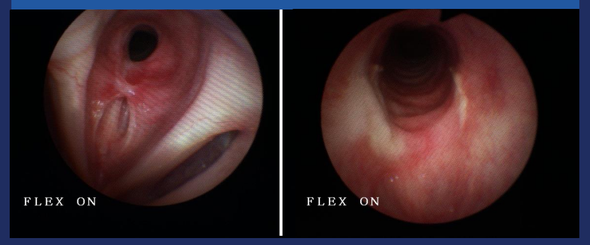
Outcome Objectives: (1) Describe factors associated with development, disease control, and rate of recurrence in patients with Idiopathic Subglottic Stenosis (ISS) and (2) evaluate the relationship between Body Mass Index (BMI) and ISS.

Methods: A retrospective chart review was performed for patients treated at the Mayo Clinic Rochester between 1996 and December 2012. All patients 16 years and older with a clinical diagnosis and/or treatment of ISS were reviewed. Patients with an identifiable etiology for stenosis including trauma, prior neck surgery, previous tracheostomy, multiple intubations (>6 lifetime intubations), prolonged intubation (>1 week), Wegener's Granulomatosis, or with antecedent explanation for their stenosis were excluded. Outcome measurements included symptom free interval, recurrence, and number of procedures performed.

Results: Features were collected on 182 female and 4 male patients. At diagnosis, 121 (65%) patients were overweight and 76 (41%) patients were obese. The mean BMI at first surgery was 28.7 kg/m^2. Ninety-one patients experienced at least one recurrence at a mean of 2.3 years following treatment. Mean number of recurrences, relative to follow-up interval, for BMI >30.0 kg/m^2 was 1.6 recurrences/year compared with 1.0 recurrences/year for BMI < 30 kg/m^2 (p=0.050). Increasing incidence of the following comorbidities was significantly associated with increases in BMI: heartburn (p=0.012), gastroesophageal reflux disease (p=0.011) hypertension (p=<0.001), cardiac history (p=0.045), hyperlipidemia/dyslipidemia (p=<0.001), and diabetes mellitus (p=0.004).

Conclusion: ISS patients with elevated BMI appear to have an increased risk of recurrent disease. Encouraging lifestyle change and weight reduction may assist in disease control.

Figure 1



Background

Subglottic stenosis is a fibrotic narrowing of the airway at the level of the cricoid cartilage, which results in dyspnea, stridor, and airway obstruction. Proposed etiologies include intubation trauma, autoimmune/inflammatory disorders, infectious processes, and congenital narrowing.[1] Roughly 5% of cases are considered idiopathic.[2] Idiopathic subglottic stenosis (ISS) develops almost exclusively in females in their third to sixth decades.[3] Several authors have suggested a possible hormonal cause due to the preponderance of female patients noted in their respective series.[3,4] A combination of both medical and surgical management is employed at Mayo to maintain airway patency.

Extraesophageal reflux has been implicated as a contributing factor in ISS. A landmark study by Koufman *et al.* identified a relationship between laryngotracheal stenosis (LTS) and laryngopharyngeal reflux (LPR).[5]

Obesity is known to be associated with an increased incidence of estrogen related tumors.[6] Obesity increases total body estrogen by the process termed 'peripheral aromatization'. Clinically, patients with obesity appear to present more frequently with ISS then non-obese patients. The relationship between BMI and ISS has not been previously addressed in the current literature.

Methods

Institutional Review Board approval at a tertiary medical center was obtained. We searched the Mayo Clinic Rochester medical record database for all patients having a diagnosis of subglottic stenosis from 1996 through 2012. Patients were excluded if they had prior neck trauma, prior neck surgery, previous tracheostomy, multiple intubations (>6 lifetime intubations), prolonged intubation (>1 week), or Wegener's Granulomatosis.

Associations of features with the indicators for overweight and obese were evaluated using Wilcoxon rank sum, chi-square, and Fisher exact tests. The duration of follow-up for recurrence-free survival was calculated from the date of tracheoscopy to the date of the first recurrence or last follow-up. Recurrence-free survival was compared among BMI categories using log-rank tests. Statistical analyses were performed using the SAS software package (SAS Institute; Cary, NC). All tests were two-sided and p-values <0.05 were considered statistically significant.

Recurrence Rate versus Body Mass Index

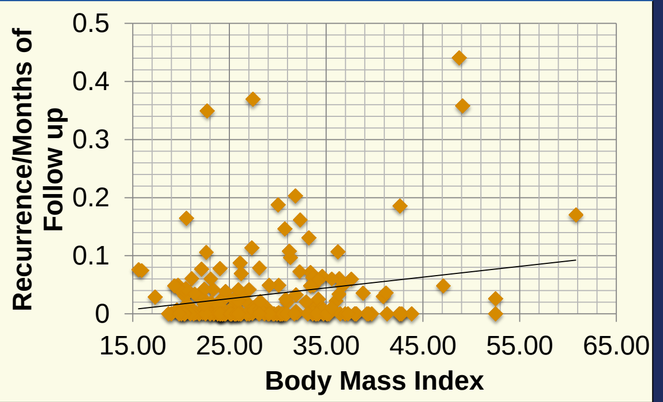


Table 1: Clinical Characteristics of 186 ISS Patients

Feature	Mean ± SD (Median; Range)
Age at onset of symptoms (N=151)	47.3 ± 13.5 (46; 15 – 84)
Age at diagnosis (N=185)	48.8 ± 13.0 (49; 19 – 84)
BMI at diagnosis	29.0 ± 7.5 (27.4; 15.6 – 60.8)
Number of treatments before Mayo (N=178)	1.0 ± 2.3 (0; 0 – 15)
Months of symptoms until diagnosis (N=150)	26.3 ± 25.6 (18; 0 – 168)
Number of endotracheal intubations (N=129)	1.3 ± 1.1 (1; 0 – 5)
MVV at diagnosis (N=126)	49.6 ± 19.9 (48; 12 – 103)
FEV_1 at diagnosis (N=145)	2.4 ± 0.6 (2.4; 0.8 – 3.8)
Number of surgeries following diagnosis at Mayo	2.4 ± 1.9 (1; 0 – 6)
Number of recurrences following diagnosis at Mayo	1.6 ± 2.1 (0; 0 – 6)
Total number of surgeries / follow-up (N=181)	1.3 ± 1.9 (0.6; 0 – 12.2)
Longest symptom-free interval in years (N=170)	3.5 ± 3.4 (2.7; 0 – 15)

Table 1: ISS Patient Clinical Outcomes Stratified By BMI

Feature	Under or Normal N=65	Over N=45	Class I Obesity N=41	Class II Obesity N=21	Class III Obesity N=14	*P*[1]	*P*[2]	*P*[3]
	Mean (Median)							
Total number of surgeries / follow-up (N=181)	0.9 (0.5)	1.1 (0.5)	1.2 (0.9)	1.7 (0.7)	2.8 (1.1)	0.20	0.13	0.050
Number of endotracheal intubations (N=129)	1.1 (1)	1.5 (1)	1.4 (1)	1.4 (1)	1.2 (1)	0.43	0.058	0.38
FEV_1 at diagnosis (N=145)	2.4 (2.3)	2.4 (2.5)	2.4 (2.5)	2.4 (2.5)	1.9 (2.1)	0.12	0.83	0.64
MVV at diagnosis (N=126)	42.3 (40)	55.1 (55)	54.3 (53)	53.3 (50)	42.1 (39)	0.019	0.003	0.21

P[1]: Comparison with the ordinal assessment of BMI | P[2]: Comparison with the indicator for overweight and obese | P[3]: Comparison with the indicator for obese

Results

- Increasing BMI correlated with a greater number of recurrences per years of follow up
- Incidence of medical comorbidities was significantly associated with increasing BMI including heartburn/GERD, hypertension, cardiac history, hyperlipidemia/dyslipidemia, and diabetes mellitus
- Declines in Maximum Voluntary Ventilation (MVV) correlated with elevations in BMI; No association was seen with Forced Expiratory Volume at 1 second (FEV_1)and BMI

Conclusions

- Elevations in BMI (>30 kg/m^2) are associated with increased rate of recurrence of ISS (p = 0.05)
- Encouraging lifestyle change and weight reduction may assist in disease control
- Hormonal alterations seen with obesity may play a role in the etiology of ISS
- Limitations
  - Retrospective nature of this study allows only for the identification of correlation between disease and exposure
  - Sampling bias is possible with any case-series study design

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