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Pathophysiology of Esophageal and gastric Symptoms

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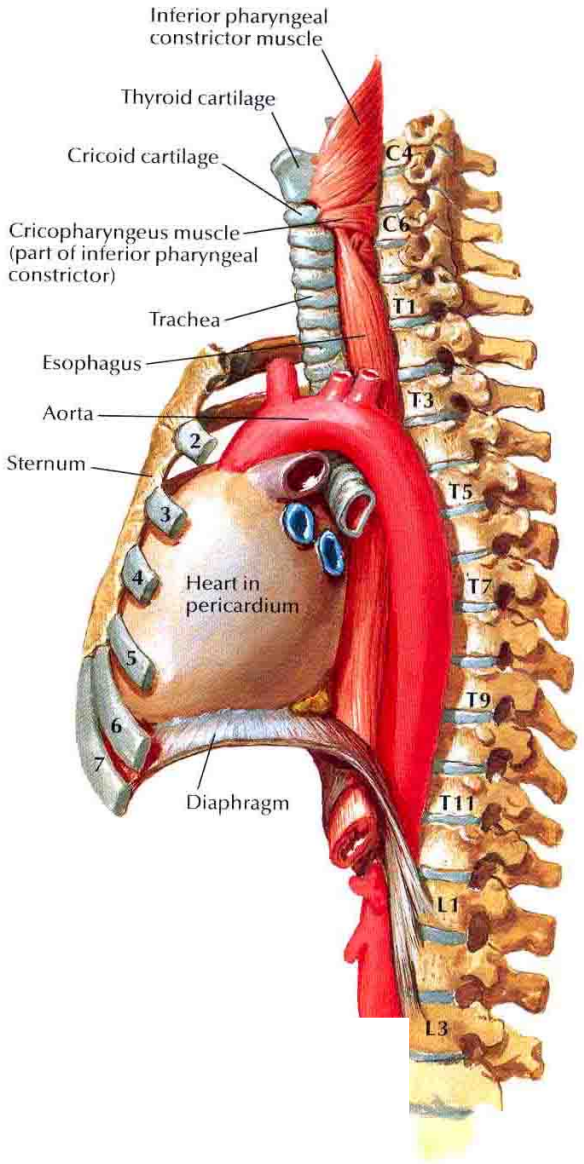
Esophageal Symptoms: Psycho-Physiologic Model

- Difficult to discuss this topic in 15 minutes and what I will try to do is to introduce why the gut-brain interaction is just as important as the anatomy and physiology.
  - *Severe abnormalities of bolus transit are obviously important and if you resolve bolus retention and relieve obstruction- people will improve.*
  - *However, the correlation between symptoms and non-obstructive motility patterns, incomplete bolus transit and other markers of abnormal mechanics is poor.*
    - *Are we missing subtle abnormalities due to poor technology*
    - *Is this all related to visceral hypersensitivity*
    - *Or is there something else driving symptom severity*

Esophageal Symptoms

- Transit related-
  - Dysphagia
  - Food impaction
  - Regurgitation
  - Aspiration
- Perception related
  - Discomfort
    - Chest pain / pressure
    - Heartburn
    - Thermal
- Fear/ Hypervigilance
  - Embarrassment
  - Choking/Death

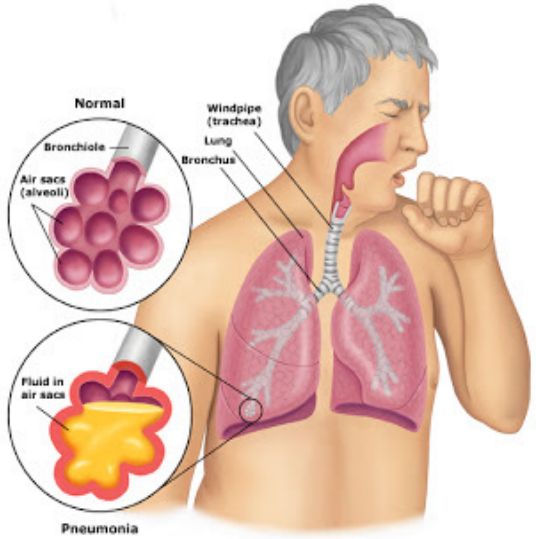


Significance: Impact

- Swallowing is something most take for granted- happens more than 1000 times a day and you don’t even notice until it stops working.
  - Approximately 1 million outpatient visits per year for this complaint.
  - 10-20% of people over the age of 50 will have dysphagia in their lifetime and the aging esophagus will likely have altered distensibility.

Significance: Impact

- Esophageal diseases, such as gastroesophageal reflux disease (GERD), achalasia, eosinophilic esophagitis (EoE) and scleroderma esophagus, are associated with major morbidity and mortality.
  - *Symptoms*
  - *Poor quality of life*
  - *Malnutrition*
  - *Aspiration*
  - *Cancer/Death*



Esophageal Symptoms
Diagnostic Approach

- Heartburn, regurgitation, dysphagia, chest pain and food impaction.
- Differential Diagnosis:
  - *GERD, EoE, Obstruction, Motor Disorder, Functional Esophageal Disorder*

- **All roads lead to endoscopy**
  - r/o mechanical obstruction, reflux injury, EoE
  - Negative- NERD, motility disorder, functional

Approach to patient with esophageal complaints:

-Dysphagia, Regurgitation, Chest pain, Food impactions

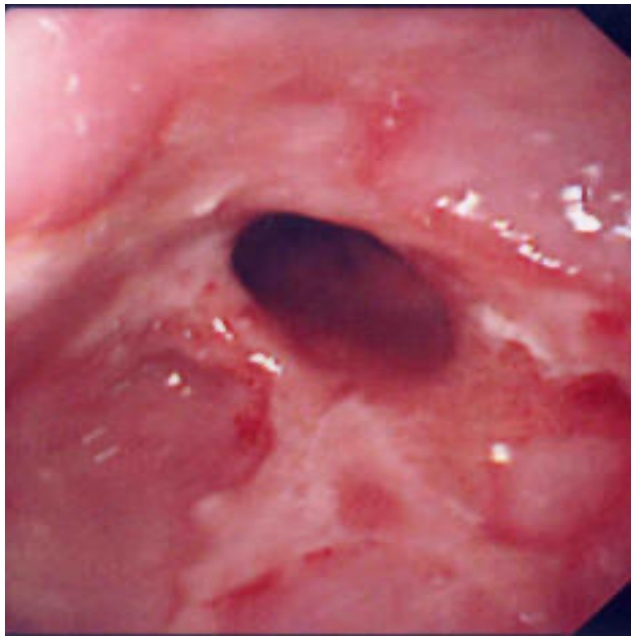
Visit 1: potentially prescribe a 4-8 week course of PPI and schedule endoscopy

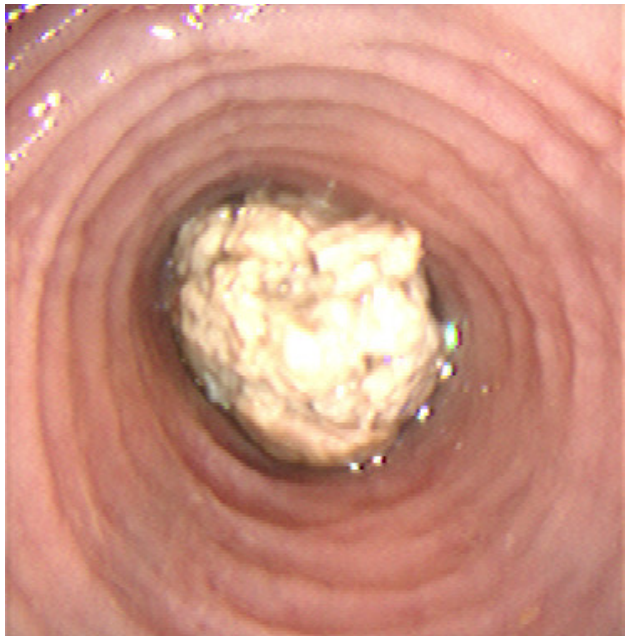
Visit 2:EGD

↓

Esophagitis- Stricture-EoE

↓





Approach to patient with esophageal complaints:

-Dysphagia, Regurgitation, Chest pain, Food impactions

Visit 1: potentially prescribe a 4-8 week course of PPI and schedule endoscopy

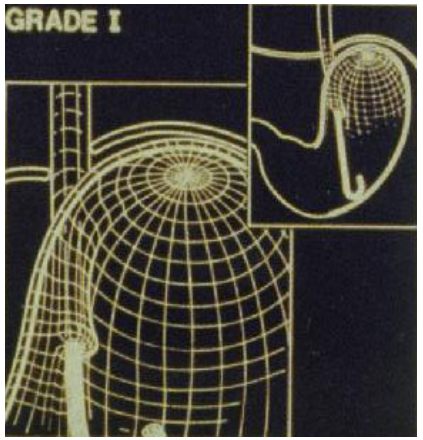
Visit 2:EGD

↓

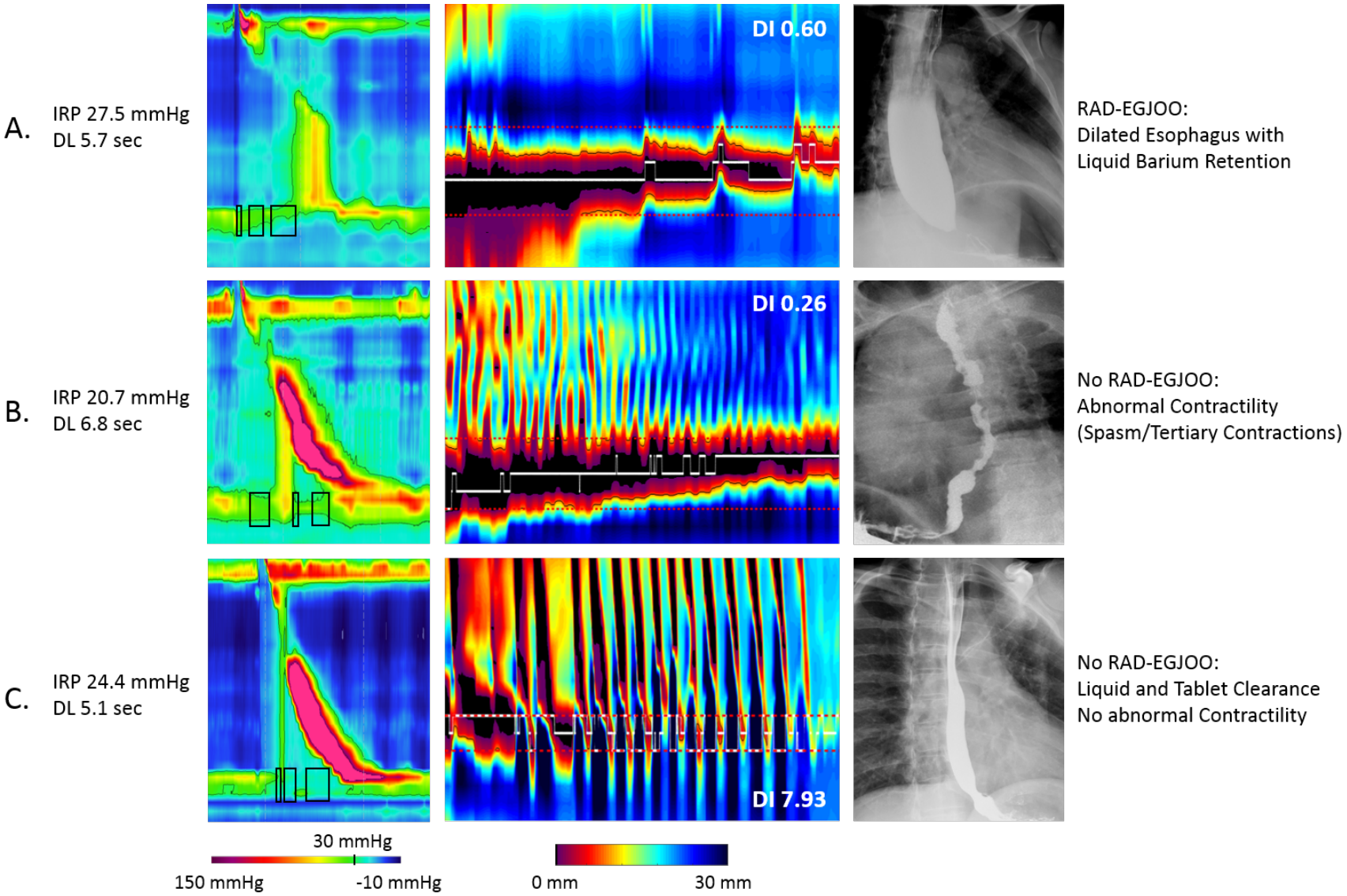
Normal or suspect EMD

↓

Visit 3: Follow up in clinic → Visit 4: Esophageal Function testing → Visit 5: Debrief Schedule endoscopy or Surgery



FUNCTIONAL LUMINAL IMAGING PROBE PANOMETRY: A METHOD TO DISTINGUISH TRUE EGJOO



Esophageal pressure Topography

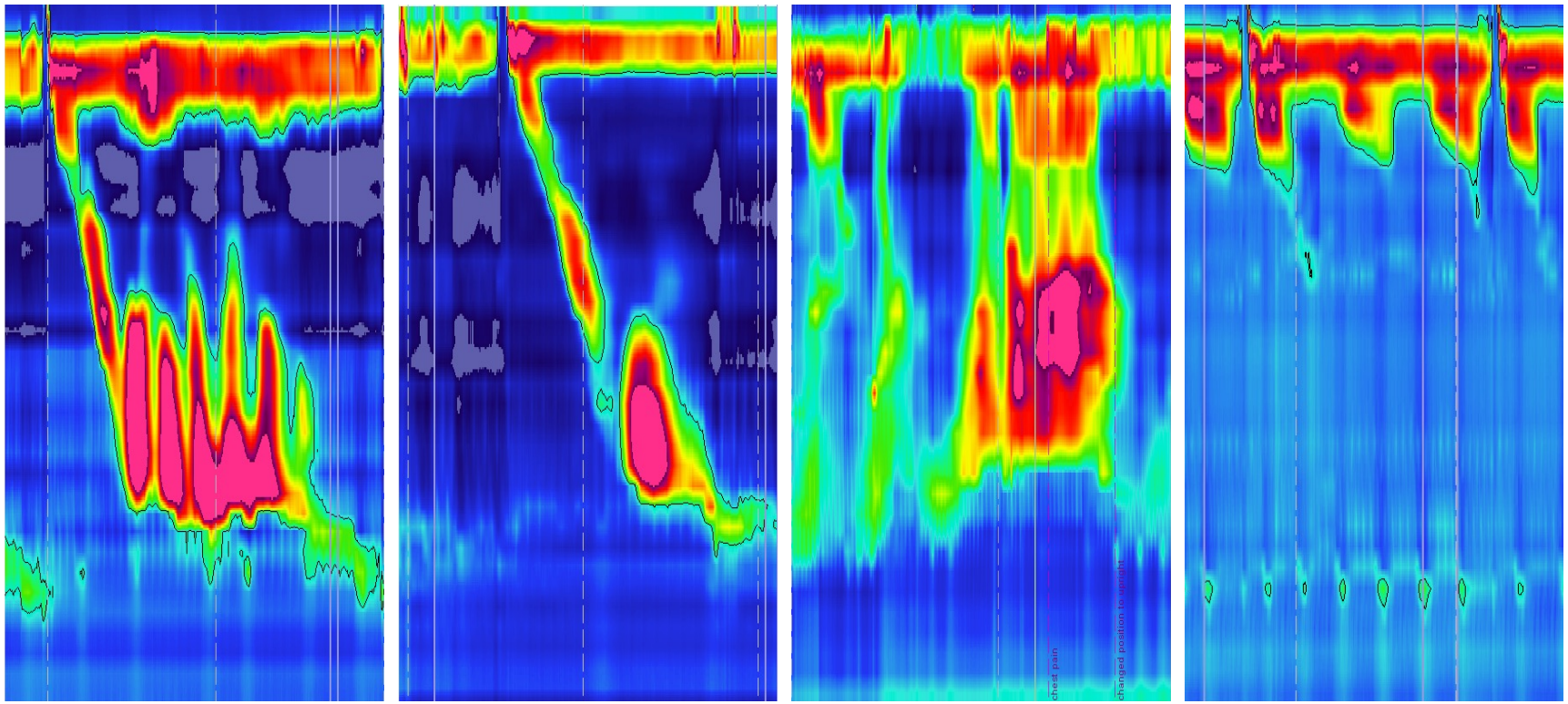
Jackhammer Esophagus- Treatment

A: Jackhammer
standard swallow- no pain

B: Jackhammer- Normal
protocol swallow + sildenafil

C: Jackhammer-Spasm
during chest pain event

D: Jackhammer-Absent Contractility
After POEM



Color Pressure scale (mmHg)

0 30 60 90 120 150 180

Our poor understanding of symptoms

- **Mechanics of Bolus Transport and prediction of symptom severity**
  - **Delicate interplay between bolus retention, EGJ obstruction, peristaltic function.**
    - ***Intrabolus pressure and esophageal diameter are the key measurements of stress and strain on the wall of the esophagus and manometry-impedance, esophagram and FLIP can help us better understand this relationship***
  - **However- the correlation between motility/impedance metrics and symptoms is poor.**
  - **There is a poor correlation between esophagram findings and symptoms outside of obstruction.**
  - **FLIP and more novel HRIM approaches have also not been able to link mechanics to symptoms in a convincing way.**

Lazarescu & Sifrim. Neurogastroenterol Motil. 2010 Dec;22(12):1292
Xiao et al. Am J Gastroenterol. 2014 Apr;109(4):521-6

ARTICLE

Esophageal Hypervigilance and Visceral Anxiety Are Contributors to Symptom Severity Among Patients Evaluated With High-Resolution Esophageal Manometry

Carlson, Dustin A. MD, MS[1]; Gyawali, C. Prakash MD[2]; Roman, Sabine MD, PhD[3]; Vela, Marcelo MD[4]; Taft, Tiffany H. PsyD, MIS[1]; Crowell, Michael D. PhD[4]; Ravi, Karthik MD[5]; Triggs, Joseph R. MD, PhD[1]; Quader, Farhan MD[2]; Prescott, Jacqueline BS[1]; Lin, Frederick T. J. MS[1]; Mion, Francois MD, PhD[3]; Biasutto, Dario MD[3]; Keefer, Laurie PhD[6]; Kahrilas, Peter J. MD[1]; Pandolfino, John E. MD, MS[1]

Author Information

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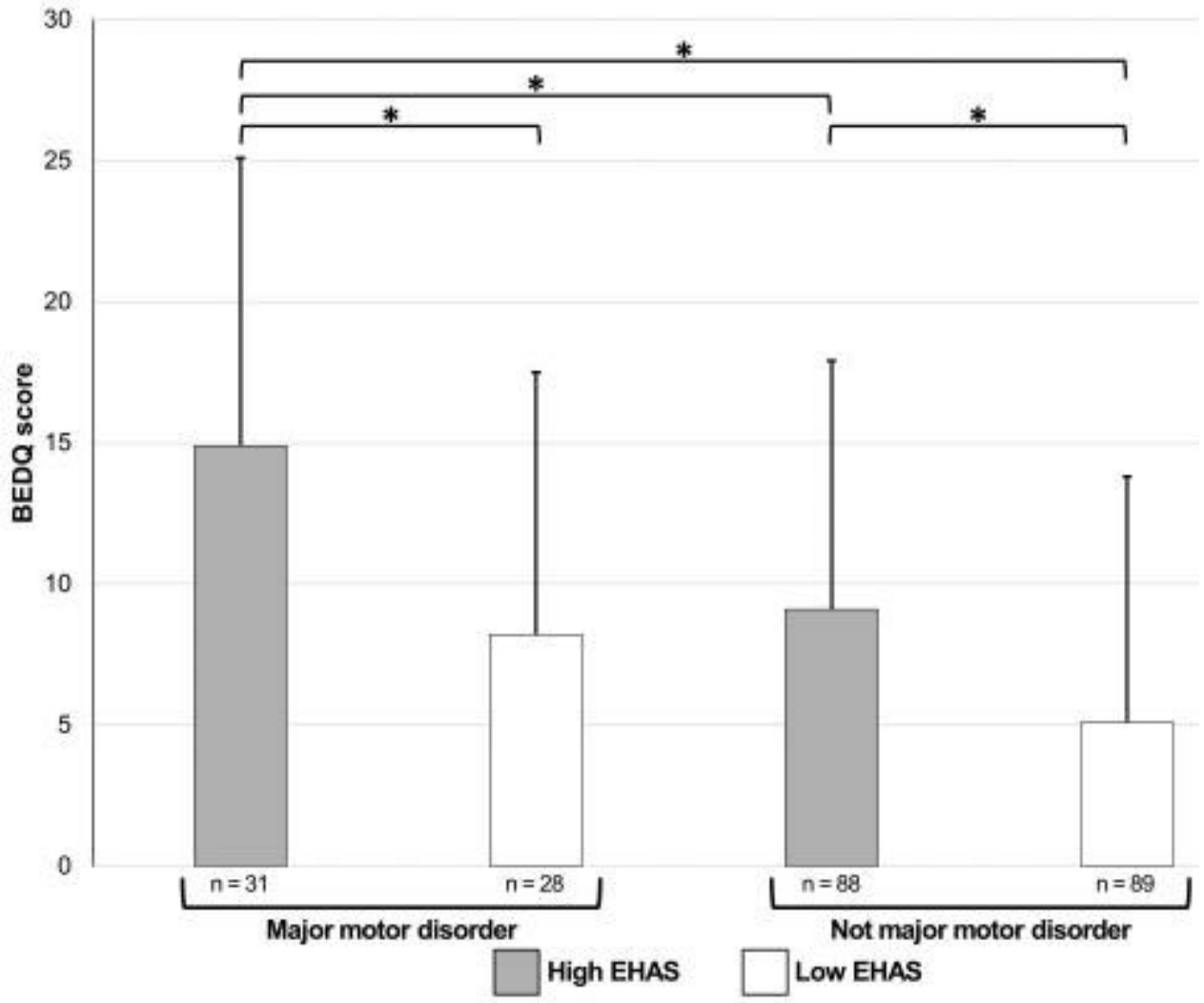
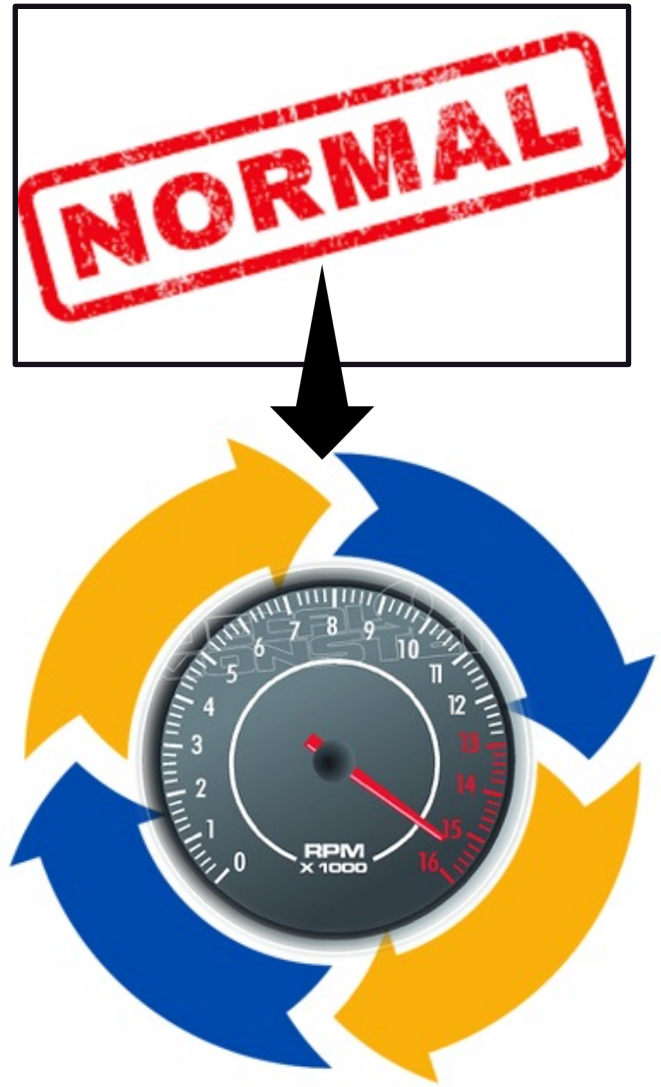
Having a major motor disorder was a significant predictor of dysphagia severity (R2adj = 0.049, P<.001), but EHAS score carried a predictive relationship of BEDQ that was two-fold higher than having a major motor disorder: R2adj = 0.118 (P<.001). This finding remained when evaluated by major motor disorder group.

HRM metrics were non-significant



Esophageal Hypervigilance and Anxiety

- Emerging as very important constructs across esophageal diseases including GERD, Achalasia, and other motility disorders
- Hypervigilance: the tendency to overly focus attention on physical sensations in the esophagus
- Symptom-Anxiety: Worry about the presence, or possibility, of esophageal symptoms



Cognitive-Affective Processes

Illness Anxiety	• Global tendency to worry about current and future illness events (flare ups, symptom exacerbation, worsening course)
Symptom-Specific Anxiety	• Worry/hypervigilance around the likelihood/presence of specific symptoms and the contexts in which they occur
Hypervigilance/ Attentional Bias	• Altered attention toward, and increased engagement with, symptoms and reminder of symptoms
Catastrophizing	• 2-pronged cognitive process in which an individual magnifies the seriousness of symptoms and consequences while viewing themselves as helpless

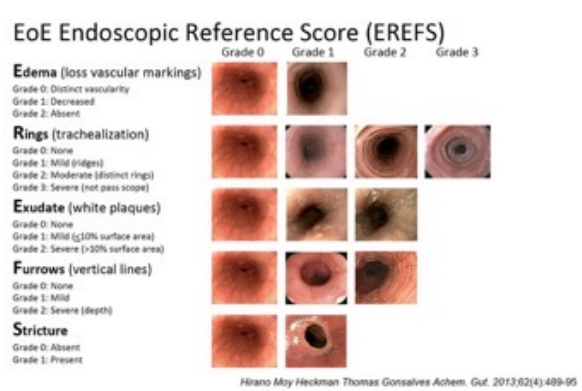
Esophageal Hypervigilance & Anxiety (EHA)

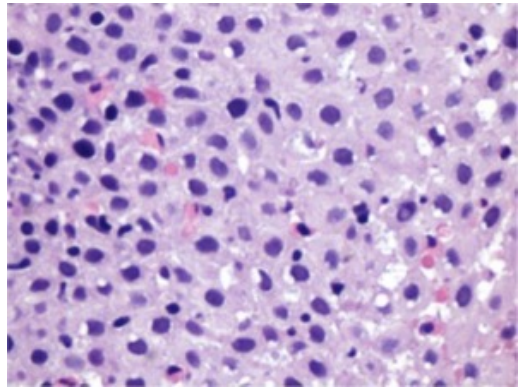
Gastroenterology
Available online 19 June 2021
In Press, Corrected Proof

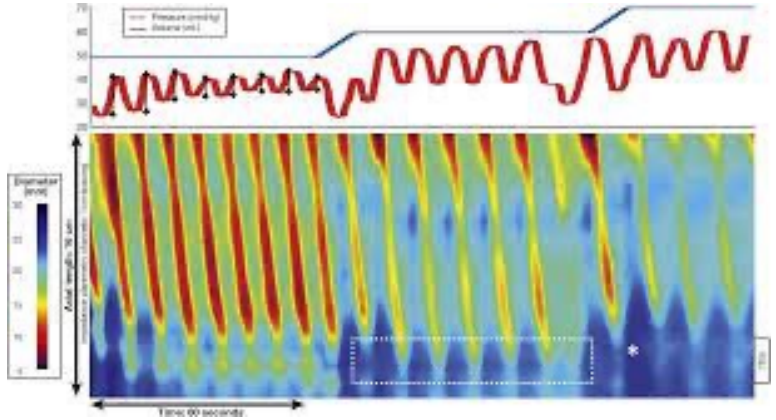
Clinical—Alimentary Tract

Esophageal Hypervigilance and Symptom-Specific Anxiety in Patients with Eosinophilic Esophagitis

Tiffany H. Taft, Dustin A. Carlson, Madison Simons, Sonia Zavala, Ikuo Hirano, Nirmala Gonsalves, John E. Pandolfino







N=103
57.8% in endoscopic remission (EREFS < 3)
38.7% in histologic remission (EOS < 15)
49.5% had dilation during EGD at time of assessment
EOS/HPF Proximal: Median = 10.5 (0 – 55.25)
EOS/HPF Distal: Median = 25.0 (0 – 50)
FLIP. Distal Distensibility Plateau: Mean = 17.88 (2.83)

45.6% had “elevated” symptoms of Hypervigilance & Anxiety (EHAS > 21)

Predictors of Dysphagia Symptom Severity (BEDQ)

		Univariate Statistics			Multivariate Statistics			
					Unstandardized Coefficient		Standardized Coefficient	
Model	Measurement	F	R^2_{adj}	ΔR^2	B	SE	β	P
1	EHAS: Anxiety	48.88	.448	.457	.526	.075	.676	<.001
2	EREFS Score	3.05	.467	.028				.086
	EHAS: Anxiety				.527	.074	.677	<.001
	EREFS				-.645	.369	-.166	.559
3	EOS/HPF	.005	.448	.000				.995
	EHAS: Anxiety				.527	.076	.678	<.001
	EREFS				-.638	.384	-.164	.103
	EOS/HPF: Proximal				.002	.026	.016	.933
	EOS/HPF: Distal				-.003	.028	-.019	.921
4	FLIP DP	.542	.443	.005				.464
	EHAS: Anxiety				.522	.076	→ .672	**<.001**
	EREFS				-.638	.394	-.149	.146
	EOS/HPF: Proximal				.003	.026	.024	.901
	EOS/HPF: Distal				-.001	.029	-.004	.982
	FLIP DP				.181	.245	.077	.464

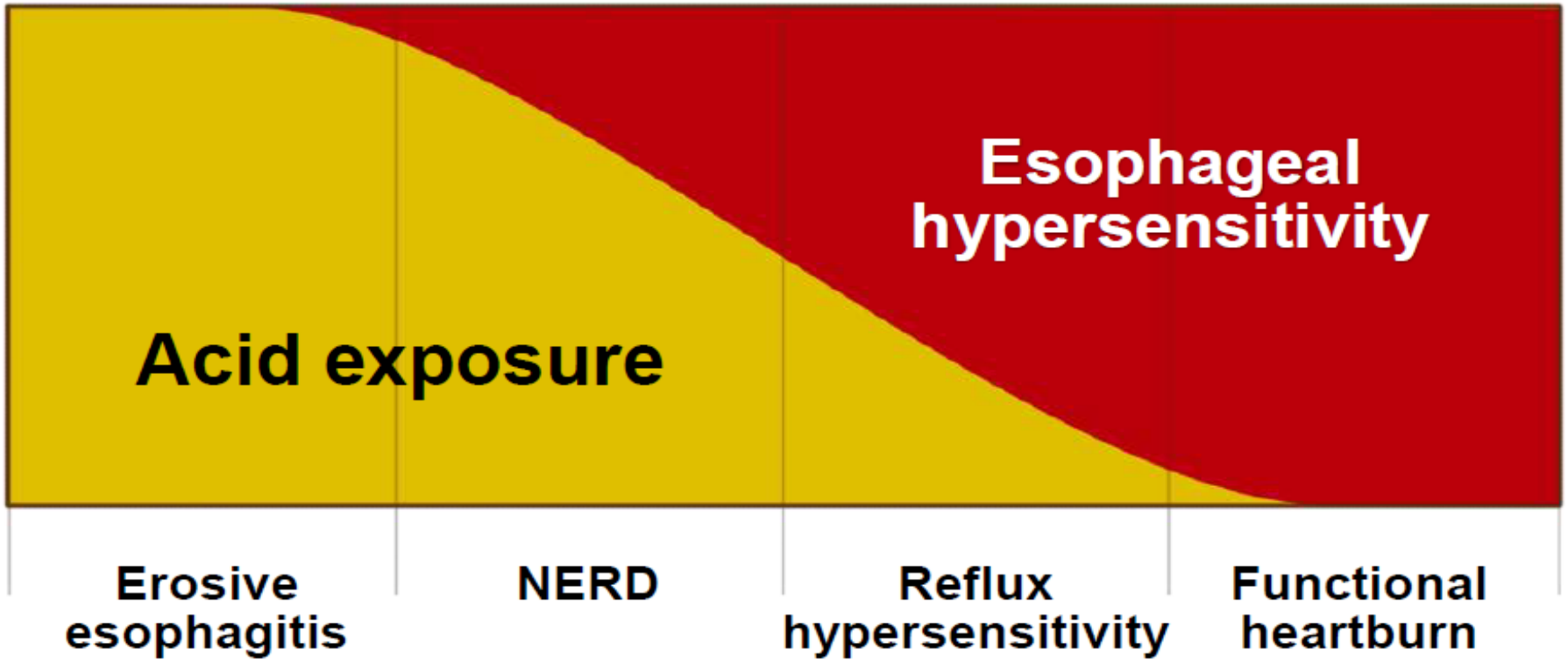
Predictors of Difficulty Swallowing (EEsAI)

		Univariate Statistics			Multivariate Statistics			
					Unstandardized Coefficient		Standardized Coefficient	
Model	Measurement	F	R^2_{adj}	ΔR^2	B	SE	β	P
1	EHAS: Anxiety	20.63	.260	.273	.314	.069	.522	<.001
2	EREFS Score + Stricture	.685	.251	.018				.508
	EHAS: Anxiety				.308	.070	.512	<.001
	EREFS				-.330	.349	-.109	.350
	Stricture Present				.794	1.20	.077	.511
3	EOS/HPF	.277	.230	.008				.759
	EHAS: Anxiety				.312	.071	.518	<.001
	EREFS				-.276	.362	-.091	.449
	Stricture Present				.927	1.23	.090	.455
	EOS/HPF: Proximal				.011	.024	.107	.642
	EOS/HPF: Distal				-.019	.027	-.163	.488
4	FLIP DP	1.16	.232	.016				.286
	EHAS: Anxiety				.306	.071	.508	**<.001**
	EREFS				-.197	.368	-.065	.595
	Stricture Present				.931	1.23	.090	.453
	EOS/HPF: Proximal				.013	.024	.120	.602
	EOS/HPF: Distal				-.016	.027	-.136	.563
	FLIP DP				.244	.226	.136	.286

GERD

GERD Dogma: Organic versus Functional

Roles of acid exposure and esophageal hypersensitivity in overlapping GERD and functional esophageal syndromes. Acid exposure and response to proton pump inhibitors decreases from erosive esophagitis to functional heartburn while esophageal hypersensitivity increases across the same spectrum.
(Adapted from Galmiche et al, UEG Journal 2013)



Neurogastroenterology & Motility

ORIGINAL ARTICLE | Full Access

Esophageal hypervigilance is prevalent across gastroesophageal reflux disease presentations

Livia Guadagnoli, Rena Yadlapati, Tiffany Taft, John E. Pandolfino, Michael Tye, Laurie Keefer

We studied 286 patients undergoing pH monitoring at Northwestern Medicine.

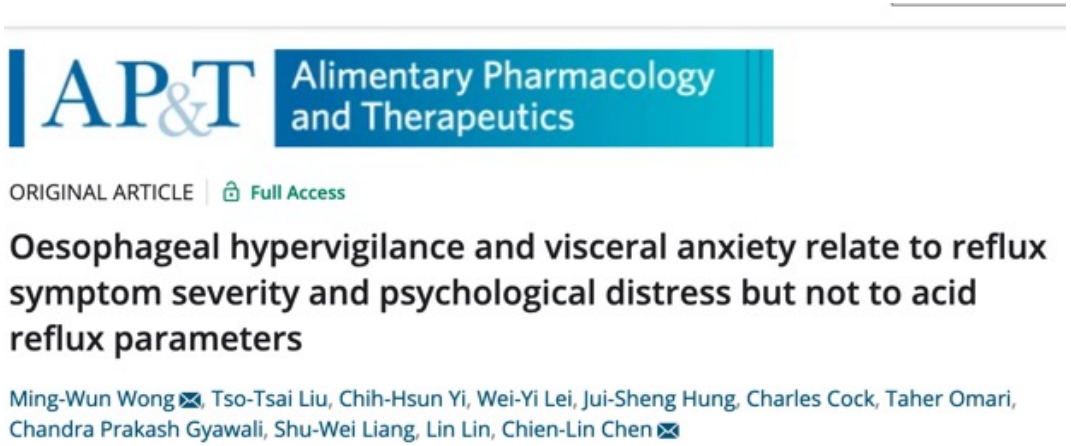
- Health related quality of life measured by the NEQOL was not associated with total Bravo (r = -0.13, p = .051) or pH impedance (r = -0.10, p = .108) acid events.
- However, elevations in hypervigilance and symptom-specific anxiety using the EHAS strongly associated with decreased HrQOL (r = -0.73, p < .001).

TABLE 3. Hierarchical linear regression for predictors of symptom severity in AET and SI samples.

	R^2adj	β	SE	*p*
AET Sample				
Model 1	0.067			0.002
Age		−0.272	0.016	
Model 2	0.092			0.038
Age		−0.244		**0.006**
EHAS Hypervigilance		0.183	0.016	**0.038**
EHAS Anxiety		0.070	0.044	0.604
SI Sample				
Model 1	0.061			0.004
Age		−0.262	0.017	
Model 2	0.093			0.027
Age		−0.238	0.017	**0.009**
EHAS Hypervigilance		0.201	0.046	**0.027**
EHAS Anxiety		0.065		0.652

Anxiety & GERD

- Between 20% and 30% of patients with GERD have anxiety (usually per HADS)



AP&T Alimentary Pharmacology and Therapeutics

ORIGINAL ARTICLE | Full Access

Oesophageal hypervigilance and visceral anxiety relate to reflux symptom severity and psychological distress but not to acid reflux parameters

Ming-Wun Wong, Tso-Tsai Liu, Chih-Hsun Yi, Wei-Yi Lei, Jui-Sheng Hung, Charles Cock, Taher Omari, Chandra Prakash Gyawali, Shu-Wei Liang, Lin Lin, Chien-Lin Chen

Neurogastroenterology & Motility

ORIGINAL ARTICLE | Full Access

The Spanish version of the esophageal hypervigilance and anxiety score shows strong psychometric properties: Results of a large prospective multicenter study in Spain and Latin America

Daniel Cisternas, Tiffany Taft, Dustin A. Carlson, Esteban Glasinovic, Hugo Monrroy, Paula Rey, Albis Hani, Andres Ardila-Hani, Ana Maria Leguizamo, Claudio Bilder, Andres Ditaranto ... See all authors

ELSEVIER

Clinics and Research in Hepatology and Gastroenterology

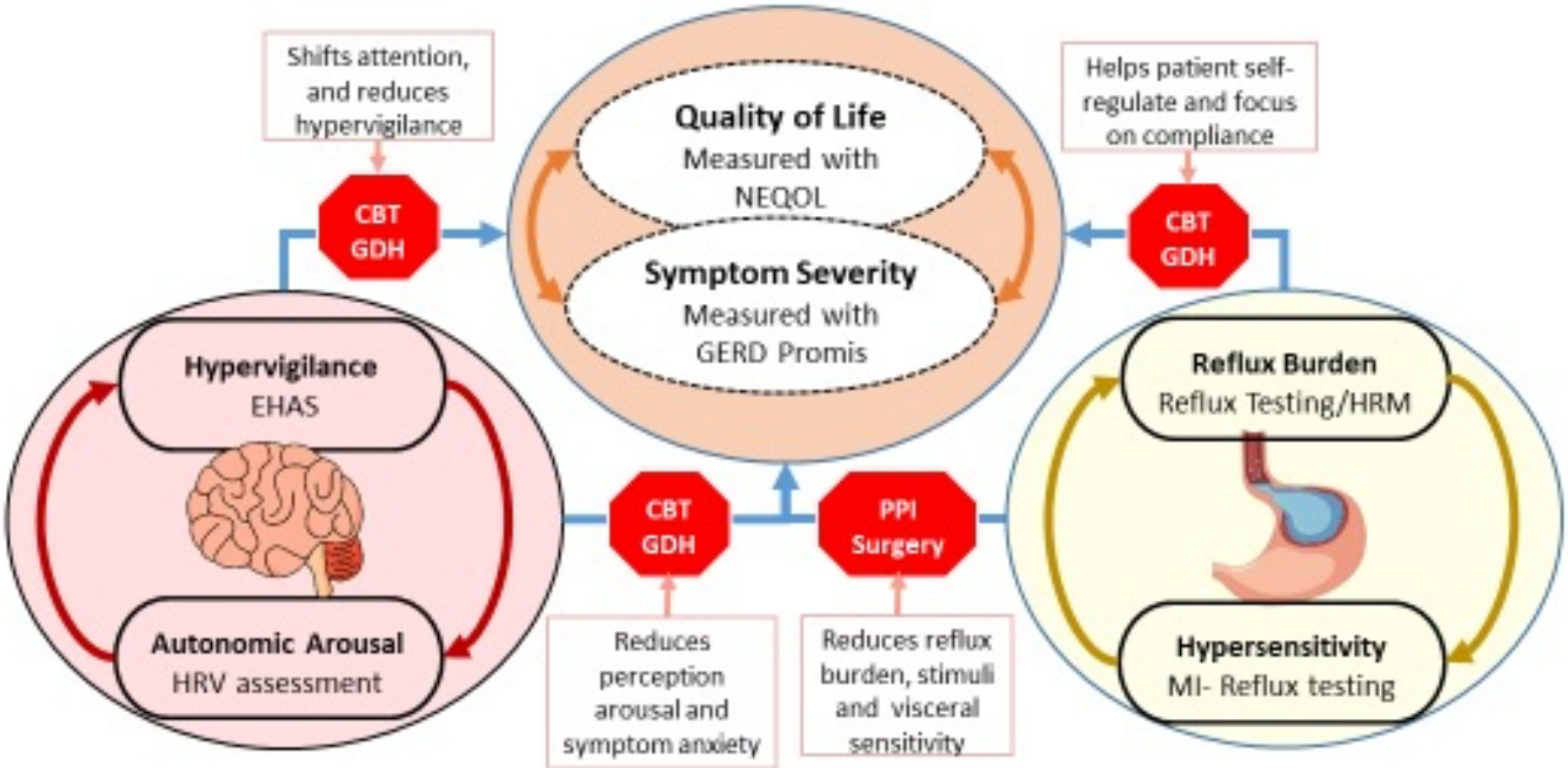
Volume 45, Issue 2, March 2021, 101672

Original article

Validation of the French version of the esophageal hypervigilance and anxiety scale

Sabine Roman, Livia Anna Guadagnoli, Audrey Hastier, Estelle Becam, Meredith Ruth Ann Craven, Marie Napoléon, John E. Pandolfino, Dustin A. Carlson, Francois Mion, Tiffany Taft

Conceptual Model of the Psycho-Physiologic Model of GERD



Esophageal Symptoms: Psycho-Physiologic Model

- *Abnormal Physiology and anatomy gets the patient to come to the doctor.*
- *However, symptom severity and QOL are driven by factors that are not just related to motility, bolus retention and visceral hypersensitivity.*
- *At some point – we have to address the gut-brain interaction as this will improve our treatment outcomes.*