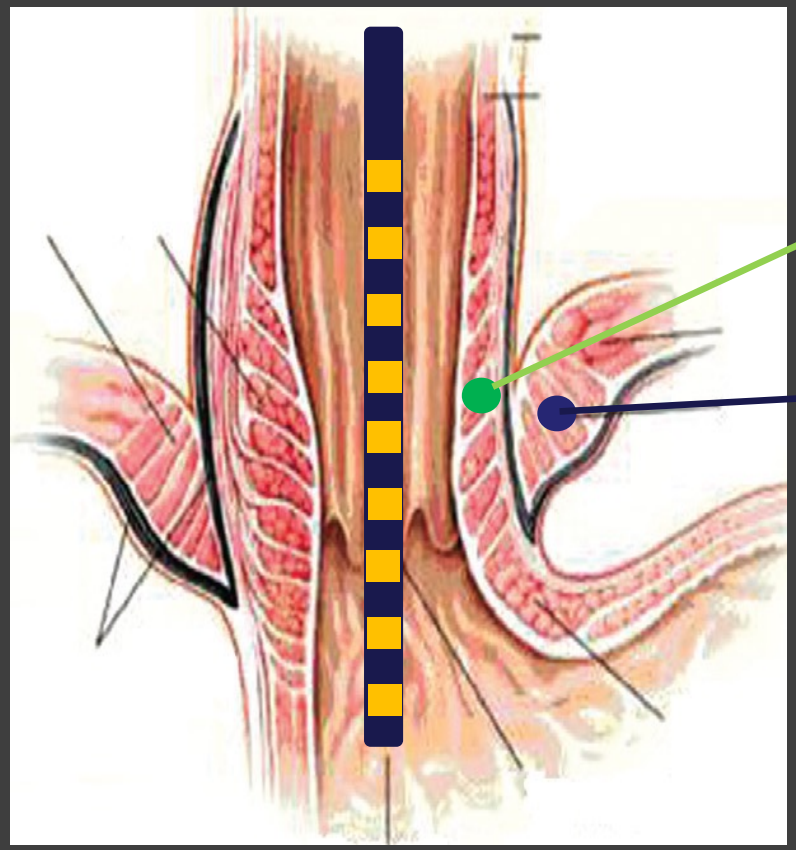
UFC

Papel do diafragma na junção esôfagogástrica na doença do refluxo gastroesofágico

Miguel Ângelo Nobre e Souza
mans@ufc.br

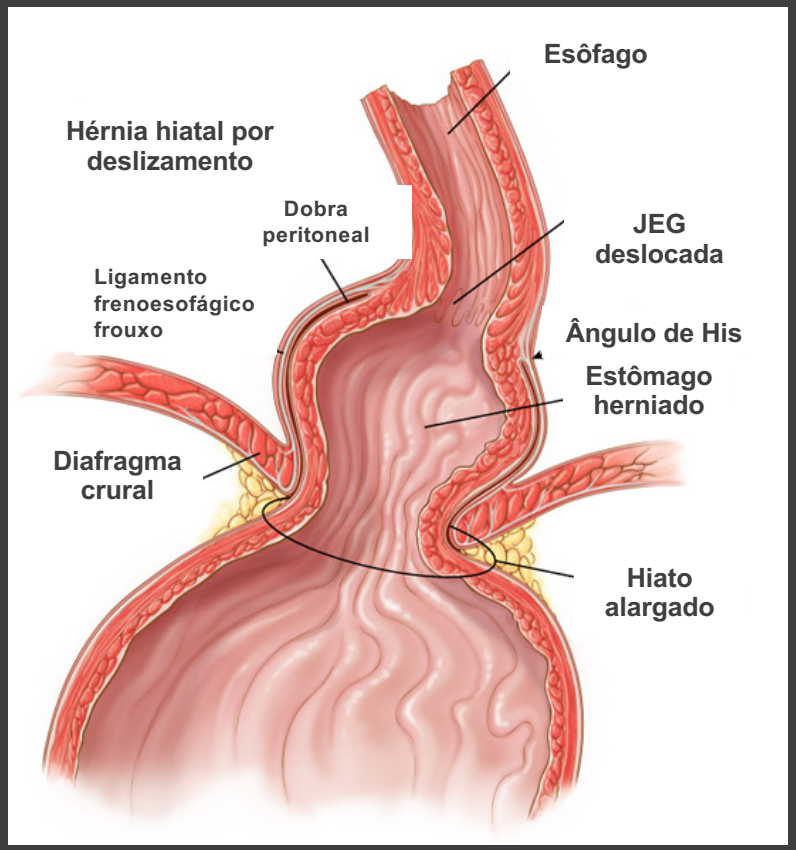
Universidade Federal do Ceará
PROGRAMA DE PÓS-GRADUAÇÃO EM CIÊNCIAS MÉDICAS

Junção Esôfago-Gástrica / Esfíncter inferior / Barreira Antirrefluxo

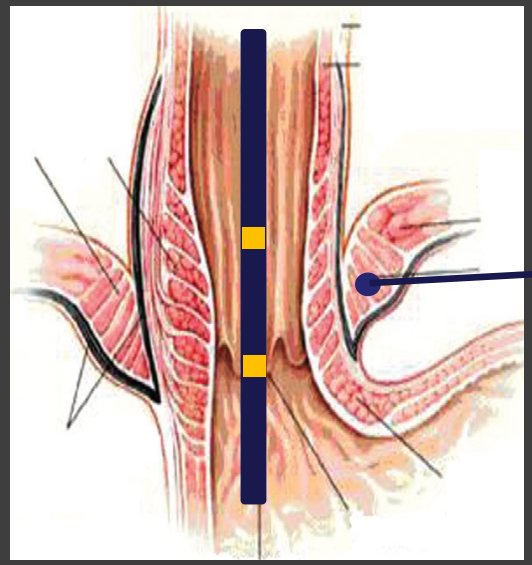


Pressão expiratória

Pressão inspiratória



Atividade elétrica do diafragma crural é inibida com a deglutição



Atividade elétrica inspiratória

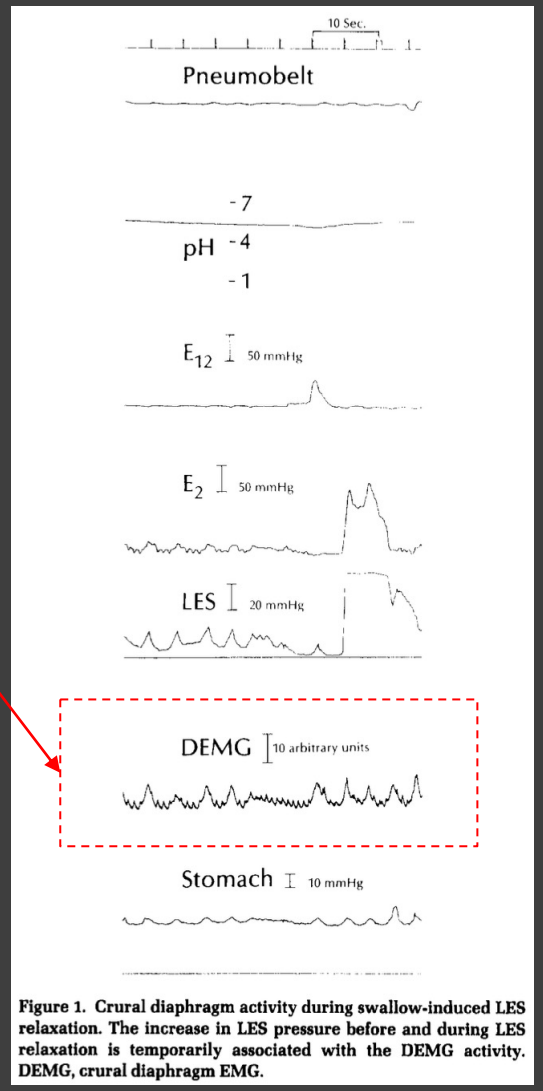
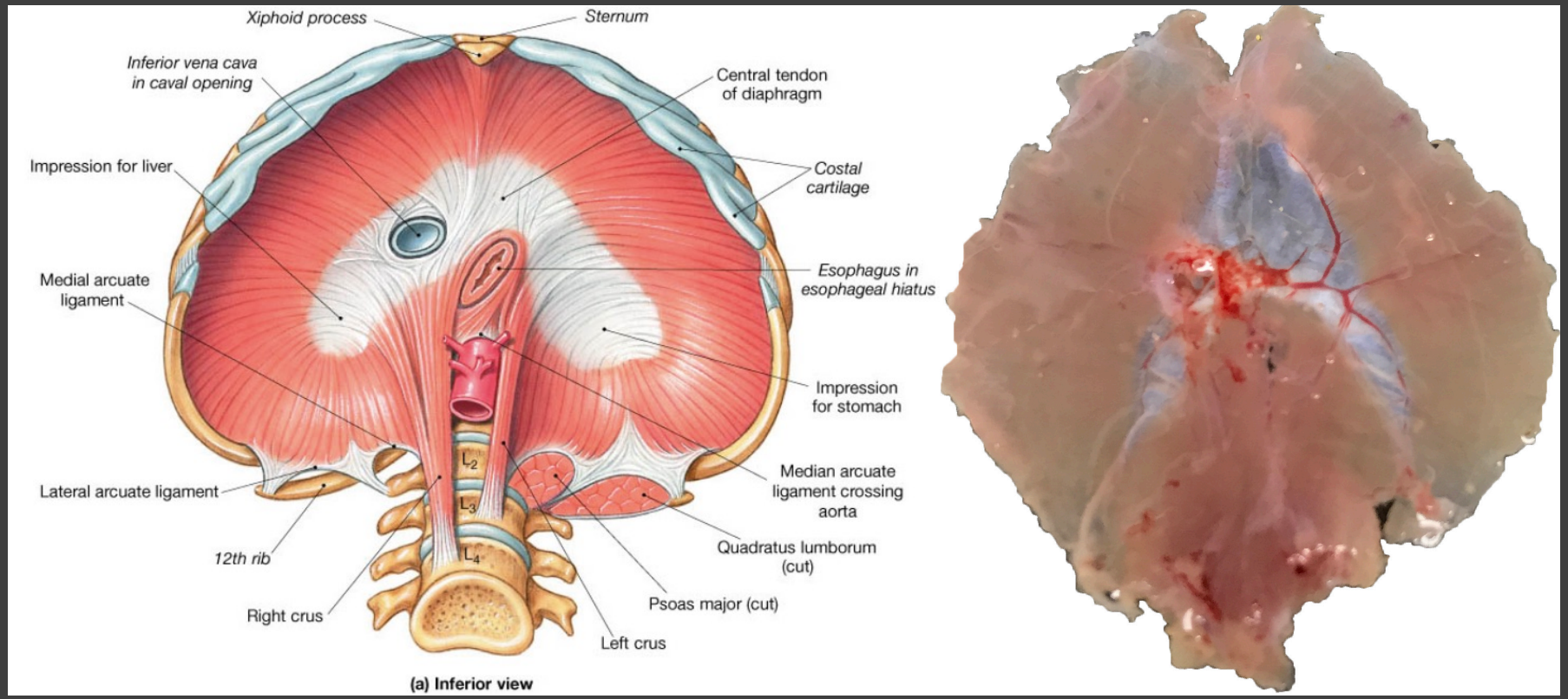


Figure 1. Crural diaphragm activity during swallow-induced LES relaxation. The increase in LES pressure before and during LES relaxation is temporarily associated with the DEMG activity. DEMG, crural diaphragm EMG.

Mittal & Fisher. Gastroenterology 1990;99:1265

O Diafragma


Xiphoid process
Sternum
Inferior vena cava in caval opening
Central tendon of diaphragm
Impression for liver
Costal cartilage
Medial arcuate ligament
Esophagus in esophageal hiatus
Impression for stomach
Median arcuate ligament crossing aorta
Lateral arcuate ligament
12th rib
Quadratus lumborum (cut)
Psoas major (cut)
Right crus
Left crus
L2
L3
L4
(a) Inferior view

Activation of the ubiquitin-proteasome pathway in the human crural diaphragm in reflux esophagitis

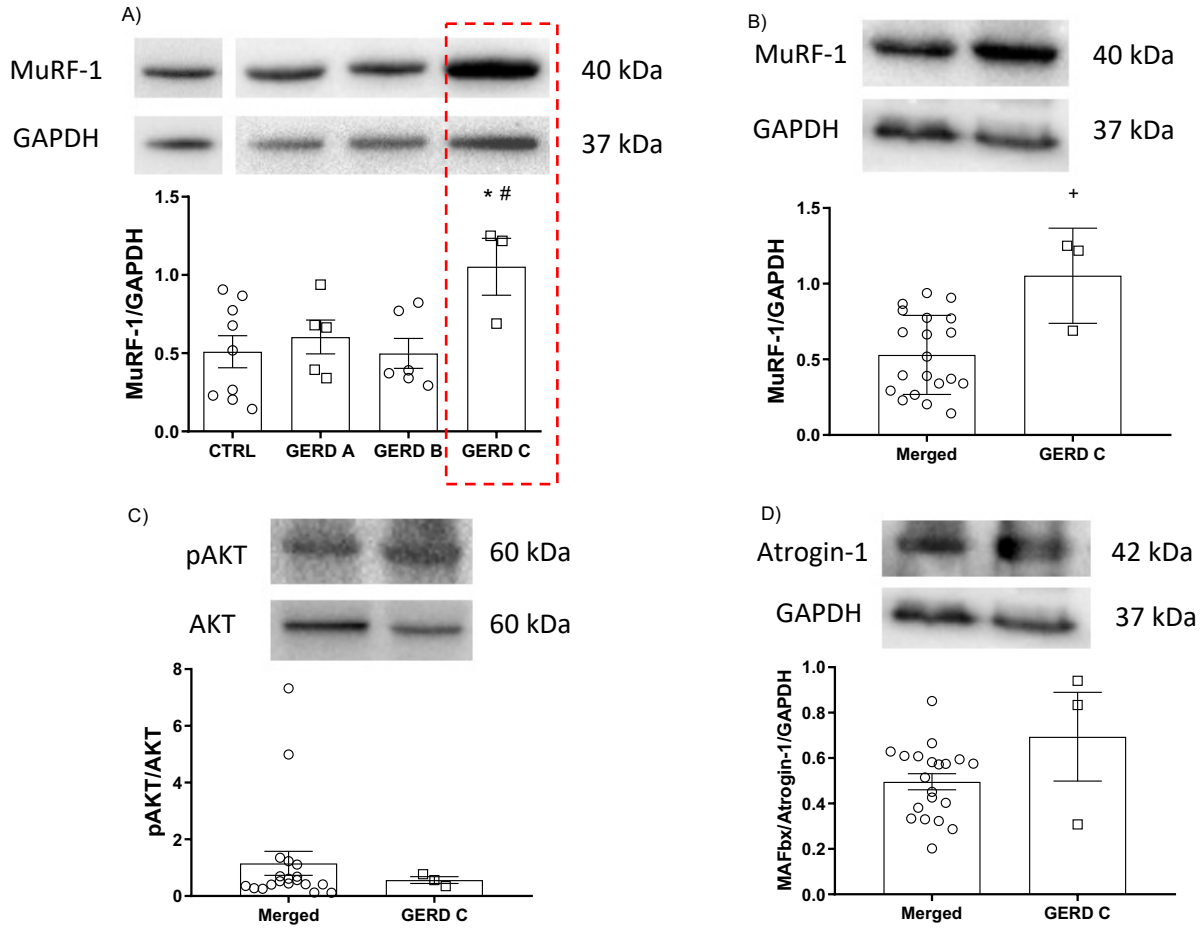


Figure 2. **Protein associated with sarcopenia pathway in crural diaphragm is increased in patients with grade C esophagitis**. MuRF-1 expression in the crural diaphragm of health volunteers (CTRL) and patients with esophagitis grade A (group GERD A), grade B (group GERD B), grade C (group GERD C) (A). MuRF-1 (B), pAKT/AKT ratio (C) and MAFbx/Atrogin-1 (D) expressions in the crural diaphragm of patients with esophagitis grade C (group GERD C) compared with groups of health volunteers, patients with esophagitis grade A and grade B together (merged). Top of each graph represents typical Western blot images. Protein expressions were normalized to GAPDH and phosphorylated AKT (pAKT) residues to total AKT content in each sample. The number of biopsies used were 3 to 20 per group. The values correspond to mean ± SEM of the biopsies studied. Statistical analysis was assessed by one-way ANOVA. *, $P < 0.05$ *vs.* CTRL, #, $P < 0.05$ *vs.* GERD B; Student's t-test; +, $P < 0.05$ *vs.* merged.

Souza MAN 2023-unpublished

Pressões ex e inspiratórias menores na DRGE

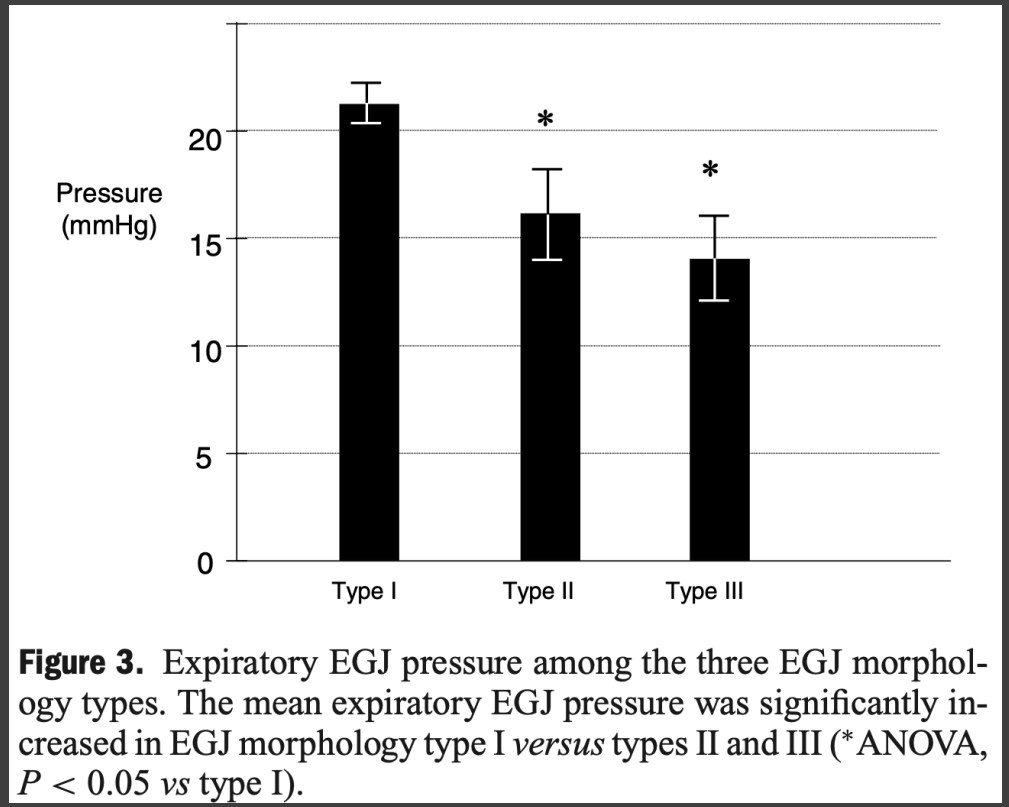


Figure 3. Expiratory EGJ pressure among the three EGJ morphology types. The mean expiratory EGJ pressure was significantly increased in EGJ morphology type I *versus* types II and III (*ANOVA, $P < 0.05$ *vs* type I).

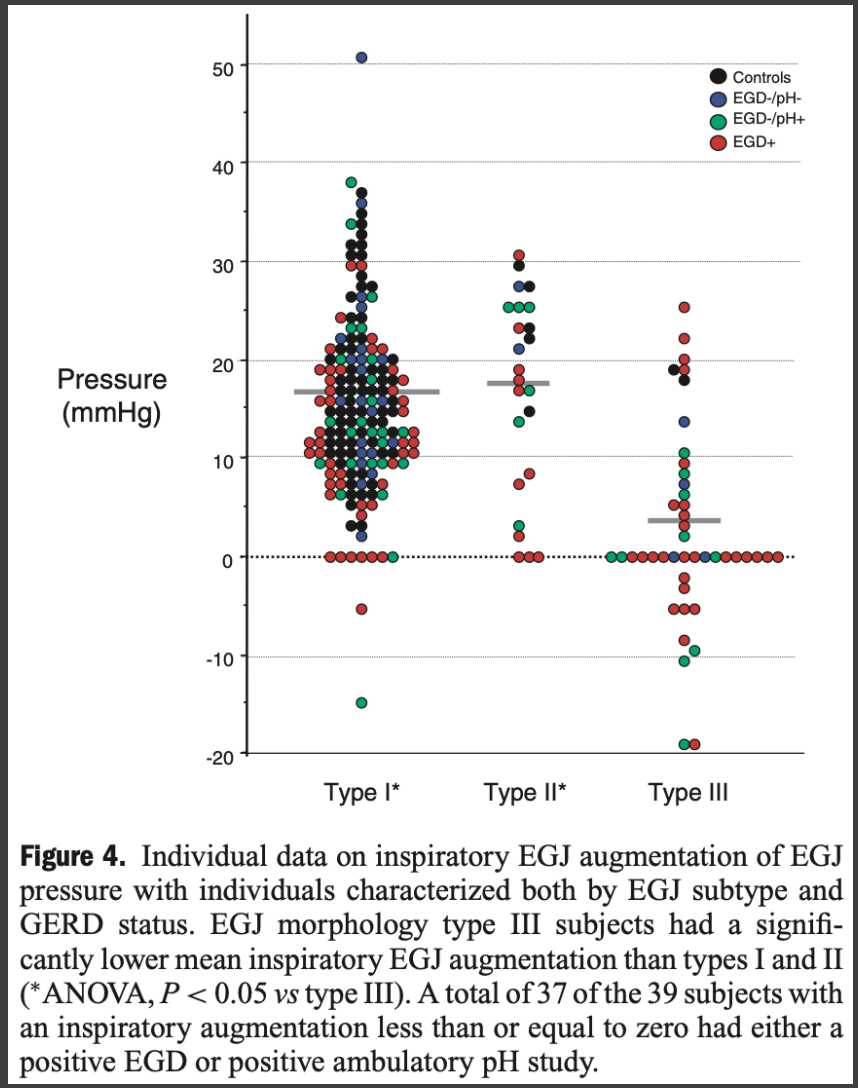


Figure 4. Individual data on inspiratory EGJ augmentation of EGJ pressure with individuals characterized both by EGJ subtype and GERD status. EGJ morphology type III subjects had a significantly lower mean inspiratory EGJ augmentation than types I and II (*ANOVA, $P < 0.05$ *vs* type III). A total of 37 of the 39 subjects with an inspiratory augmentation less than or equal to zero had either a positive EGD or positive ambulatory pH study.

Pandolfino et al. Am J Gastroenterol 2007;102:1056

Pressões da JEG e diagnóstico de DRGE

High-Resolution Manometry of the EGJ: An Analysis of Crural Diaphragm Function in GERD

Table 2. EGJ Pressure Component Separation and Pressure Profile Among the Subject Groups

	Controls	EGD−/ pH−	EGD−/ pH+	EGD+
LES-CD separation (cm)	0.2 (0.1)	0.4 (0.2)	0.9 (0.2)*	1.2 (0.2)*†
Expiratory EGJ pressure (mmHg)	24.0 (1.1)	20.5 (2.7)	18.6 (1.9)*	16.8 (1.2)*
Inspiratory EGJ augmentation (mmHg)	16.9 (1.0)	16.7 (2.1)	11.5 (1.9)*†	10.0 (1.2)*†

ANOVA, $*P < 0.05$ *vs* controls, $^{\dagger}P < 0.05$ *vs* EGD+.

Table 4. The Association Between EGJ Morphology and Pressure Profile and GERD

	Regression Coefficient	SE	*P* Value
Expiratory EGJ pressure (mmHg)	–0.04	0.02	0.02
LES-CD separation (cm)	0.45	0.18	0.01
EGJ pressure augmentation (mmHg)	–0.06	0.02	0.0005

Modelo de regressão logística:

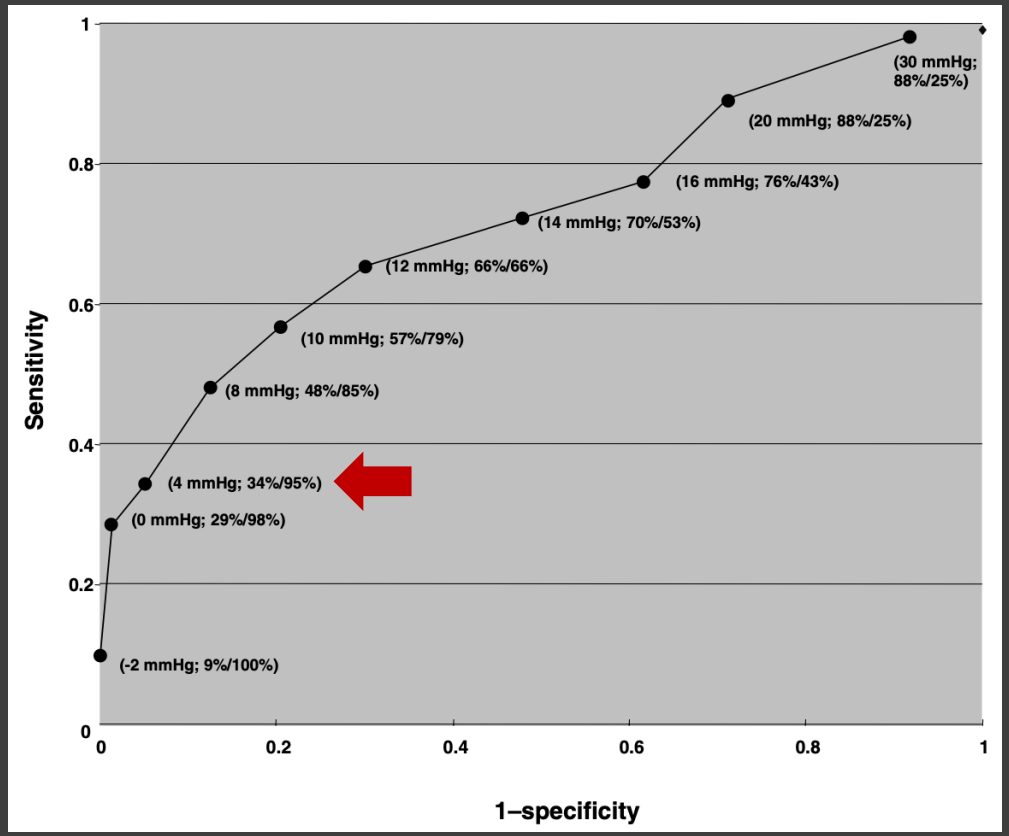
Somente Pins, idade e IMC significantes.

Pandolfino et al. Am J Gastroenterol 2007;102:1056

Predição de DRGE pelo aumento da pressão inspiratória da JEG

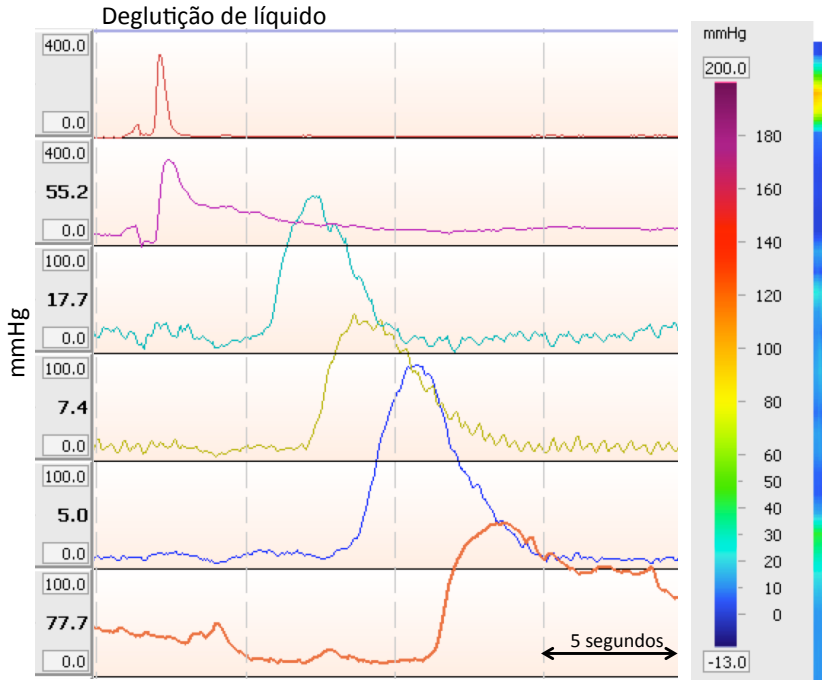
ROC analysis of the pressure value for inspiratory EGJ augmentation in predicting GERD

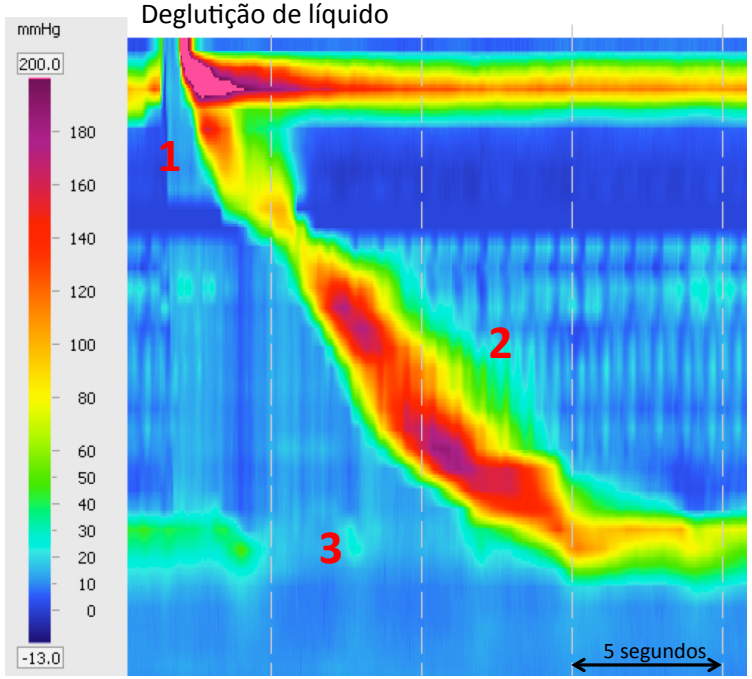
Inspiratory augmentation < 4 => 95% specificity



Pandolfino et al. Am J Gastroenterol 2007;102:1056

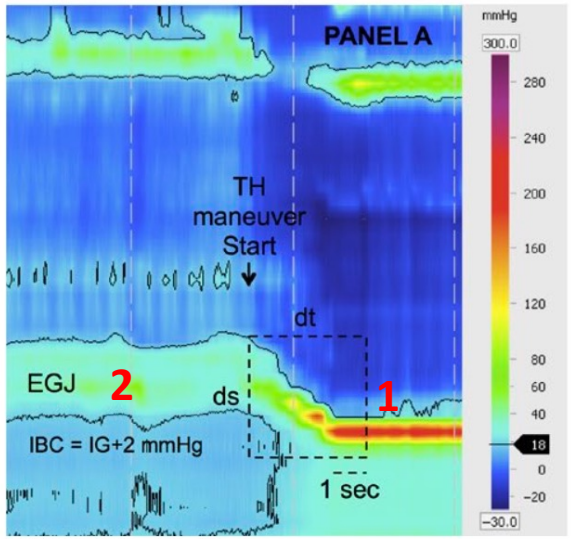
Motilidade esofágica normal

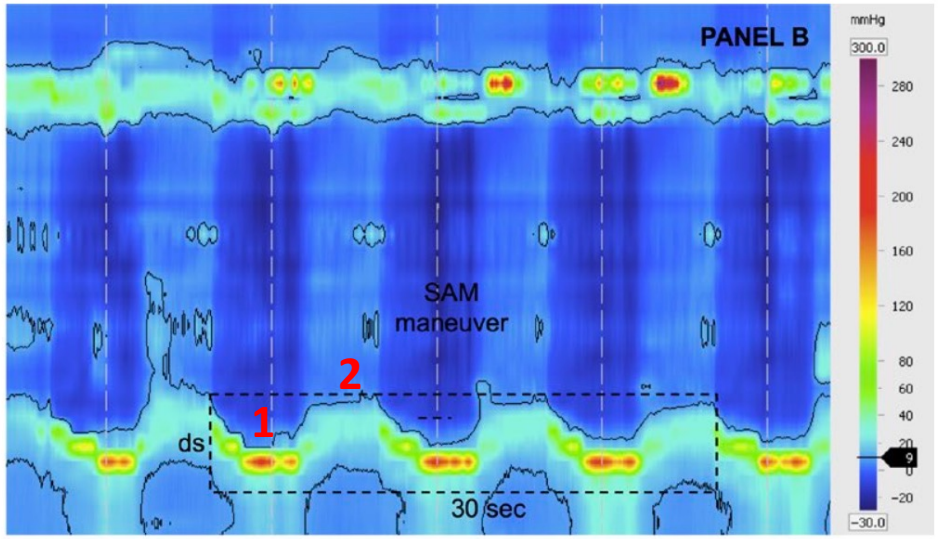




Padrão motor normal:

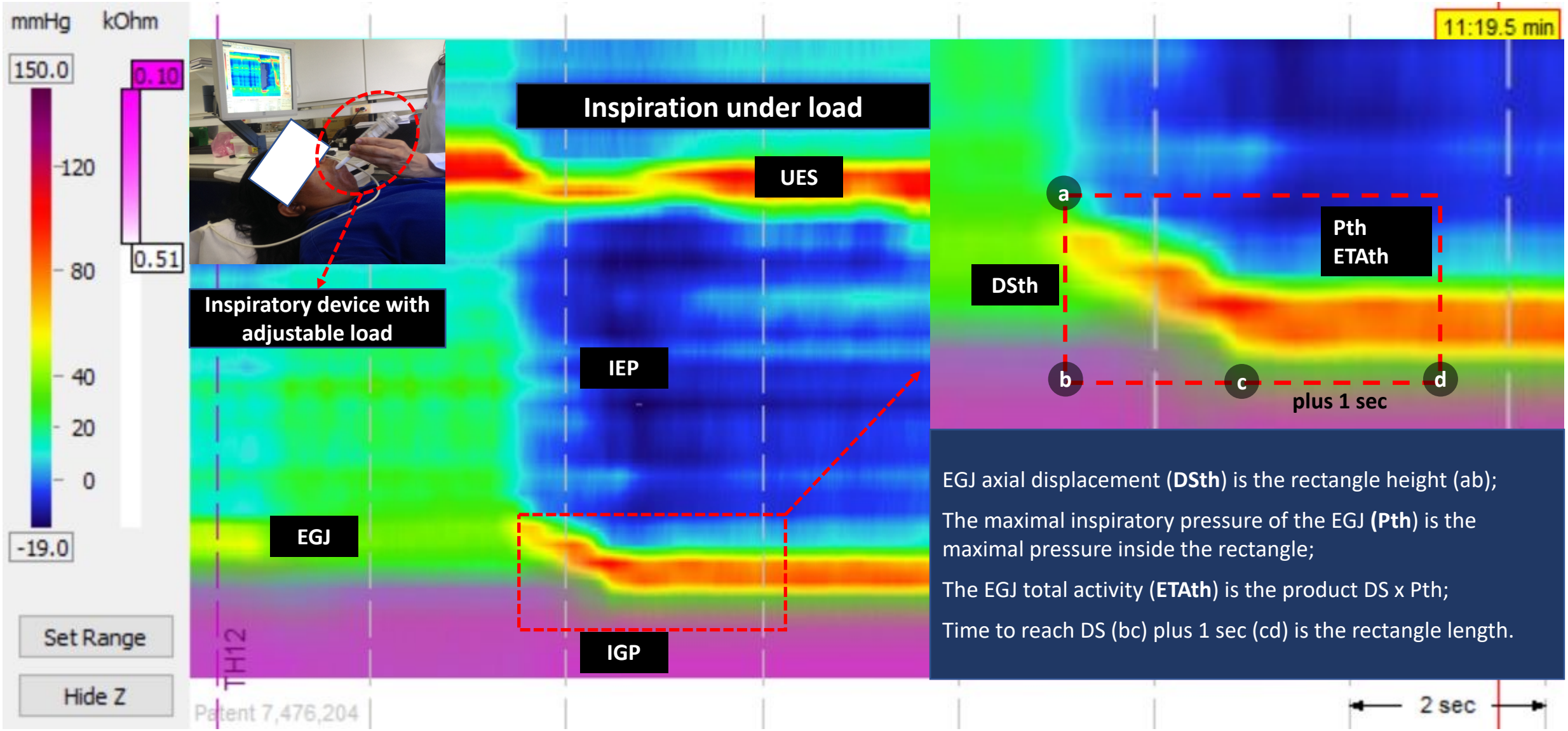
1. Esfincter superior abre;
2. Corpo esofágico com contrações sequenciais;
3. Esfincter inferior relaxa.





Junção esôfago-gástrica(EGJ) durante manobras inspiratórias:

1. Pressão inspiratória;
2. Pressão expiratória.



EGJ axial displacement (**DSth**) is the rectangle height (ab);

The maximal inspiratory pressure of the EGJ **(Pth**) is the maximal pressure inside the rectangle;

The EGJ total activity (**ETAth**) is the product DS x Pth;

Time to reach DS (bc) plus 1 sec (cd) is the rectangle length.

Anatomical and functional deficiencies of the crural diaphragm in patients with esophagitis

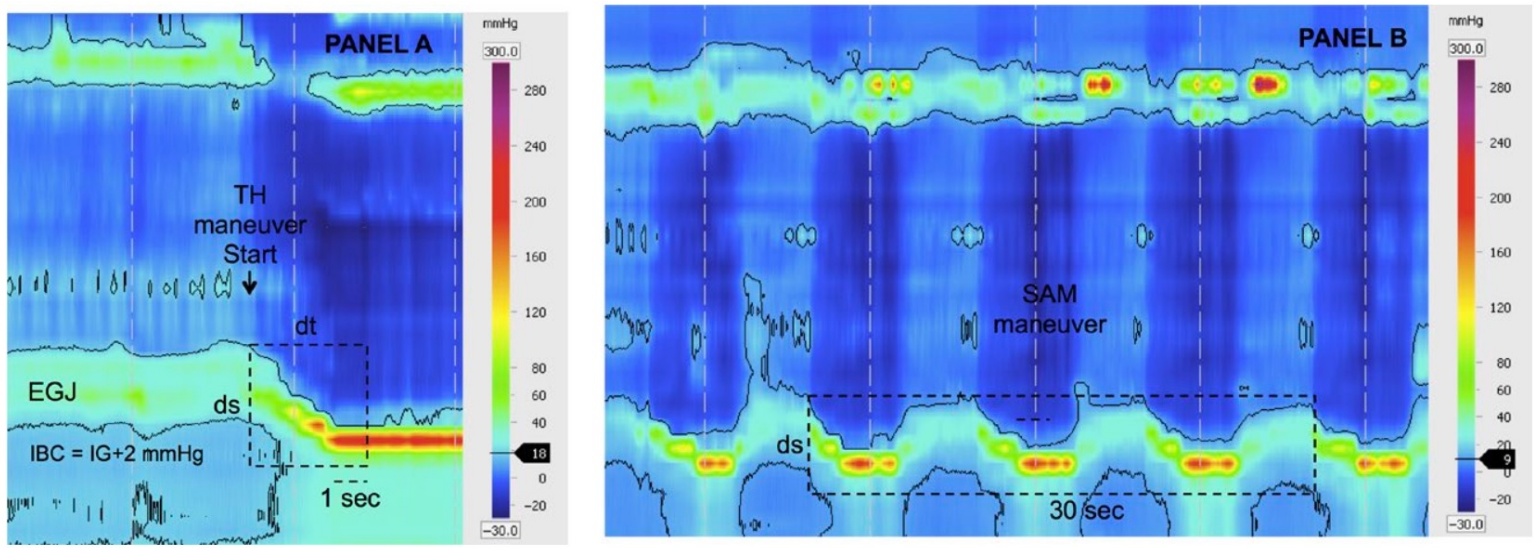


FIGURE 1 The EGJ contractile index (EGJ-CI) was determined with a DCI tool box that enclosed the esophagogastric junction (EGJ) from the start of the inspiratory threshold (TH) maneuver until 1 second after the CD reached its lowest position (A). In the case of the sinus arrhythmia maneuver (SAM), the box duration was 30 seconds, corresponding to three respiratory cycles (B). Isobaric contours (IBC) were 2 mm Hg above intragastric pressure (IG)

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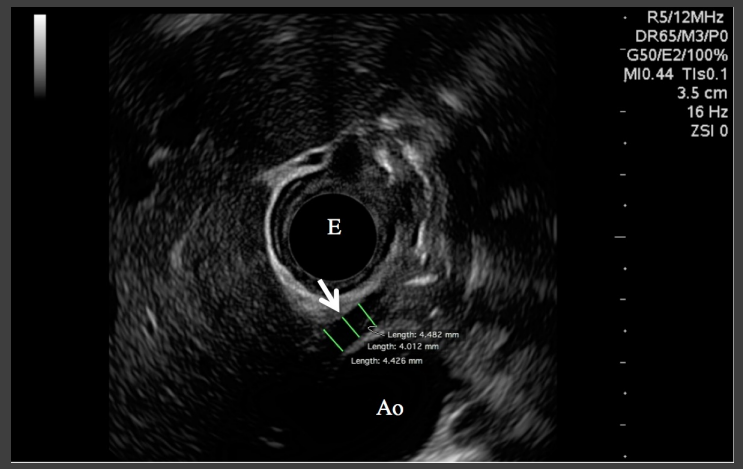
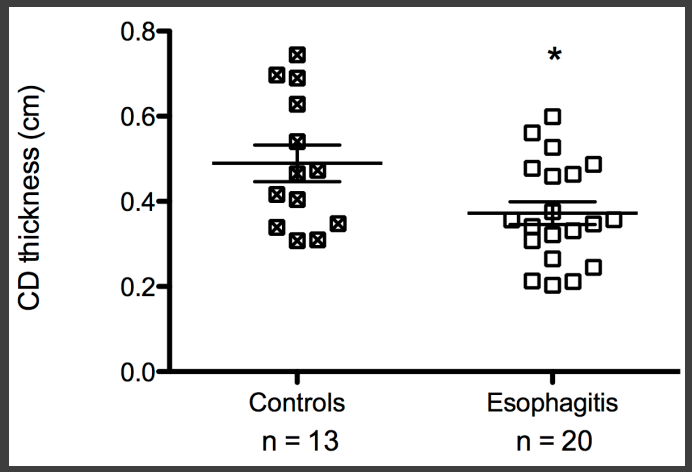
Deficiência Crural

Ramo crural mais fino na esofagite

Laboratório de Pesquisa em Gastroenterologia - UFC





Souza MAN et al. Neurogastroenterol Motil 2016; 1–8

Anatomical and functional deficiencies of the crural diaphragm in patients with esophagitis

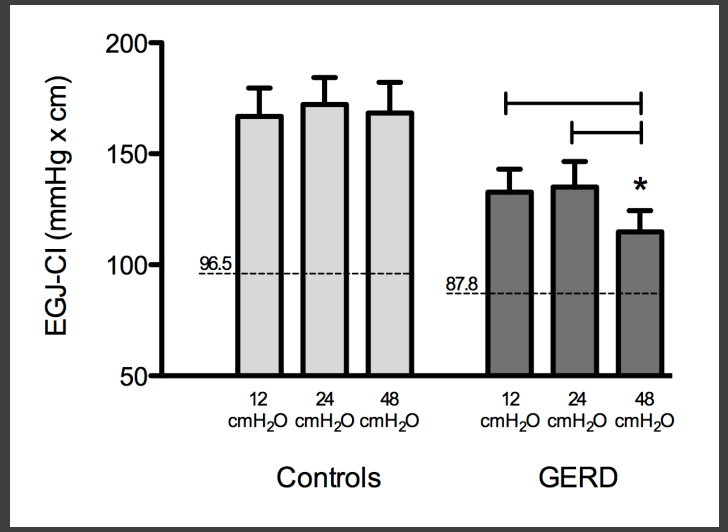
TABLE 3 The EGJ motility deficit in esophagitis patients is unveiled by respiratory maneuvers under increasing inspiratory loads

		Inspiratory load		
Parameter	**Group**	**TH12**	**TH24**	**TH48**
EGJ-CI (mm Hg×cm)	Controls	166.9 ± 12.7	172.2 ± 12.2	168.4 ± 13.8
	Esophagitis	132.8 ± 10.3[a]	135.1 ± 11.4[b]	114.8 ± 9.6[c]
EGJ total activity (mm Hg×cm)	Controls	1270 ± 70.6	1338 ± 80.8	1280 ± 72.5
	Esophagitis	1282 ± 110.4	1241 ± 91.6	1065 ± 73.2[d]

[a]*P* = .06.
[b]*P* = .041.
[c]*P* = .006.
[d]*P* = .049.
Mean ± SEM; two-tail, unpaired *t*-test between controls (n=30) and esophagitis (n=20).
EGJ, esophagogastric junction; SAM, sinus arrhythmia maneuver; TH, threshold maneuver under 12, 24, or 48 cmH_2O inspiratory loads.

Souza MAN et al. Neurogastroenterol Motil 2016; 1–8

Anatomical and functional deficiencies of the crural diaphragm in patients with esophagitis



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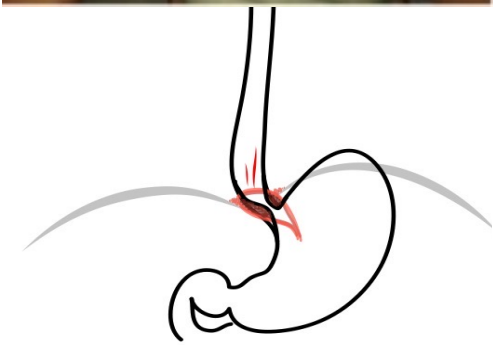
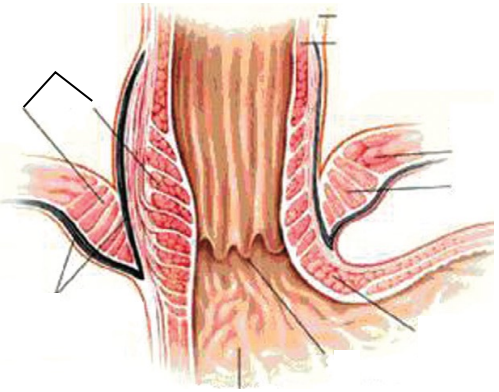




Inspiratory muscle training improves antireflux barrier in GERD patients

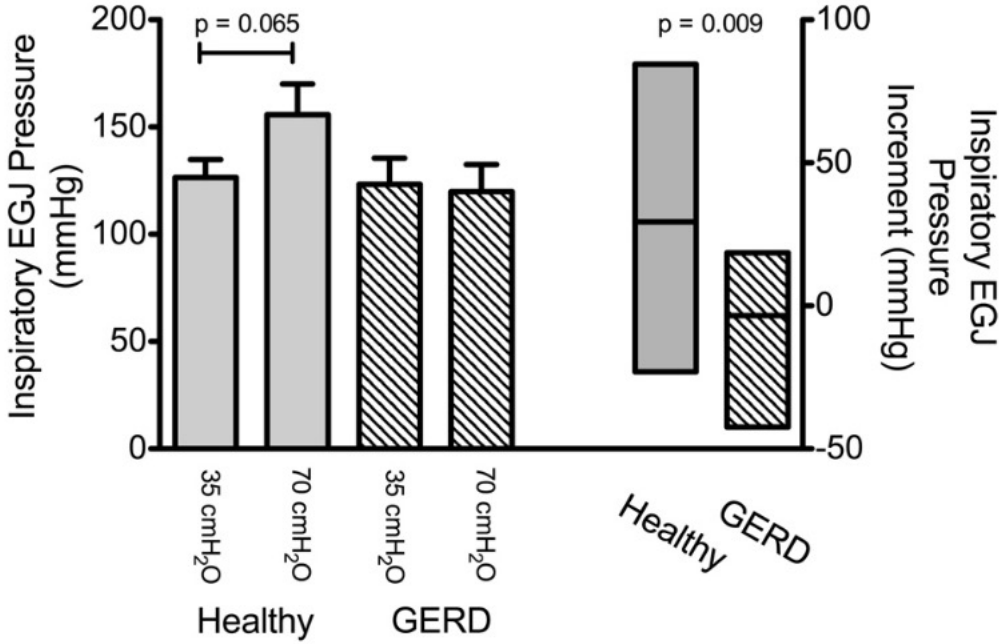


Fig. 3. Increasing inspiratory load from 35 to 70 cmH_2O yielded a greater inspiratory EGJ pressure in the healthy group but not in the GERD one (bars at *left*). The increment in inspiratory EGJ pressure across the 35- and the 70-cmH_2O loads was significantly higher for the healthy group (floating bars at *right*). Data are means ± SE at the bars (paired *t*-test) and minimum, maximum, and mean at the floating bars (unpaired *t*-test).

Souza et al. Am J Physiol Gastrointest Liver Physiol 305: G862–G867, 2013

Inspiratory muscle training improves antireflux barrier in GERD patients

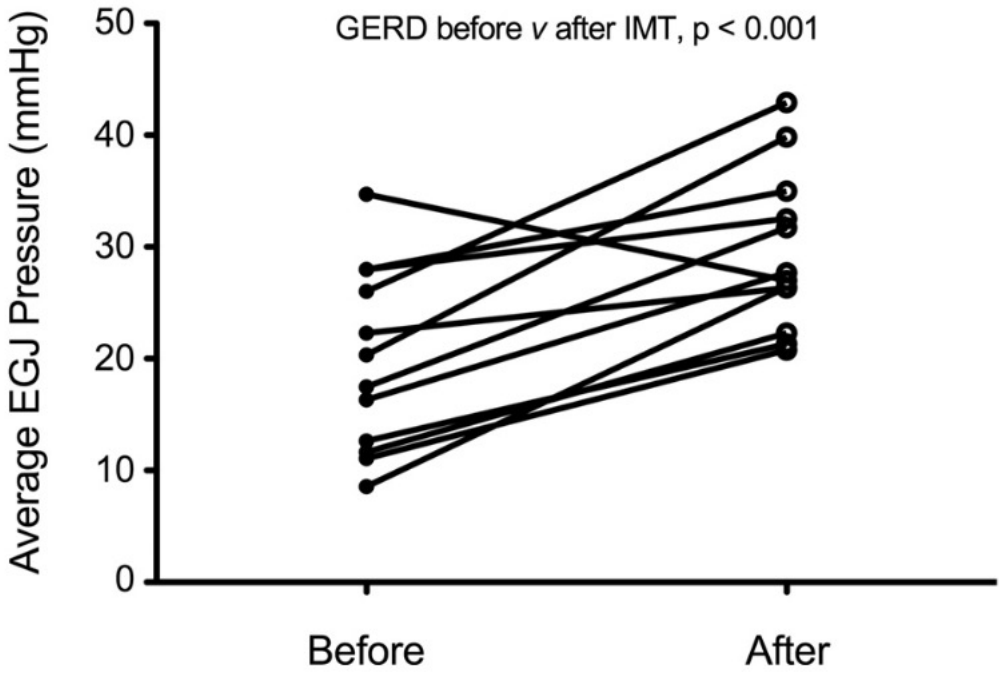


Fig. 1. Average resting esophagogastric junction (EGJ) pressure in gastro-esophageal reflux disease (GERD) volunteers increased significantly after inspiratory muscle training (IMT). EGJ pressure was the average of inspiratory and expiratory pressures during a 15-s swallow-free period (paired *t*-test).

Souza et al. Am J Physiol Gastrointest Liver Physiol 305: G862–G867, 2013

Inspiratory muscle training improves antireflux barrier in GERD patients

Table 1. *Inspiratory EGJ pressures across inspiratory loads of 17, 35, and 70 cmH_2O increased significantly after IMT*

Inspiratory Load	Healthy Volunteers (n = 7): EGJ pressure (No IMT)	GERD Volunteers (n = 12): EGJ Pressure (IMT)		
		Before	After	P
17 cmH_2O	137.3 ± 16.2	110.9 ± 11.5	141 ± 11.3	0.002
35 cmH_2O	120.2 ± 6.5	123.3 ± 12.2	148.6 ± 10.6	0.015
70 cmH_2O	154 ± 16.4	119.9 ± 12.6	149.2 ± 10.1	0.008

Values are means ± SE. IMT, inspiratory muscle training; GERD, gastroesophageal reflux disease; EGJ, esophagogastric junction. P values before vs. after IMT by paired t-test.

Souza et al. Am J Physiol Gastrointest Liver Physiol 305: G862–G867, 2013

Inspiratory muscle training improves antireflux barrier in GERD patients

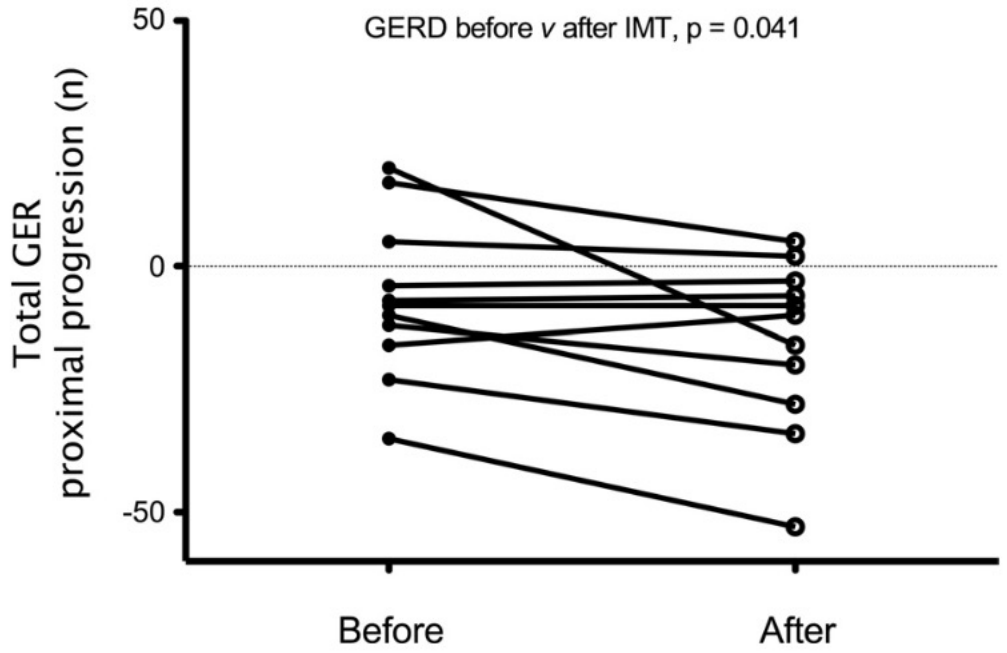


Fig. 4. Total GER proximal progression decreased significantly after IMT. Data presented as the difference between the number of proximal reflux and nonprogressing reflux (paired *t*-test).

Souza et al. Am J Physiol Gastrointest Liver Physiol 305: G862–G867, 2013

Effects of Diaphragmatic Breathing on the Pathophysiology and Treatment of Upright Gastroesophageal Reflux: A Randomized Controlled Trial

Halland, Magnus MD[1,2]; Bharucha, Adil E. MD[1,2]; Crowell, Michael D. PhD[1,2]; Ravi, Karthik MD[1,2]; Katzka, David A. MD[1,2]

Author Information

The American Journal of Gastroenterology 116(1):p 86-94, January 2021. | ***DOI:*** 10.14309/ajg.0000000000000913

Positive Effect of Abdominal Breathing Exercise on Gastroesophageal Reflux Disease: A Randomized, Controlled Study

Eherer, A J MD[1]; Netolitzky, F[1]; Högenauer, C MD[1]; Puschnig, G[1]; Hinterleitner, T A MD[1]; Scheidl, S MD[2]; Kraxner, W MD[1]; Krejs, G J MD[1]; Hoffmann, Karl Martin PD, MD[3]

Author Information

American Journal of Gastroenterology 107(3):p 372-378, March 2012. | ***DOI:*** 10.1038/ajg.2011.420

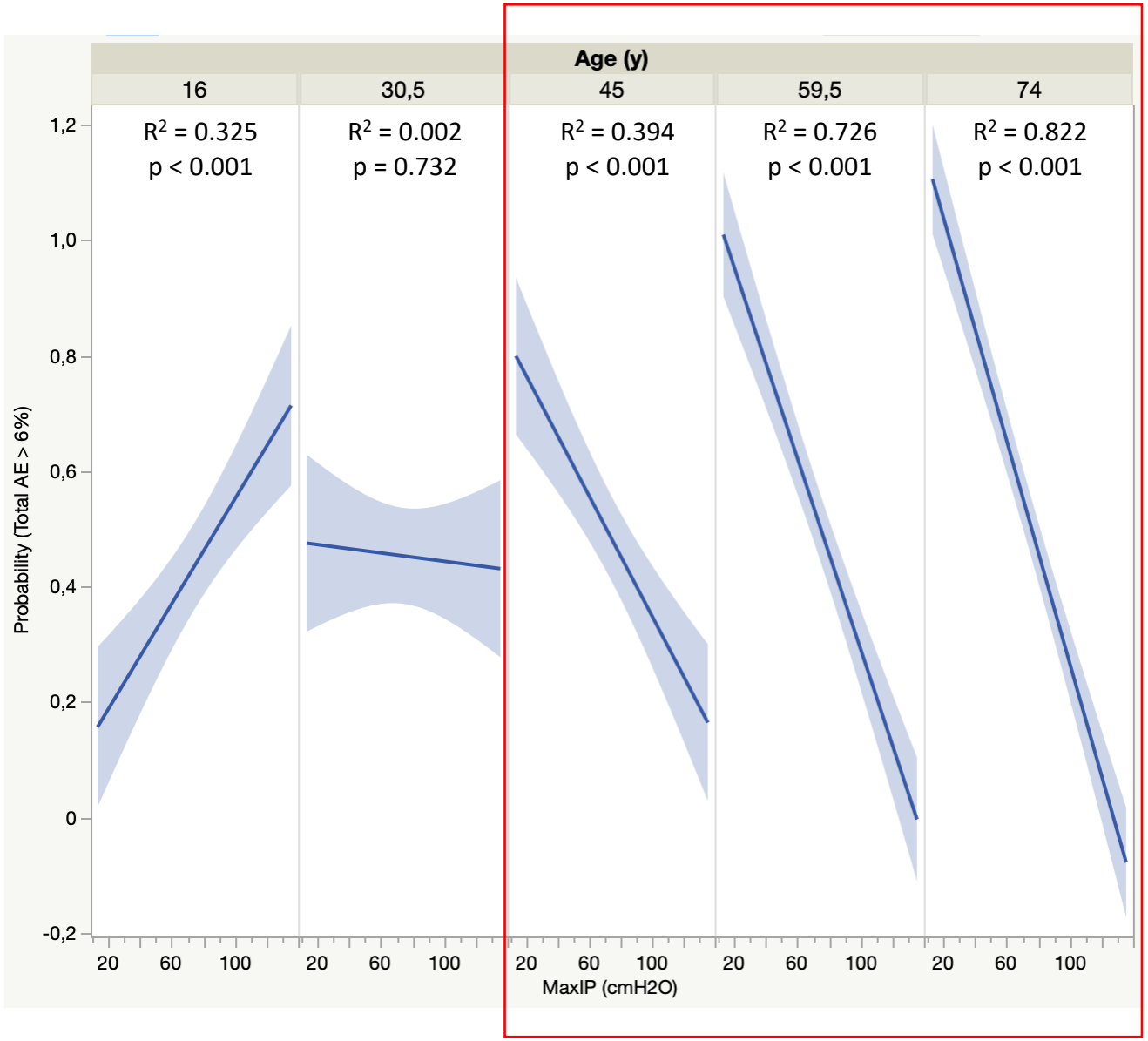
Respiratory physiotherapy can increase lower esophageal sphincter pressure in GERD patients

Renata Carvalho de Miranda Chaves [1], Milena Suesada, Fabiane Polisel, Cláudia Cristina de Sá, Tomas Navarro-Rodriguez

Affiliations + expand

PMID: 23026445 DOI: 10.1016/j.rmed.2012.08.023

Distal esophageal acid exposure is associated with inspiratory oral pressure, a measurement of the diaphragm strength, particularly with ageing



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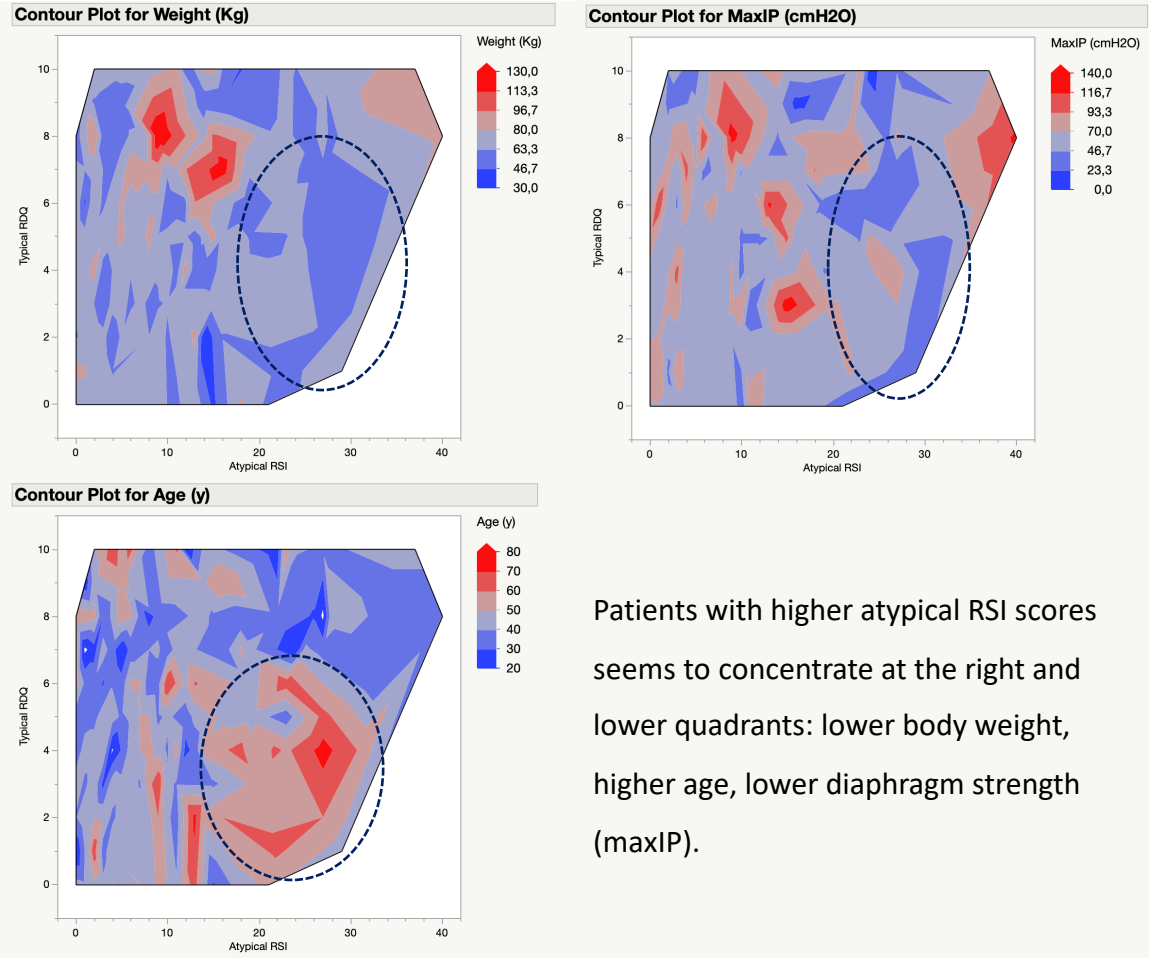
Surface plots of body weight, age, and MaxIP in the domains of typical and atypical symptoms of GERD



Patients with higher atypical RSI scores seems to concentrate at the right and lower quadrants: lower body weight, higher age, lower diaphragm strength (maxIP).

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Atypical GERD symptoms scores are higher in the patients with low MaxIP.

The Lo-maxIP cluster had a higher atypical RSI score (p = 0.01) and a lower BW (p = 0.006) than the Hi- maxIP one.

Individual RDQ or RSI symptoms not shown in the table were not different between the groups.

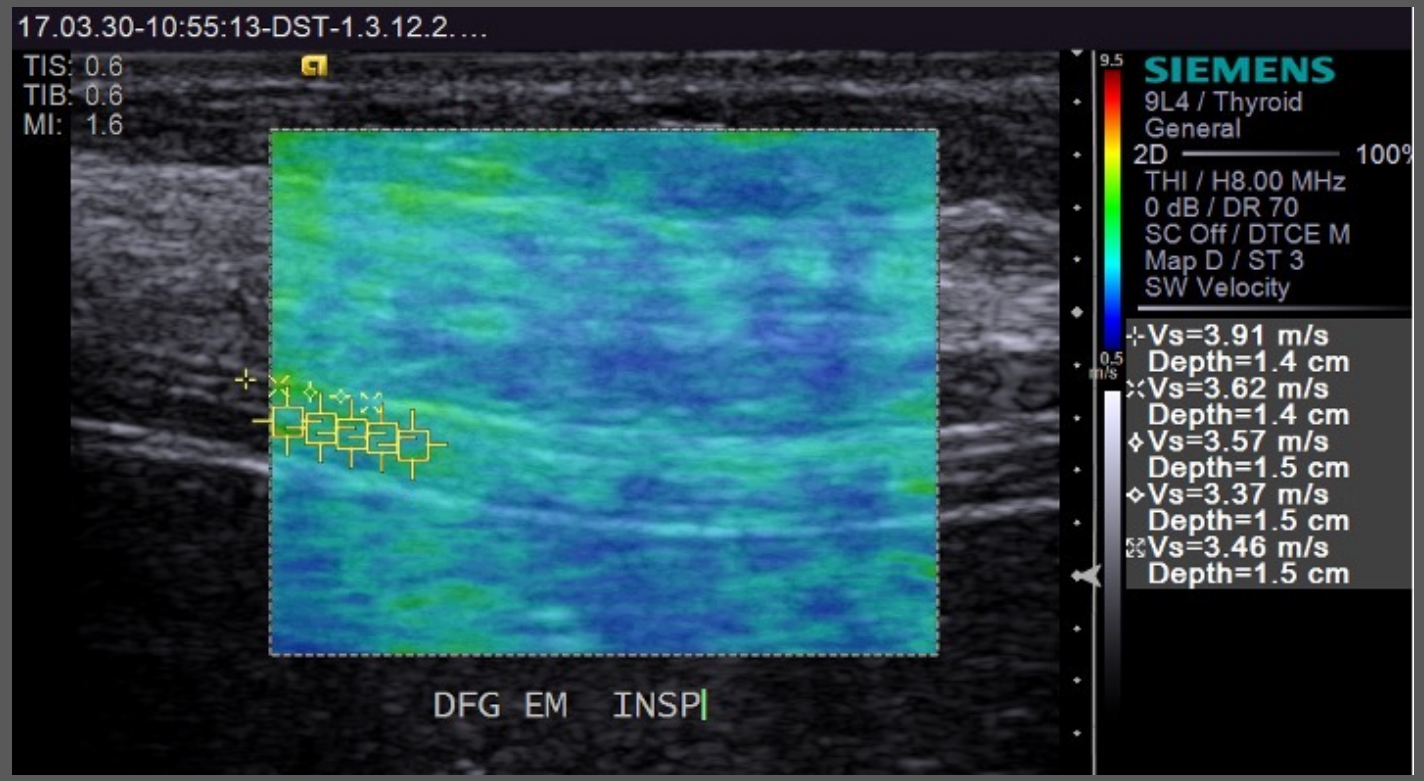
Symptom	Low maxIP n = 464	High maxIP n = 152	p
Age	45.9 ± 14.9	39.3 ± 11.3	<0.01
BW	68.3 ± 16.2	73.2 ± 19.7	<0.01
RDQ	6 (0 - 18)	5 (0 – 16)	0.34
Typical RDQ[1]	2 (0 – 7)	1.5 (0 – 7)	0.91
Dyspepsia RDQ[2]	3 (0 – 8)	2 (0 – 7)	0.05
Atypical RSI[3]	4 (0 – 15)	2 (0 – 14)	0.01
Excess throat mucus	0 (0 – 3	0 (0 – 2)	0.02
Difficulty swallowing	0 (0 – 3	0 (0 – 2)	0.06
Breathing difficulties	0 (0 – 2)	0 (0 – 1.7)	0.01

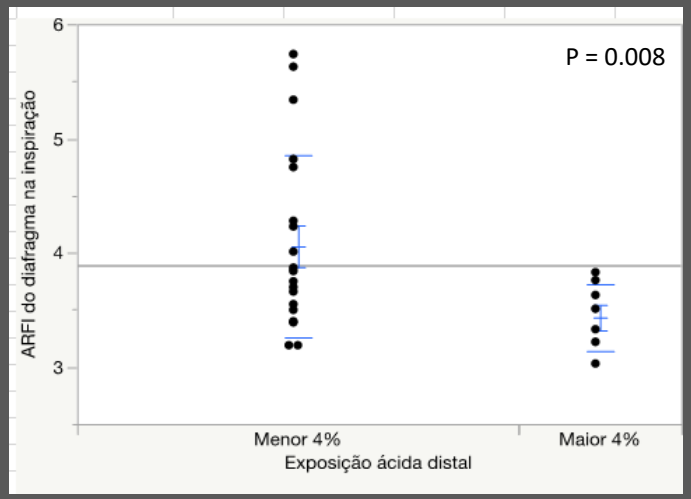
[1] Heartburn + Regurgitation; [2] Epigastric burning + pain
[3] Without heartburn, regurgitation, chest pain, indigestion
maxIP – maximal inspiratory pressure; BW – body weight
Mean ± SD; median (percentile10 – percentile90)

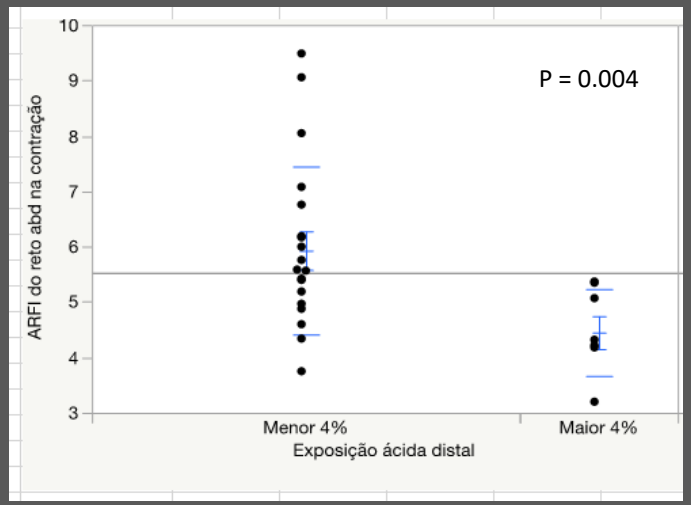
Souza, MAN et al. DDW 2022

DDW2023
Digestive Disease Week®
MAY 6-9, 2023 | CHICAGO, IL
EXHIBIT DATES: MAY 7-9, 2023

ELDERLY SUBJECTS WITH HIGHER DISTAL ESOPHAGEAL ACID EXPOSURE HAVE DIAPHRAGM AND RECTUS ABDOMINIS MUSCLES WEAKNESSES







Valores normais da motilidade esofágica após cirurgia antirrefluxo

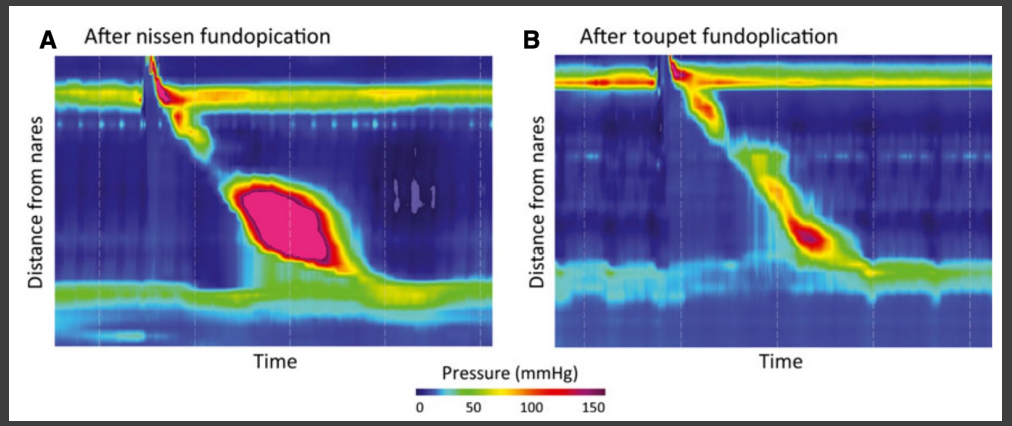


Table 1 Normal values of UES and EGJ parameters after fundoplication

	After Toupet fundoplication					After Nissen fundoplication						
				Percentiles					Percentiles			
	Mean	SD	Median	5th	95th	Mean	SD	Median	5th	95th	*p*-value	5th–95th Chicago*
UES												
UES resting pressure (mmHg)	88.1	53.5	79.7	19.9	243.0	64.3	27.9	59.2	31.4	121.9	0.08	26.3–85.1
UES residual pressure (mmHg)	1.4	4.2	1.9	−7.0	11.3	2.6	4.0	1.4	−3.2	11.2	0.32	0.1–11.9
EGJ												
EGJ length (cm)	3.9	0.8	3.9	2.0	5.1	3.9	0.7	4.0	2.4	5.3	0.96	n.a.
EGJ intra-abdominal length (cm)	2.7	1.1	2.8	0.1	4.4	2.7	0.8	2.8	0.1	4.0	0.91	n.a.
EGJ resting pressure (mmHg)	12.7	5.7	12.1	3.1	26.4	19.0	8.3	18.2	1.5	34.0	<0.01	5–31.6
IRP (mmHg)	7.4	2.9	7.2	3.1	15.0	13.0	4.7	13.0	5.1	24.4	<0.01	<14.7
IBP average max (mmHg)	13.7	3.4	13.7	8.6	21.5	15.2	3.6	14.6	9.9	22.6	0.18	<15
IBP at LESR (mmHg)	1.9	3.5	2.9	−4.6	8.3	5.6	5.2	6.0	−7.8	13.2	<0.05	n.a.

- ✓ Após fundoplicatura:
- ✓ Pjeg média com valores normais;
- ✓ IRP maior

Weijenborg et al. Neurogastroenterol Motil 2015; 27:929–935.

JEG antes e após Nissen
Manometria de alta resolução

Table 3. Esophagogastric Junction Profile Pressures and Esophageal Motility by High-resolution Manometry in Pre- and Post-operative Patients.

	Normal values range	Pre-operative patients (n = 25) median (IQR) [minimum-maximum]	Post-operative patients (n = 25) median (IQR) [minimum-maximum]	*P*-value[a]
Mean basal EGJ pressure (mmHg)	10-35	10.0 (5.7-15.6) [−4.8-39.9]	15.8 (10.2-23.7) [5.2-57.0]	< 0.05
Minimal basal EGJ pressure (mmHg)	4.8-32.0	1.8 (−1.1-6.5) [−11.2-11.0]	7.3 (4.6-13.9) [−0.3-42.0]	< 0.001
IRP (mmHg)	< 15	2.0 (0.0-3.3) [−2.9-10.9]	6 (2.9-11.4) [0.1-38.9]	< 0.001
IBP (mmHg)	< 15	10.0 (6.2-14.1) [0.3-33.3]	13.9 (11.7-20.8) [3.7-49.9]	< 0.05
DCI (mmHg·sec·cm)	500-4300	859.0 (430.0-1574.0) [94.0-3204.0]	1008.0 (725.0-1968.0) [278.0-4439.0]	< 0.05
CFV (cm/sec)	2.6-5.3	4.3 (3.1-5.4) [2.4-16.5]	2.9 (2.0-4.0) [1.1-7.5]	< 0.01
Double-peaked waves (%)	≤ 15	0.0 (0.0-0.0) [0.0-22.0]	10.0 (0.0-20.0) [0.0-78.0]	< 0.01
Mean wave duration (sec)	2.7-5.4	3.1 (2.6-3.9) [2.2-5.3]	3.5 (3.2-4.7) [2.3-8.0]	< 0.01
Hiatal hernia by HRM		11 (44%)	0 (0%)	

[a]Wilcoxon test.
IRQ, interquartile range; EGJ, esophagogastric junction; IRP, integrated relaxation pressure; IBP, intra-bolus pressure; DCI, distal contractile integral; CFV, contractile front velocity; HRM, high-resolution manometry.

Katarzyna et al. J Neurogastroenterol Motil 2017; 23(1):55-63.

A pressão basal (média) e o IRP aumentam após fundoplicatura

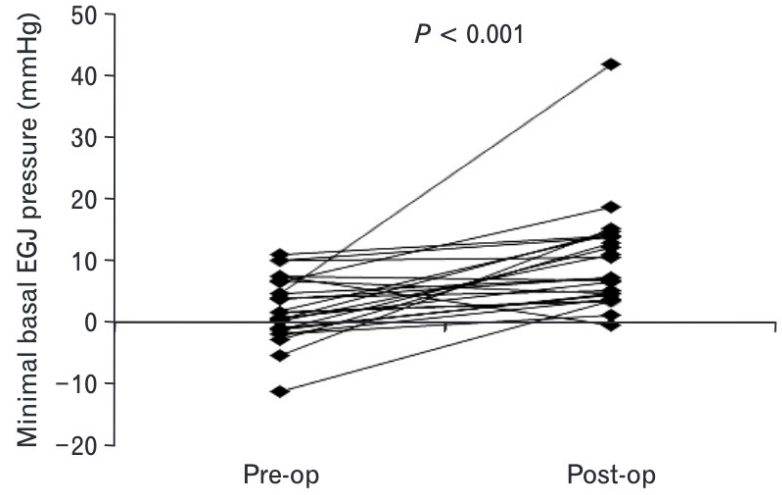


Figure 1. Individual changes of minimal basal esophagogastric junction (EGJ) pressure in pre-operative (pre-op) and post-operative patients (post-op): in 22 patients increase while in 3 patients decrease of minimal basal EGJ pressure were shown after fundoplication (normal values range: 4.8-32.0 mmHg).

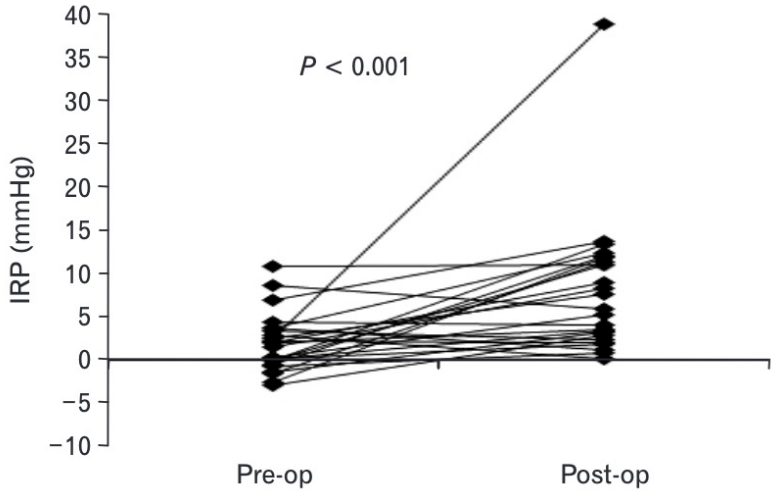


Figure 2. Individual changes of integrated relaxation pressure (IRP) in pre-operative (pre-op) and post-operative patients (post-op): in 19 patients increase while in 6 patients decrease of integrated relaxation pressure were shown after fundoplication (normal values range: < 15 mmHg).

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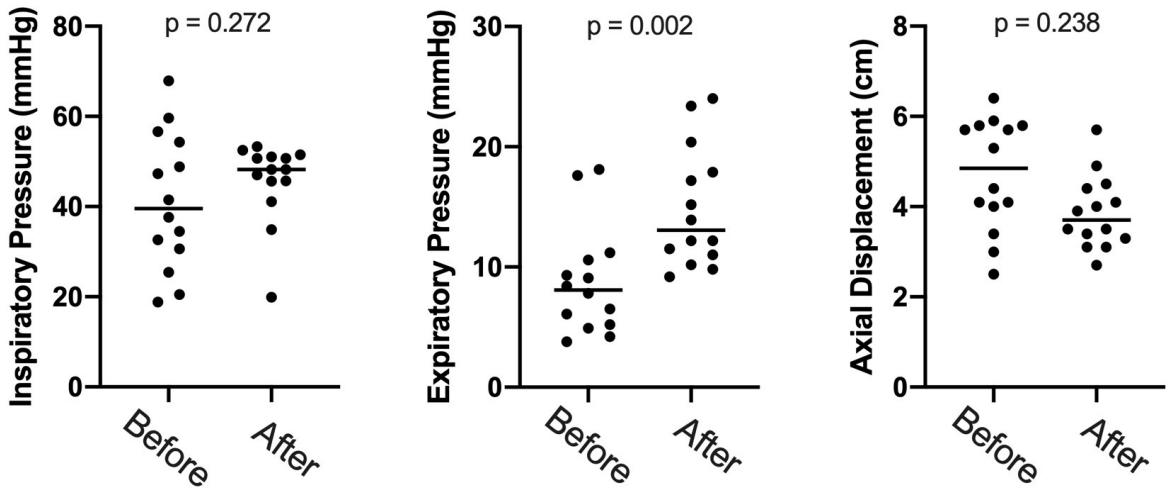
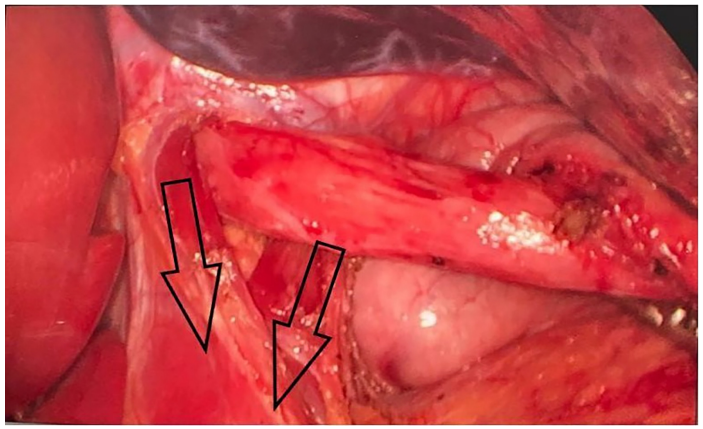
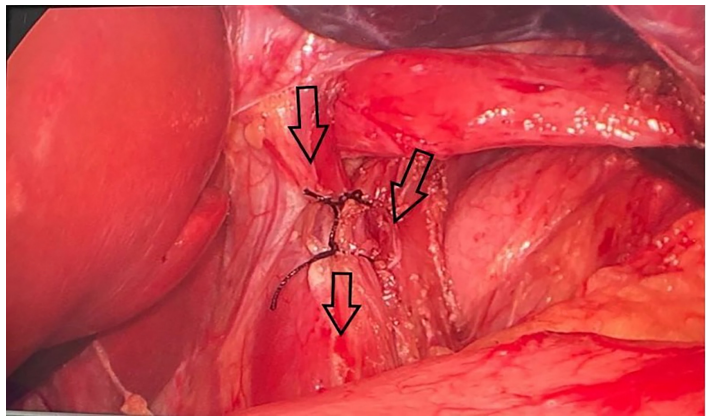
Pressure dynamics of the esophagogastric junction at rest and during inspiratory maneuvers after Nissen fundoplication







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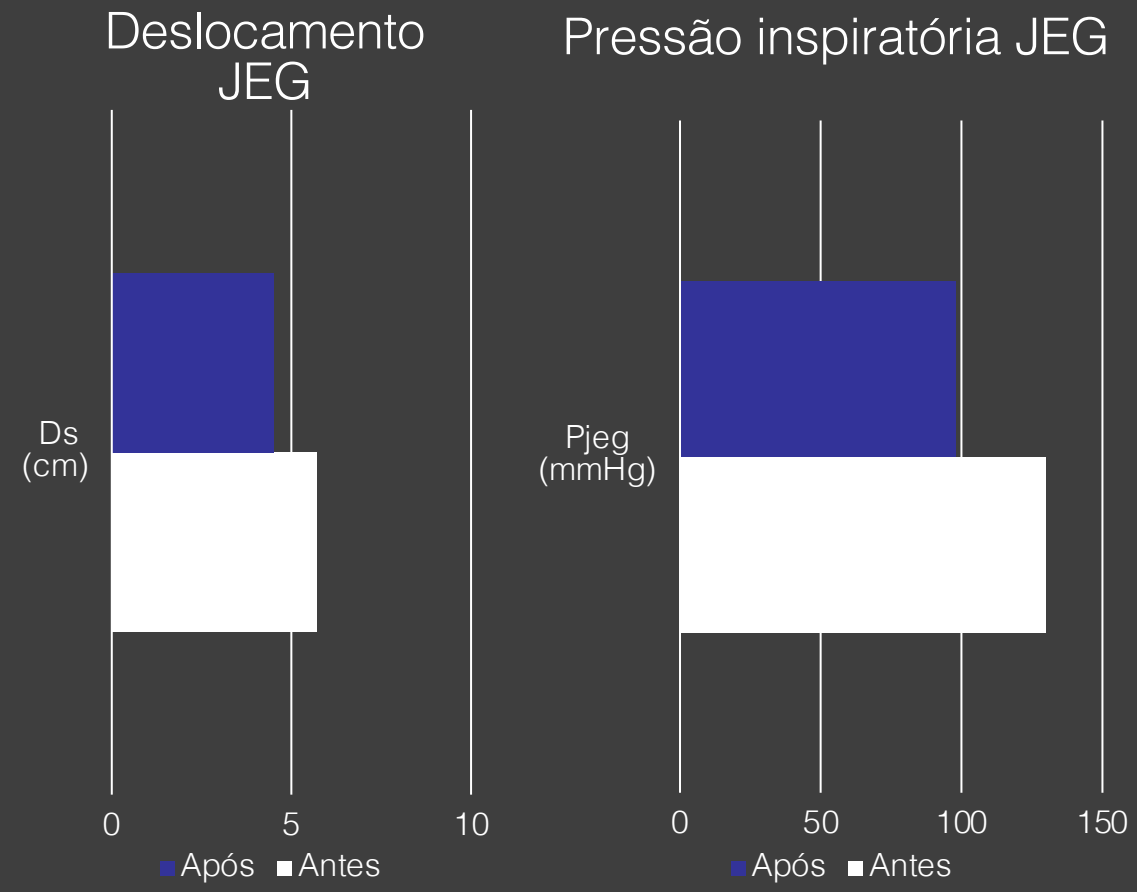
Pressão inspiratória e mobilidade da JEG é menor após Nissen

Table 5. HRM variables assessed during the Threshold Maneuver protocol, before and after NF.

Variables	Before NF Median (min; max)	After NF Median (min;max)	*p* value
Pth12 (mmHg)	145.6 (86.2; 268.1)	102.7 (58.7; 132)	0.004
DSth12 (cm)	5.8 (2.8; 8.9)	5.3 (3.0; 6,8)	0.116
ETAth12 (mmHg.cm)	784.2 (470.8; 1957,1)	530.6 (275.9; 749,3)	0.009
Pth24 (mmHg	134.8 (59.7; 273.3)	98.7 (23.1; 130.8)	0.004
DSth24 (cm)	5.7 (3,4; 9.9)	5.0 (2.8; 7.3)	0.069
ETAth24 (mmHg.cm)	794.8 (202.98; 1694.46)	485.0 (120.1; 661.5)	0.004
Pth36	130.6 (52; 255.5)	91.6 (47.9; 132.0)	0.011
DSth36 (cm)	6.0 (2.7; 10.4)	4.9 (2.7; 6.1)	0.075
ETAth36 (mmHg.cm)	736.3 (140.4; 1839.6)	466.8 (131.5; 739.2)	0.004
Pth48 (mmHg)	129.7 (52.4; 249)	97.9 (44.3; 137.1)	0.011
DSth48 (cm)	5.7 (2.8; 9.5)	4.5 (1.8; 6.5)	0.017
ETAth48 (mmHg.cm)	842.1 (214.8; 1817.7)	393.2 (99.5; 788.4)	0.006

The parameters measured during respiratory the maneuvers (TH) were all inspiratory, under increasing resistances of 12, 24, 36, and 48 cmH_2O (axial displacement – DSth, EGJ pressure – Pth, and EGJ total activity – ETAth).

* The pressure data recorded during the TH maneuver, will be followed by the value of the load set on the device. Example: For load set at 12mmHg, the metric descriptions are DSth12 , Pth12, etc.



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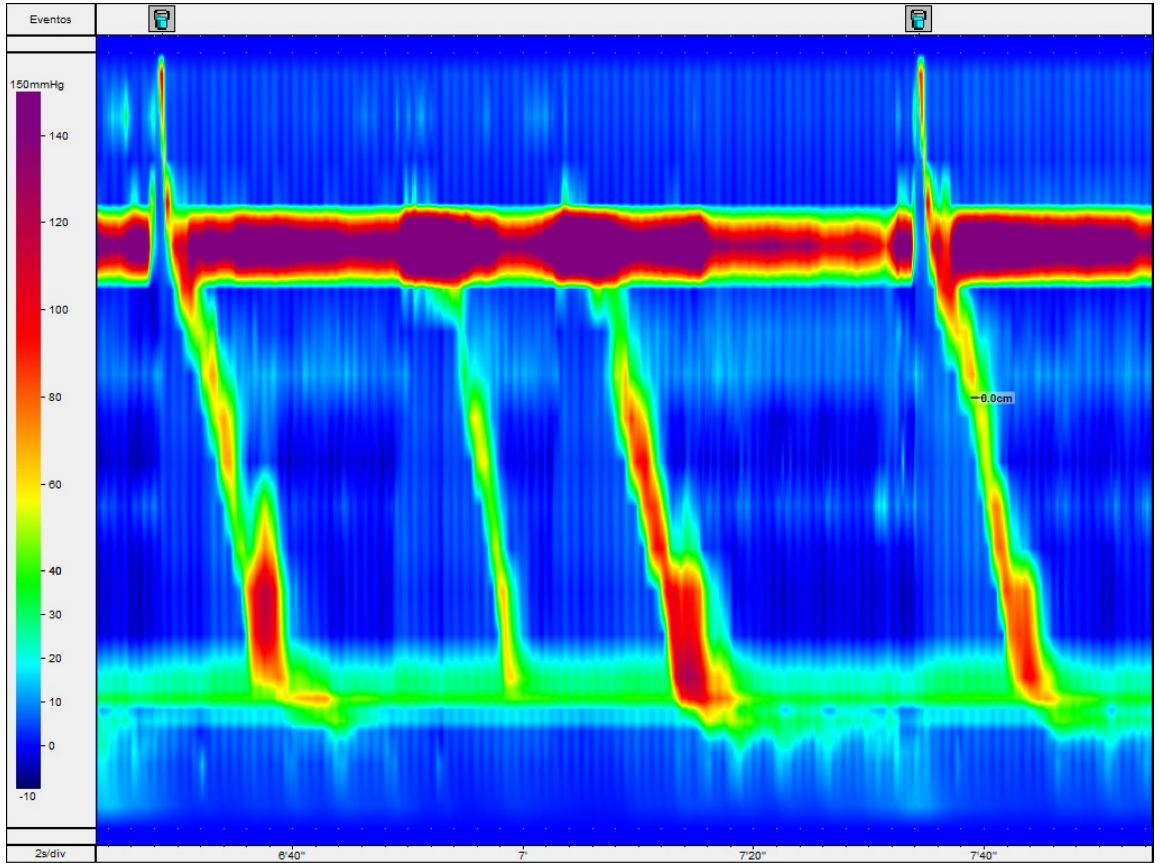
….pós fundoplicatura normal

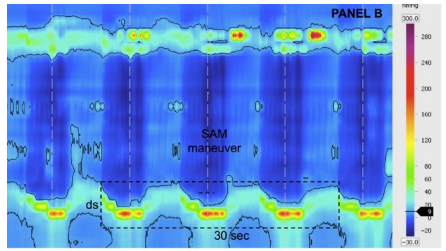


Padrão motor normal:

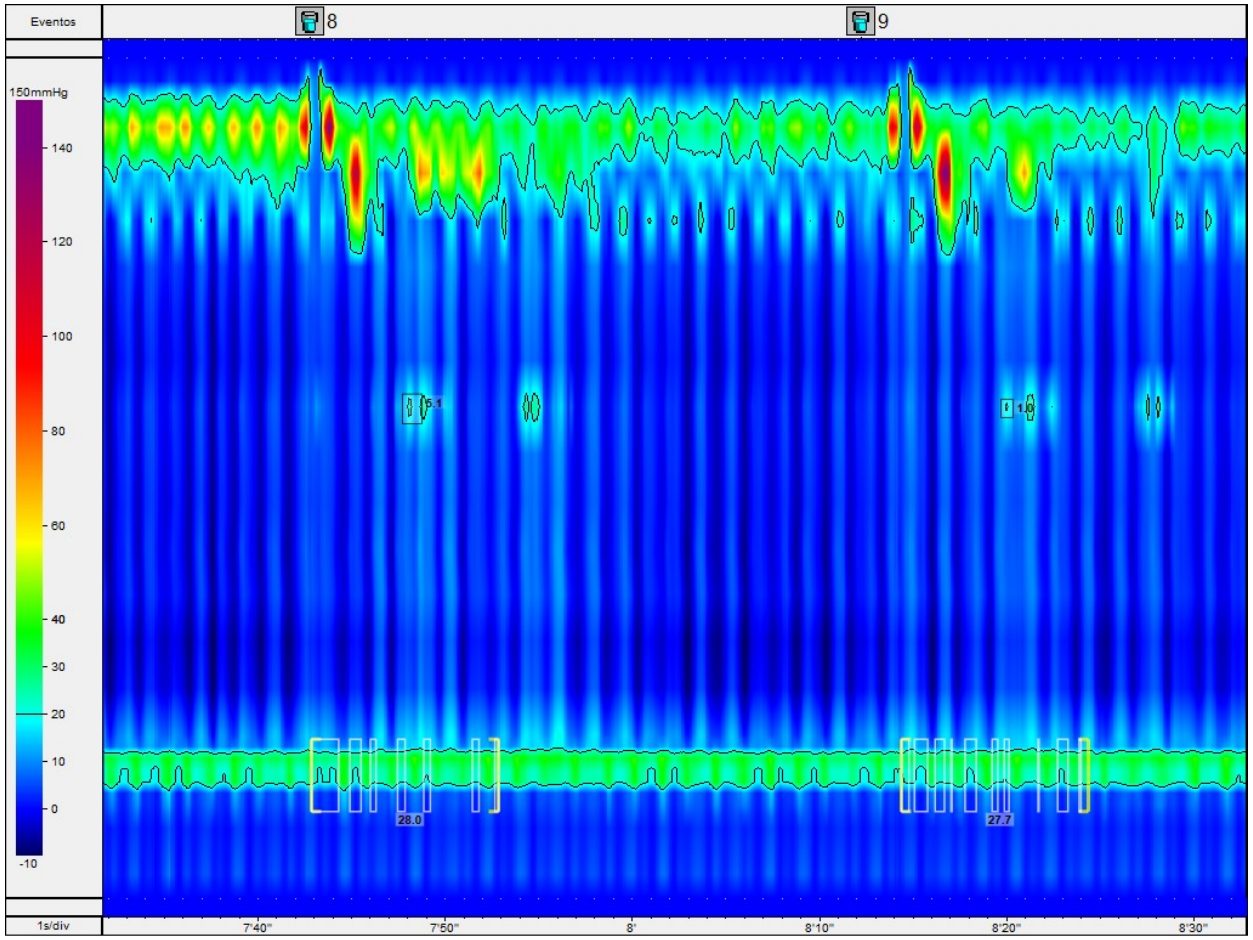
1. Esfincter superior abre;
2. Corpo esofágico com contrações sequenciais;
3. Esfincter inferior não relaxa completamente:
    1. P95 IRP = 25 mmHg

Junção esôfago-gástrica(EGJ) durante manobras inspiratórias:

1. Pressão inspiratória menor;
2. Pressão expiratória maior.



…pós fundoplicatura anormal



Padrão motor anormal:

1. Esfincter superior abre;
2. Corpo esofágico sem atividade motora;
3. Esfincter inferior não relaxa e IRP muito elevado.

Conclusões

- ✓ Conceito novo: deficit diafragmático (inspiratório) na DRGE;
- ✓ A pressão inspiratória da JEG (diafragma) parece prever melhor a presença de DRGE;
- ✓ Um deficit diafragmático e de outros músculos se associam com maior exposição ácida do esôfago, após 40 anos de idade;
- ✓ Um deficit inspiratório se associa mais com sintomas atípicos de DRGE;
- ✓ A pressão expiratória aumenta e o relaxamento da JEG é incompleto após fundoplicatura;
- ✓ A pressão inspiratória e mobilidade da JEG são menores após fundoplicatura;
- ✓ A cirurgia antirrefluxo hipercompensa o deficit de pressão inspiratória.