

esophageal circular smooth muscle tissue constructs were bioengineered using collagen hydrogel. (2) The muscle constructs were placed around a 2.5cm long hollow chitosan tube. (3) Biodegradable surgical glue was applied between the smooth muscle constructs and along their circumference. The constructs were maintained around the scaffold in culture. (4) Semi-solid material was pipetted through the lumen of the tube to check for flow, leakage and muscle integrity. (5) The constructs were taken off and tested for the ability to contract in response to Acetylcholine (ACh) and relax in response to vasoactive intestinal peptide (VIP). Results: (1) The bioengineered 2cm-long esophageal tube construct, maintained its luminal patency and its structural integrity in vitro >1 month. One end of the scaffold was clamped while the other was left intact. The scaffold, with the tissue constructs around it, expanded while pipetting a semi-solid solution through their lumen. The construct was able to restore its original dimensions once the solution was cleared through. No signs of leakage were observed and the tissue constructs did not disrupt due to pressure applied from the semi-solid bolus. (2) Real time force generation was studied on the tissue constructs after being taken off the scaffold. ACh caused a contraction of 45 μ N and VIP caused a relaxation of -35 μ N. Summary: We show the production of an esophageal tissue using a tubular biodegradable scaffold and esophageal smooth muscle cells. The construct was able to withstand the pressure of a semi-solid material pushed through its lumen. Conclusion: We successfully bioengineered a continuous esophageal tube using primary isolated circular smooth muscle cells. The semi-solid material mimicked the texture of a food bolus. This construct could be suitable for esophageal reconstruction. This work was supported by NIH/NIDDK RO1 DK042876.

Su1875

Esophageal Biofeedback Using Balloon Distension of the Esophagus and Swallowing-Related Visual, Olfactory, and Gustatory Stimuli in the Treatment of Severe Dysphagia With Tube Feeding

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INTRODUCTION: It is reported that tactile, gustatory, and visual biofeedback stimuli modulate neural substrates of deglutition (1). And that sacral nerve stimulation initially activates a region of the frontal cortex, which is normally active during focused attention, while subsequent stimuli activate the caudate nucleus, which is involved in learning and reward processing (2). The purpose of this pilot study was to modulate the altered neuronal substrate of swallowing through the stimulation of tensoreceptors with esophageal balloon distention combined with visual, olfactory, and gustatory stimuli in patients with severe dysphagia and feeding tube. **METHODS:** Seventeen patients (43 \pm 13 years) with severe dysphagia (Castell dysphagia severity scale = 6 \pm 2; 1= no dysphagia at any time, 7= unable to eat by mouth) after unsuccessful prior therapies were studied [clinical assessment, dysphagia severity, radiology, endoscopy, and esophageal manometry (MMS, Netherlands)] and compared with 12 healthy subjects for manometry studies. **Biofeedback:** 1) Slight inflation of the balloon in the mid esophagus was performed three times in a single session. 2) The patients received a graphic and precise description of how a normal person swallowing mechanism functions. 3) On waking, they rinsed out their mouths with water. 4) Patients were asked to look at, smell, chew and then discharge the food. 5) Then they were asked to try and swallow food while bearing in mind the working of the swallowing system that had been explained to them. Steps 3-4-5 were followed at home, every morning until healing. **Means \pm SD, binominal 95% confidence interval, and nonpaired Student two-tailed t test with alpha=0.05. RESULTS:** All patients recovered completely the mechanism of swallowing in 36.9 \pm 25 (CI: 24-49) days. The 3 patients who were initially feeding tube dependent progressed to total oral intake after 13 \pm 10.5 (CI: -1.6-27.6) days of treatment. Patients with dysphagia compared with healthy subjects showed impaired peristalsis (p=0.008), lesser esophageal medial amplitude [47 \pm 21 (CI: 35-59) Vs. 88 \pm 54 (CI: 57-119) mmHg, respectively; p=0.022], and lesser esophageal upper duration [3 \pm 0.7 (CI: 2.5-3.4) Vs. 3.6 \pm 0.5 (CI: 3.3-3.9) s, respectively; p=0.034]. Lower esophageal sphincter pressure was not different between patients with dysphagia (14 \pm 6 (CI: 10.2-17.7) mmHg and healthy subjects (20.8 \pm 11.2 (CI: 14.4-27.2) mmHg, p=0.082. **CONCLUSION:** This successful outcome with our innovative Dysphagia Therapy Program suggests that the stimulation of esophageal tensoreceptors combined with visual, olfactory, and gustatory biofeedback stimuli, can modulate the neural substrates of swallowing reprogramming the physiological mechanism of swallowing in patients with severe dysphagia. **REFERENCES:** (1) Humbert IA et al. *Neuroimage* 2012;59:1485-90. (2) Lundby L et al. *Dis Colon Rectum* 2011;54:318-323.

Su1876

Determination of Normal Esophageal Pressure Responses to a Rapid Multiple Swallow Challenge Test. Results of a Multicenter Study in Healthy Volunteers

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Recent studies have suggested that a rapid multiple swallow challenge test can detect motor abnormalities not detected during conventional high resolution esophageal manometry (Marin et al. *Gut* 2012;61:A424). However, data of normal manometric values using this test is scarce. **AIM:** To determine normal values of a rapid multiple swallow challenge test performed in sitting position in healthy volunteers using high-resolution esophageal manometry. **METHODS:** 57 healthy volunteers (28 female, 29 male, age range 18-68 yrs) were recruited from seven centers from Europe and America. In each subject we evaluated the responses to rapid drink of 200 ml of water with a straw in sitting position, performed immediately after the standard protocol of high resolution esophageal manometry. In each subject we evaluated the time and the number of pharyngeal swallows required to drink 200 ml of water, lower esophageal sphincter (LES) pressure and esophageal body pressure during and after swallow, and esophago-gastric pressure gradient during swallow. Perception of esophageal symptoms was assessed by a 1-4 questionnaire. Results are expressed as mean \pm SD **RESULTS:** Subjects needed 14.0 \pm 5.5 pharyngeal swallows during 25.4 \pm 10.8 seconds to drink 200 ml of water. During that period, there was a general inhibition of esophageal pressures, both LES (mean IRP -1.4 \pm 3.0 mmHg) and esophageal body pressures

(Only 5 % of healthy subjects had two or more brief pressure episodes >20 mmHg, longer than 3 cm, duration 1.3 \pm 0.7 sec) resulting in a low esophago-gastric pressure gradient (-2.07 \pm 3.22 mmHg). 2.0 \pm 3.4 sec after the last swallow 23 % of subjects had a normal peristaltic contraction, whereas 75 % had no contraction and 2 % had a simultaneous contraction LES pressure returned to pre-swallow levels (-1.0 \pm 12.0 mmHg greater than pre-swallow; p=0.535) immediately after swallow cessation. Only 13 % of subjects reported mild symptoms (score 1.8 \pm 1.5), mainly dysphagia 25 % and chest pain 75 % **CONCLUSION:** Rapid multiple swallow of 200 ml of water in sitting position may be a well tolerated, easy to perform challenge test of esophageal function. It is characterized by inhibition of esophageal LES and body pressures during swallow, and either no contractile post-swallow activity, or a normal post-swallow peristaltic contraction.

Su1877

Chicago Classification Normal Reference Range Significantly Altered When Patients Over Age 50 Included

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Background: High-resolution Manometry (HRM) based on spatiotemporal plots is increasingly replacing conventional manometry based on linear waves. Chicago classification based on its characteristic parameters including integrated relaxation pressure (IRP) and distal contractile integral (DCI) showed higher diagnostic value than the previously used conventional criteria. However, the current normal cut-off values used by the Chicago classification system are based on a limited sample of individuals from 19 to 48 years of age without considering the elderly. Therefore, we aimed to investigate the normal values for Chicago classification across a more diverse age spectrum from 20 to 67 years of age. Then, we compared the difference between the young and older age groups. **Methods:** From March to September 2012, 54 asymptomatic healthy people (M:F=27:27, age:20-67) were prospectively enrolled in this study based on their responses to the ROME III questionnaire. To evaluate the influence of age and sex on manometric profiles, we attempted to enroll the same number of subjects of each sex within each decade. A HRIM catheter with 32 circumferential pressure and 16 impedance sensors was used. The manometry profiles were analyzed by one investigator using Bioview software. **Results:** Fifty-four subjects with 10 swallows each constituted the final sample (a total of 540 swallows). Mean IRP and DCI were 2.98 \pm 2.33 mmHg and 1051.69 \pm 1002.16 mmHg \cdot s \cdot cm, respectively. Mean distal latency (DL) and contractile front velocity (CFV) were 7.00 \pm 0.81 sec and 4.14 \pm 1.01 cm/sec, respectively. Comparison of those \leq 50 years (n=42, M:F=22:20, mean age=33 \pm 9 years old) and those > 50 years (n=12, M:F=5:7, age=57 \pm 5 years old) revealed a higher mean IRP (4.61 \pm 2.56 mmHg in >50 years vs. 2.52 \pm 2.06 mmHg in \leq 50 years old, P<0.01) and DCI (1856.77 \pm 1530.60 mmHg \cdot s \cdot cm in > 50 years vs. 821.67 \pm 652.56 mmHg \cdot s \cdot cm in \leq 50 years old, P=0.02) in the > 50 years old group. Moreover, DL showed a tendency to be longer in the \leq 50 years old group (7.11 \pm 0.84 sec in > 50 years vs. 6.63 \pm 0.57 sec in \leq 50 years old, P=0.06). However, there was no significant difference in CFV between the two groups. No significant difference was found between males and females. **Conclusions:** The key parameters determining the Chicago classification are affected by age, especially IRP and DCI. Larger prospective studies including the elderly are needed to provide age relevant normative values for the Chicago Classification system.

Su1878

Normal Values Determination for High Resolution Esophageal Manometry Using Sitting Viscous Solution Swallows. Results of a Multicenter Study in Healthy Volunteers

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Introduction: It has been suggested that a more physiologic esophageal manometry study protocol, including non-liquid solutions and a sitting position, could improve the test performance. For the specificity determination of putative findings it is necessary to determine normal values **Aim:** To determine normal values for sitting viscous solution swallows in healthy volunteers using high-resolution esophageal manometry (HREM) **Methods:** Healthy volunteers were recruited from seven centers in Spain and America. Sitting swallows with an apple sauce-like standardized solution were analyzed using HREM. Analysis was performed as recommended by Bredenoord et al in the last Chicago classification revision (*Neurogastroenterology and Motility* 2012;24(Suppl 1):57). **Results:** 59 volunteers (29 females (48.1%)) with a total of 468 swallows were analyzed. 132 of this swallows (in 18 volunteers) were analyzed using impedance and HREM. 47 volunteers had at least 7 evaluable swallows, so that the whole study could be diagnosed using the Chicago classification. Mean age was 34 years (18-68 years). Table 1 shows results for significant variables. None of them demonstrated any gender-related difference. Using the aforementioned Chicago classification for whole study, 26/47 (55.3%) were classified as normal, 7/47 (14.9%) as weak peristalsis with small defect, 7/47 (14.9%) as weak peristalsis with large defects, 5/47 (10.6%) as frequent failed peristalsis, 1/47 (2.1%) as EGJ outflow obstruction and 1/47 (2.1%) as rapid contractions with normal latency. 88/132 (66.6%) of swallows evaluated with impedance showed complete bolus transit. 13/18 (72.2%) volunteers showed at least one swallow with incomplete bolus transit. Using Chicago single swallow classification, 78/83 (93.9%) of normal, 4/11 (36.4%) of small break, 6/19 (31.6%) of large break and 0/19 of failed peristalsis showed complete bolus transit, respectively. There was a significant difference in bolus transit when comparing normal to non-normal swallows (p<0.001), but not when comparing small to large breaks (p=1). **Conclusion:** Normal values have been determined. Remarkably, upper limit of CFV and lower limit of DL are higher than normal values previously described for supine-water swallows. On the other hand, upper limit for DCI seems much lower. Impedance information suggests that even in a sitting position, normal peristalsis is still a significant predictor of bolus transit. Any functional relevance of the small and large breaks distinction could not be demonstrated.

Variable	Mean +/-Standard Deviation	Percentile 5	Percentile 95
EGJ basal pressure (mean)	20.16 +/- 11.79 mmHg	4.93 mmHg	44.5 mmHg
EGJ pressure (respiratory minimum)	12.07 +/- 10.76 mmHg	-0.67 mmHg	36.34 mmHg
Integrated relaxation period 4 seconds (IRP 4s)	4.76 +/- 4.28 mmHg	-0.8 mmHg	12.75 mmHg
Gap number	0.59 +/- 0.47	0	1.4
Contractile velocity front (CVF)	4.66 +/- 2.52 cm/s	2.35 cm/s	11.67 cm/s
Distal latency (DL)	6.81 +/- 0.99 s	5.50 s	8.96 s
Distal Contractile Integral (DCI)	1082.02 +/- 804.38 mmHg/cm/s	26.32 mmHg/cm/s	2948.55 mmHg/cm/s

Su1879

Lymphocytic Esophagitis With or With No Apoptoses: Two Unequal Subgroups in the Wide Ranging Concept of Lymphocytic Esophagitis

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BACKGROUND & AIMS: Lymphocytic esophagitis is ill defined and lymphocyte-rich inflammatory lesions of esophageal squamous epithelium are believed to show non-specific histological changes. This study was performed to investigate the histological and molecular criteria in lymphocytic esophagitis. **METHODS:** We collected 33 biopsies from 28 patients with lymphocytic esophagitis, which were diagnosed between 2010 and 2012 (17 men and 11 women, mean age = 60.8 and 61.1 years, respectively). Grading was performed by the number of lymphocytes (50/HPF cut off value) and according to Purdy et al. The inflammatory infiltrate was characterized by using the XTRACT robot (STRATIFYER, Cologne, Germany), quantitative real-time-PCR (FOXP3, CXCL9, CXCL13, IGHM, CD3, CD4 and CD8) and immunohistochemistry (CD4, CD8, TIA, GranzymB and Caspase 3). Spearman rank test was used to calculate the correlation between these parameters. **RESULTS:** Apoptoses could be detected in 83% of severe cases (15/18) and in 47% of mild cases (7/15) without differences between the two grading systems. High levels of cytotoxic T-cells were present in 80% of severe cases with apoptoses (12/15) and in 5 cases without visible apoptoses in H&E stain, mostly mild cases. The overall number of lymphocytes correlated with the number of apoptoses (p = 0,002) and the number of CD8 positive lymphocytes (p = 0,005). Cases with apoptoses showed high levels of CD8 positive lymphocytes. A positive correlation between spongiosis and levels of cytotoxic T-cells could be demonstrated (p = <0,0001). Evaluation of clinical data revealed a correlation between high levels of cytotoxic lymphocytes and a wavy mucosal surface (p = 0,025), reddening of esophageal epithelium (p = 0,017) and a stipplelike exudate (p = 0,015). Within the group with apoptoses a strong correlation between cytotoxic T-cells (= CD8) and regulatory T-cells (= FOXP3) (p = <0,0001) was found. Expression of CXCL9 correlated with the expression of CD4 and CD8 (p = 0,05 and p = 0,0042, respectively). **CONCLUSIONS:** Our data suggest that the term "lymphocytic esophagitis" should only be used as an umbrella-term in several diseases and therefore we suggest "lymphocyte-rich esophagitis" to be used for further subdivisions. Two different subgroups of this lymphocyte-rich variant of chronic esophagitis can be distinguished: Lymphocyte-rich esophagitis with apoptosis (LEA) and lymphocytic esophagitis with no apoptosis (LENA). Apoptotic keratinocytes are useful in grading LEA, as they can be found in large numbers predominantly in severe forms. The number and localization of apoptoses distinguishes esophageal Crohn's disease and lichen planus from LEA. Further studies should focus on the question, whether our findings are a hint to an autoimmunologic mechanism or not.

Su1880

Achalasia Symptom Response After Heller Myotomy Segregated by Subtypes on High Resolution Manometry (HRM)

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Achalasia has been classified into three subtypes on HRM. Earlier reports suggest incomplete symptom resolution for subtype 1 (absence of pressurization or spastic contractions) and subtype 3 (spastic esophageal body contractions), but a combination of treatment strategies (botulinum toxin injection, pneumatic dilation, Heller myotomy) were utilized. We assessed if symptomatic response varied if only a single treatment strategy, i.e. Heller myotomy, was employed. **METHODS:** Subjects with achalasia on HRM (Given Imaging, Los Angeles, CA) with integrated residual pressure (IRP) >15 mmHg referred for Heller myotomy were eligible for inclusion. Chicago criteria designated achalasia subtypes (subtype 1: no esophageal pressurization; subtype 2: panesophageal pressurization in ≥20% swallows; subtype 3: spastic contractions in ≥20% swallows). Symptom questionnaires assessed severity and frequency of esophageal symptoms (dysphagia, regurgitation, chest pain, heartburn) before and after myotomy on a 5 point Likert scale (0=no symptoms, 4=severe symptoms several times a day); symptomatic state over the previous two weeks were recorded on a 10 point global symptom scale (GSS, 0=extremely dissatisfied, 10=extremely satisfied); satisfaction with surgery was recorded on a similar scale. All subjects underwent Heller myotomy with partial fundoplication. Data were analyzed to determine predictors of GSS improvement. **RESULTS:** Over a 5 year study period, 60 subjects (55.5 ±2.4 yr, 55% F) fulfilled study criteria and completed symptom questionnaires, 9 (15%) with subtype 1, 35 (58%) with subtype 2 and 16 (27%) with subtype 3 achalasia. Mean IRP was 29.7 ±1.3 mmHg, and was lower in subtype 1 compared to the other two groups (p=0.05). Baseline symptoms included dysphagia (solids:85%, liquids:73%), regurgitation (84%) and chest pain (35%); GSS was 7.2 ±0.3. Upon follow-up 2.2 ±0.2 yr after Heller myotomy, GSS was rated 1.9 ±0.4 (p <0.001 compared to pre-myotomy scores), with a surgical satisfaction score of 8.7 ±0.3. Numerically, subtype 1 had the highest proportion of residual symptoms (GSS 3.1±1.3) compared to subtypes 2 and 3 (GSS 1.6±0.4, 1.7±0.8, p=ns for all comparisons). On univariate analysis,

female gender (p=0.004), higher IRP (p=0.05); and transit symptoms (regurgitation, dysphagia for liquids and solids, p≤0.03 for each) predicted improvement in GSS; achalasia subtype, age and chest pain did not. On multivariate analysis, only female gender remained an independent predictor (p=0.014), and dysphagia for solids trended towards significance (p=0.059); achalasia subtype was not a predictor. **CONCLUSIONS:** When a uniform surgical approach is utilized, despite residual symptoms, symptomatic outcome and satisfaction with therapy are similar for achalasia subtypes. Female gender and severity of preoperative dysphagia for solids may predict better post-surgical outcome.

Su1881

Characterization of Patients With Lymphocytic Esophagitis, an Emerging Clinicopathologic Disease

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Background: Lymphocytic Esophagitis (LyE) is a recently described clinicopathological condition in patients with upper GI symptoms and a prominent esophageal mucosal lymphocytic infiltrate. Little is known about this disease and consensus does not exist regarding the defining features and clinical associations. **Aim:** To characterize patients with LyE, compare them to non-LyE controls, and identify risk factors for the condition and outcomes. **Methods:** We conducted a review at the University of North Carolina- Chapel Hill of all patients ≥18 years old who had undergone upper endoscopy with esophageal biopsy between January 1, 2000 and June 1, 2012. Archived pathology slides were independently re-reviewed by study pathologists, and LyE was diagnosed if there were ≥ 10 lymph/hpf (hpf=0.24mm2) and no eosinophils or granulocytes. Three non-LyE controls groups were also defined in patients who had undergone EGD with biopsy: patients with GERD (defined by clinical symptoms and a mixed inflammatory pattern on biopsy); patients with eosinophilic esophagitis (EoE) (defined by consensus guidelines); and patients with a normal esophageal biopsy. Data were extracted from electronic medical records including: patient demographics, comorbidities, tobacco/alcohol abuse, medications, endoscopic findings, treatment, and outcomes. Descriptive statistics were used to characterize patients diagnosed with LyE, and bivariate analysis was performed to compare LyE cases and non-LyE controls. **Results:** 29 adults were diagnosed with LyE, with the first diagnosis made in 2004 (mean age 57; 59% female; 62% white; see Table). The most common symptom at presentation was dysphagia (71%). 52% had a prior diagnosis of GERD and 59% were on a PPI at time of diagnosis. 42% had a history of alcohol use, and 64% had a history of tobacco use. Endoscopic findings included strictures (41%), rings (31%), erythema or erosive esophagitis (40%), and hiatal hernia (28%); 38% of patients required dilation. After histology re-review, 85% of LyE patients were found to have more than 20 lymph/hpf. In comparison to the normal, GERD and EoE controls, patients with LyE tended to be non-white (38% vs 20%, 5%, and 5%, respectively; p = 0.06), were more commonly tobacco users (p=0.02), and less likely to have seasonal allergies (p=0.02). **Conclusion:** LyE is predominantly found in middle-aged smokers. Most patients present with dysphagia and are commonly found to have strictures requiring dilation on endoscopy. LyE should be considered as a diagnostic possibility in patients with these characteristics undergoing upper endoscopy.

Characteristics of patients with LyE compared to control patients

	LyE	Normal	GERD	EoE	P value
N	29	20	20	20	
Age in years (Mean ± SD)	57 ± 16	57 ± 12	61 ± 15	61 ± 15	<0.001
Female (%)	59	75	60	50	0.43
Race (%) Caucasian Black Hispanic	62 34 4	80 20 0	95 5 0	95 5 0	0.06
Allergy History (%) Drug Food Seasonal	41 8 4	55 5 20	50 10 20	32 16 42	0.46 0.68 0.02
Alcohol use (%)	42	45	55	61	0.34
Tobacco use prior and current (%)	64	30	55	55	0.02
Endoscopic Findings (%) Normal Hiatal Hernia Erosive Esophagitis Stricture Rings Erythema	17 28 14 41 31 28	35 40 25 15 15 30	20 55 40 27 20 20	10 10 0 35 55 10	0.24 0.02 0.01 0.23 0.03 0.40
Dilation during endoscopy (%)	38	20	20	35	0.39

Su1882

Individualized Flavored Liquid Thickener Improves Swallowing in Dysphagic Amyotrophic Lateral Sclerosis Patients

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Background. Oropharyngeal dysphagia is an early and incapacitating symptom in Amyotrophic Lateral Sclerosis (ALS). Taste receptors in the oral cavity contribute to trigger and enhance deglutition performance 1). Aims. To assess in dysphagic ALS patients whether a) the taste of thickened liquid can affect swallowing function and b) by modifying taste of the thickened liquid in the daily diet can improve the swallowing function. Patients and Methods. Twenty ALS patients (M:12, F:8, mean age 62.3 years, range 55-72) requiring thickened liquid for swallowing impairment were recruited. At study enrollment each patient was weighted and filled in the validated Swallowing Disturbance Questionnaire (SDQ) 2) consisting of 15 questions. The questions consider several swallowing dysfunctions (labial retention, chewing, liquid/solid dysphagia), respiratory symptoms (cough, dysphonia, respiratory difficulties or infections), and for each of them the patient scores the degree of severity from 0 to 3 so to obtain a cumulative maximal score of 45. In the following 6 weeks, patients continued their usual diet. At the end of the first 6 weeks each patient was asked to fill in the SDQ and to taste 5 differently flavored thickeners: acid, sweet, bitter, salty, and neutral lipid cream. The taste indicated as most agreeable by the patient was then used by the patient in the diet for the following 6 weeks, at the end of which the patient was weighted and filled in the SDQ. Results. No patient chose salty or cream taste; 9 patients