Thunderstorm Asthma in Seasonal Allergic Rhinitis: The TAISAR Study

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An Introduction to Thunderstorm Asthma

- Notable event in Melbourne, Australia on November 21, 2016
  - 3,400 ED visits and 10 fatalities
- Vast majority of patients experienced seasonal allergic rhinitis (SAR)
  - Wagga Wagga event in Oct. 1997
  - SAR, Ryegrass Pollen (RGP) Sensitization
- Development of Thunderstorm Asthma (TA)
  - Air particles are swept up into clouds and broken down to smaller sizes
  - Wind gusts concentrate these smaller particles, which can then be inhaled
- Current guidelines for preventing TA and identifying high-risk patients is unclear
- TAISAR study aims to identifying risk factors for TA and hospital presentation

Methods: Study Population and Procedures

- TAISAR was a multicenter cohort study that included adults (age >/= 18 y/o) living in Melbourne with self-reported SAR and/or past diagnosis of TA
  - Eligibility Criteria:
    i. Written Consent
    ii. Self-Reported History of SAR
- Recruited patients seen for a single-visit between Oct. 21-Dec. 18, 2018
  - Completed interviewer-administered questionnaire
  - Spirometry, skin-prick testing, FeNO levels
  - Blood Tests
  - 5-Item Asthma Control Questionnaire (ACQ)
  - SNOT-22

Methods: Statistical Analyses

- Participants classified into 1 of 3 groups:
  1. Isolated SAR (I-SAR)
  2. Outpatient TA (O-TA)
  3. Hospitalized TA (H-TA)
- Multinomial Logistic Regression with I-SAR as the reference group
- 3 Binary Variables then created to model…
  a. Factors associated with TA in the whole group
  b. Factors associated with hospitalization in the whole group
  c. Factors associated with hospitalization among those with TA
- Binary variables used to conduct separate logistic regression analyses with results reported as crude and adjusted multinomial ORs
- Receiver operating characteristic (ROC) curves also plotted

Results: Demographics and Questionnaires

TABLE I. Demographic characteristics among the TAISAR cohort (N = 228) with I-SAR, O-TA, and H-TA

Characteristic	Total responses (n)	I-SAR (n = 80)	O-TA (n = 84)	H-TA (n = 64)	*P* value
Female sex	228	66% (53 of 80)	67% (56 of 84)	55% (35 of 64)	.253
Age (y), mean (SD)	228	49.6 (16.4)	42.8 (13.8)	42.8 (13.5)	**.004**
Reported White ethnicity	223 of 228	81% (64 of 79)	56% (45 of 81)	40% (25 of 63)	**<.001**
Country of birth: Australia	227 of 228	68% (54 of 79)	48% (40 of 84)	42% (27 of 64)	**.003**
Parents' country of birth: Australia	228	55% (44 of 80)	39% (33 of 84)	27% (17 of 64)	**.002**
Smoking status					
Current	228	6% (5 of 80)	12% (10 of 84)	3% (2 of 64)	
Ex-smoker	228	33% (26 of 80)	12% (10 of 84)	16% (10 of 64)	
Nonsmoker	228	61% (49 of 80)	76% (64 of 84)	81% (52 of 64)	**.033**
Other conditions					
Aspirin/NSAID sensitivity	224 of 228	6% (5 of 79)	5% (4 of 83)	11% (7 of 62)	.353
Eczema	224 of 228	25% (20 of 79)	25% (21 of 83)	29% (18 of 62)	.875
Allergic rhinitis	224 of 228	99% (78 of 79)	100% (83 of 83)	97% (60 of 62)	.194
Nasal polyps	224 of 228	4% (3 of 79)	4% (3 of 83)	8% (5)	.466
Food allergies	224 of 228	27% (21 of 79)	28% (23 of 83)	27% (17)	1.00
Any comorbidities*	227 of 228	73% (58 of 79)	75% (63 of 84)	73% (47 of 64)	.928
ACQ score, median (IQR)	226 of 228	0 (0.0-0.8)	0.8 (0.0-1.4)	1.6 (0.6-2.4)	**<.001**
>1.5		14% (11 of 80)	23% (19 of 84)	50% (32 of 62)	**<.001**
SNOT-22 score, median (IQR)	228	37.0 (19.0-54.0)	37.5 (23.5-51.0)	35.0 (25.0-51.0)	.984
BMI, kg/m^2, median (IQR)	225 of 228	26.8 (23.4-29.7)	26.9 (24.0-31.7)	28.8 (24.5-34.0)	**.031**
Asthma history					
Previous asthma diagnosis, % (no.)	228	41% (33 of 80)	51% (43 of 84)	100% (64 of 64)	**<.001**
Current asthma symptoms (in the last 12 mo)	140	73% (24 of 33)	79% (34 of 43)	84% (54 of 64)	.391
Previous asthma hospitalization	138 of 140	41% (13 of 32)	35% (15 of 43)	71% (45 of 63)	**<.001**
Previous asthma intubation	139 of 140	9% (3 of 32)	9% (4 of 43)	6% (4 of 64)	.777

Results: Demographics and Questionnaires

- 228 total participants
  - 35% I-SAR (n = 80), 37% O-TA (n = 84), 28% H-TA (n = 64)
  - 63% were females (n = 144) and 59% were of White ethnicity (n = 134)
    - Relation of White ethnicity to O-TA and H-TA?
  - Average Ages: 49.6 years for I-SAR and 42.8 years for both O-TA and H-TA
- All patients in the H-TA group reported previous asthma diagnosis
  - 51% for O-TA group and 41% for I-SAR group ($P < .001$)
- Poorly controlled asthma seen with H-TA group → median ACQ Score of 1.6
  - ACQ Score 0.8 for O-TA group and 0.0 for I-SAR group
- SNOT-22, Asthma and Rhinitis treatments

Results: Laboratory and Clinical Tests

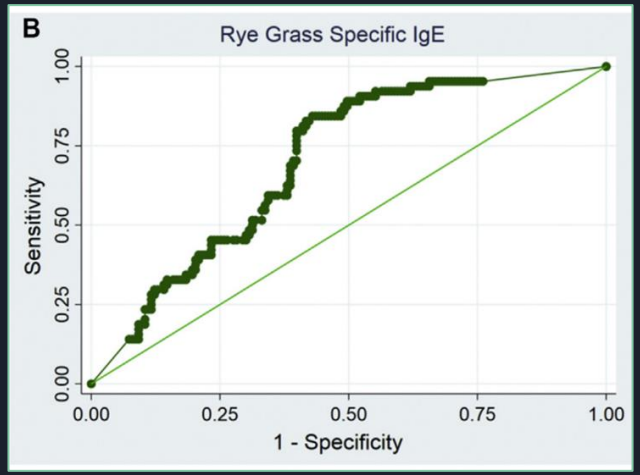
- RGP-specific IgE concentrations
  - 1.8 kU/L in I-SAR group (IQR 0.0-8.4 kU/L)
  - 26.2 kU/L in O-TA group (IQE 2.3-57.8)
  - 27.4 kU/L in H-TA group (IQR 13.9-79.1 kU/L)
- Testing for RGP-spIgE was negative in 36% (29 of 80) of the I-SAR group
  - Also negative for 23% (19 of 84) of O-TA group
  - Only 5% (3 of 64) of the H-TA group ($P < .001$)
- Serum eosinophil counts
  - Median count of 0.3 for O-TA and H-TA groups (IQR 0.1-0.4 for O-TA and 0.2-0.5 for H-TA)
  - Median count 0.2 for I-SAR group (IQR 0.1-0.2)
- Spirometry and FeNo
  - Lung function substantially lower within H-TA group
  - FeNO level was elevated (>/= 50 ppb) in both the O-TA and H-TA groups

Results: Multinomial Logistic Regression Analyses

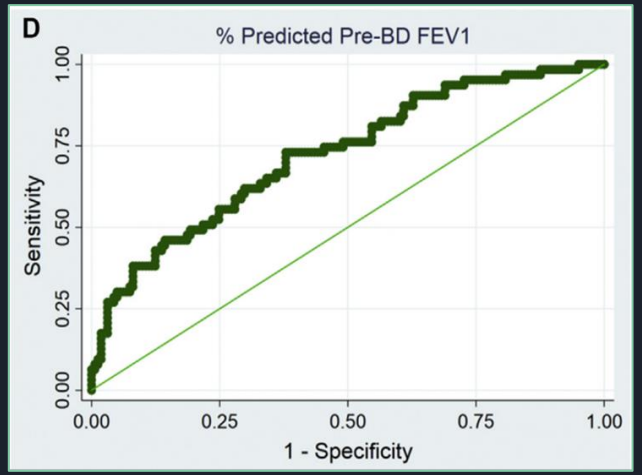
- Eosinophil count > 0.3 associated with OR of 3.7 for patients in the O-TA group (95% CI = 1.99-6.84 [P <.001]) and remained significant after adjustment
- Moderate-higher level of RGP-spIgE was associated with increased risk of previous TA
- Prebronchodilator FEV1 below the LLN was associated with an increase risk of H-TA (95% CI = 3.09-18.00)
- Elevated FeNO associated with increased risk of O-TA and H-TA in crude analysis
- Poorly controlled asthma (ACQ > 1.5) was associated with an increase risk of H-TA (95% CI = 2.98-15.01)

	Crude mOR* (95% CI), *P* value			Adjusted mOR* (95% CI), *P* value		
Variable	**No.**	**O-TA**	**H-TA**	**No.**	**O-TA**	**H-TA**
Eosinophil count	225			198		
>0.3 × 10^9 cells/L		3.70 (1.88-7.30) <.001	3.67 (1.78-7.57) <.001		2.59 (1.10-6.08)† .029	1.98 (0.80-4.90)† .141
RGP-spIgE‡	227			200		
Low (0.35-3.49 kU/L)		1.92 (0.96-3.80) .063	11.56 (3.33-40.17) <.001		1.53 (0.65-3.61)† .334	15.69 (3.24-76.00)† .001
Moderate (3.5-17.49 kU/L)		4.84 (2.49-9.42) <.001	17.95 (6.89-46.79) <.001		5.18 (2.33-11.51)† <.001	25.11 (8.06-78.23)† <.001
High (17.5-51 kU/L)		6.47 (3.14-13.32) <.001	7.35 (3.42-15.80) <.001		6.91 (2.93-16.30)† <.001	8.75 (3.49-21.93)† <.001
Very High (>51 kU/L)		8.67 (2.86-26.23) <.001	9.28 (2.99-28.80) <.001		8.62 (2.58-28.78)† <.001	8.57 (2.50-29.43)† .001
Pre-BD spirometry	204			202		
FEV_1 % predicted		1.00 (0.98-1.01) .606	0.95 (0.93-0.97) <.001		1.00 (0.97-1.02)§ .689	0.94 (0.92-0.97)§ <.001
FVC % predicted		0.99 (0.97-1.01) .573	0.96 (0.94-0.98) .001		0.99 (0.96-1.02)§ .479	0.96 (0.94-0.99)§ .019
FEV_1/FVC % predicted		1.00 (0.97-1.03) .966	0.93 (0.90-0.96) <.001		1.00 (0.96-1.04)§ .919	0.93 (0.90-0.97)§ .001
FEV_1 < LLN	228	2.45 (1.00-6.02) .050	7.46 (3.09-18.00) <.001	207	2.33 (0.88-6.19) .09	8.00 (2.96-21.65) <.001
Post-BD spirometry	224			202		
FEV_1 % predicted		1.00 (0.98-1.02) .850	0.96 (0.93-0.98) <.001		1.00 (0.97-1.02)§ .915	0.95 (0.93-0.98)§ .001
FVC % predicted		1.00 (0.97-1.02) .802	0.98 (0.95-1.00) .082		1.00 (0.97-1.02)§ .731	0.98 (0.95-1.01)§ .146
FEV_1/FVC % predicted		1.00 (0.97-1.03) .949	0.93 (0.90-0.97) <.001		1.00 (0.96-1.04)§ .903	0.93 (0.89-0.97)§ .001
FENO level	204			178		
>50 ppb		2.92 (1.19-7.15) .019	3.46 (1.38-8.68) .008		1.87 (0.62-5.71)† .269	1.48 (0.45-4.83)† .517
ACQ score	226			198		
>1.5		1.83 (0.81-4.15) .145	6.69 (2.98-15.01) <.001		1.61 (0.59-4.45)† .352	5.00 (1.70-14.50)† .003

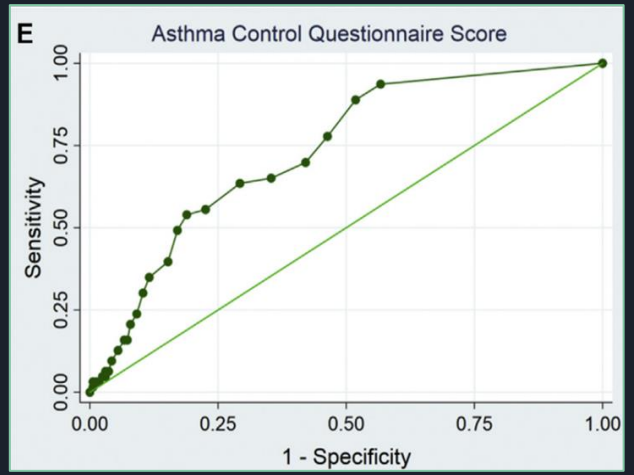
Results: ROC Curves



RGP-spIgE
concentration



FEV1 %
Predicted Value



ACQ
Score

Summary of Findings

- Raised eosinophil levels, elevated RGP-spIgE concentration, lower lung function, and poorly controlled asthma in people with SAR during high pollen season were associated with a history of TA
- Among individuals with a history of TA, poorly controlled asthma, elevated RGP-spIgE concentration, and evidence of obstruction on pre-bronchodilator spirometry were associated with higher risk of hospital presentation
- Increased risk of hospitalization for TA:
    1. RGP-spIgE concentration > 10.1kU/L
    2. Pre-bronchodilator FEV1 percent predicted value < 90%
    3. ACQ Score > 0.2

Discussion and Future Directions

- Looking back at the event from Melbourne on November 21, 2016…
  - All 10 patients who passed away had RGP-spIgE concentration > 10.1kU/L
  - No spirometry data available but all patients who passed known to have asthma
- Current Australian guidelines for prevention of TA?
  - Further studies to compare treatment modalities
  - Utility of biomarkers and baseline asthma control
- Limitations
  - Variations in serum IgE concentrations
  - Most cases in relation to a single TA event
  - Self-reported histories of SAR
  - No pediatric data
- Effects of climate change and air pollution?