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EXPORT DATE:24 Jan 2016

Doulami, G.a , Triantafyllou, S.a , Natoudi, M.b , Albanopoulos, K.b , Menenakos, E.b , Filis, K.c , Zografos, G.c , Theodorou, D.a

“Normal Values of 24H Multichannel Intraluminal Impedance pH-Metry in a Greek Obese Population Based on Montreal Definition of Gerd”

(2016) Obesity Surgery, 26 (1), pp. 126-131.

ABSTRACT: Background: Although several studies reporting normal values of 24h multichannel intraluminal impedance pH (MIIpH) have been published, none of them has ever studied obese individuals. The purpose of this study is to determine overall frequency and duration of reflux episodes (acid and non-acid, supine-upright, post and preprandial) in obese asymptomatic volunteers. Methods: Obese volunteers were enlisted during their preoperative evaluation for bariatric surgery. Volunteers had no gastroesophageal reflux disease (GERD) symptoms and no evidence of esophageal mucosal injury on endoscopy. Participants underwent a 24h MIIpH. Results: In this prospective observational study, data of 22 obese individuals were analyzed. Mean age was 41.9 years and mean BMI was 47.1 kg/m2. Mean total reflux episodes was 55.6 and 95th percentile was 99.7. Mean percentage of total time with pH &lt;4 was 2.59 % and 95th percentile was 8.57 %. Mean percentage of bolus exposure was 1.84 % with 95th percentile being 4.47 %. Postprandial acid reflux episodes were statistical significant more frequent in comparison to preprandial acid reflux episodes (19.41 vs. 15, p = 0.008). Mean acid clearance duration was 3.6 times higher than median bolus clearance duration (56.05 and 15.55 s, respectively, p = 0.868). Conclusion: Our study is the first to provide normal values of 24h MIIpH of asymptomatic obese. Normal values of 24h MIIpH of obese asymptomatic individuals differ from the reported normal values of non-obese healthy individuals; having more reflux episodes and equal or slightly higher median bolus exposure and acid clearance. Our results imply that new cut-off values should be employed in order to define GERD in obese individuals. © 2015, Springer Science+Business Media New York.

Doulami, G., Triantafyllou, S., Natoudi, M., Albanopoulos, K., Leandros, E., Zografos, G., Theodorou, D.

GERD-Related Questionnaires and Obese Population: Can They Really Reflect the Severity of the Disease and the Impact of GERD on Quality of Patients’ Life?

(2015) Obesity Surgery, 25 (10), pp. 1882-1885. Cited 2 times.

ABSTRACT: Introduction: There is a strong association between obesity and gastroesophageal reflux disease (GERD). GERD-related questionnaires have been developed in order to objectify symptoms. However, none of them has been tested in obese population. Purpose: The purpose of this study is to evaluate if GERD score and GERD-Health-Related Quality of Life (HRQL) can reflect severity of the disease and screen obese patients for GERD preoperatively. GERD’s impact on the quality of life of obese patients is being assessed with the use of EORTC-QLQ C30. Patients-Methods: Obese patients during their preoperative evaluation were recruited regardless of the presence of GERD symptoms. A targeted GERD symptom history was obtained. Patients completed GERD score, GERD-HRQL, and EORTC-QLQ C30, and then, a 24-h multichannel intraluminal impedance pHmetry (MIIpH) was conducted. Results: Forty-seven consecutive obese patients with mean age 39.91 years and mean BMI 46.94 kg/m2 were included in the study. GERD score and GERD-HRQL have a positive linear correlation with DeMeester score (p = 0.001 and p < 0.001, respectively). EORTC QLQ-C30 does not correlate with DeMeester score. Conclusions: GERD-related questionnaires could be used in obese population as preoperative screening tool for GERD. However, our results indicate that the quality of life of obese patients is not affected by the existence of GERD. © 2015, Springer Science+Business Media New York.

Tasioudi, K.E.a , Sakellariou, S.a , Levidou, G.a , Theodorou, D.b , Michalopoulos, N.V.b , Patsouris, E.a , Korkolopoulou, P.a , Saetta, A.A.a

Immunohistochemical and molecular analysis of PI3K/AKT/mTOR pathway in esophageal carcinoma

(2015) APMIS, 123 (8), pp. 639-647. Cited 1 time.

ABSTRACT: Among the numerous signaling pathways involved in tumorigenesis, PI3K-AKT-mTOR is a key one that regulates diverse cellular functions. However, its prognostic value in esophageal carcinoma remains unclear. In our study, we examined the immunohistochemical expression of phosphorylated (p-) AKT, mTOR, p70S6K and 4E-BP1 along with the mutational status of PIK3CA and AKT1 genes by High Resolution Melting Analysis and Pyrosequencing in 44 esophageal carcinomas. The results were correlated with the clinicopathological characteristics of the patients in an effort to define their possible prognostic significance. Total p-mTOR cytoplasmic expression, assessed in 10 random areas, was positively correlated with tumor stage (Kruskal-Wallis ANOVA, I/II vs III/IV, p = 0.0500). Μoreover, maximum p-mTOR cytoplasmic immunoexpression, estimated in hot spot areas, was positively associated with tumor grade (Mann-Whitney U test, I/II vs III, p = 0.0565). Interestingly, p-4E-BP1 immunoreactivity was negatively correlated with tumor histological grade (Mann-Whitney U test, I/II vs III, p = 0.0427). No mutation was observed in exons 9 and 20 of PIK3CA gene and in exon 4 of AKT1 gene. In conclusion, our findings depict the presence of activated PI3K/AKT/mTOR pathway in esophageal cancer bringing forward p-mTOR and p-4E-BP1 for their potential role in esophageal carcinogenesis. Additional studies are warranted to validate our findings. © 2015 APMIS. Published by John Wiley & Sons Ltd.

Theodorou, D., Doulami, G., Memos, N., Kokoroskos, N., Vrakopoulou, G.-Z., Triantafyllou, S., Kleidi, E., Katsaragakis, S., Zografos, G.

Is there room for improvement in esophageal cancer surgery? Results of a prospective protocol for individualization of surgical treatment

(2014) Esophagus, . Article in Press.

ABSTRACT: Background Despite improvements in multimodality approach, overall survival of esophageal cancer (EC) is still very low. Because of the rarity of the disease and the lack of large prospective studies, several controversies exist regarding the optimal type of surgery and the use of adjuvant and neoadjuvant therapy. Traditionally, the debate for the extent lymphadenectomy is between transhiatal esophagectomy with 1-field lymphadenectomy (THE-1FL) and transthoracic esophagectomy with 2-field lymphadenectomy (TTE-2FL). The purpose of this study is to evaluate the effect of optimal patient selection for submission to each procedure, on overall survival. Methods Patients with EC were prospectively enrolled in a database and a protocol of individualized surgical treatment of EC (PISTEC) was applied to patients with resectable disease. PISTEC is based on patient's physical status and disease stage, with intent to select the appropriate surgical procedure for each patient. Results From 01/2006 to 12/2011, 61 patients with EC were individualized according to the PISTEC. Of them, 52.4 % were submitted to THE-1FL and 31.1 % to TTE-2FL. The 30-day mortality rate was 4.9 %. The 5-year overall survival rate was 54.9 % and recurrence was observed in 27.5 % of patients. The estimated 5-year overall survival of patients with stages 0, I, II, III and IV was 100, 100, 92.9, 45 and 0 %, respectively. Conclusion The algorithm proposed by the PISTEC aims at balancing perioperative risks with oncological benefit. When type of surgery is individualized, the outcomes regarding survival are favorable. This effect could probably be enhanced with the concurrent application of neoadjuvant treatment. © 2014 The Japan Esophageal Society and Springer Japan.

Doulami, G., Theodorou, D.

Comment on "peroral esophageal myotomy (POEM) and laparoscopic Heller myotomy produce a similar short-term anatomic and functional effect"

(2014) Surgery (United States), 155 (3), p. 582.

Larentzakis, A., Theodorou, D.

Erratum: A multicenter study of survival after neoadjuvant radiotherapy/chemotherapy and esophagectomy for ypT0N0M0R0 esphageal center (Annals of Surgery (2014) 259 (e67))

(2014) Annals of Surgery, 260 (1), p. 21.

Natoudi, M.a , Theodorou, D.a , Papalois, A.b , Drymousis, P.a , Alevizos, L.a c , Katsaragakis, S.a , Zografos, G.a , Leandros, E.a , Menenakos, E.a

Does tissue ischemia actually contribute to leak after sleeve gastrectomy? An experimental study

(2014) Obesity Surgery, 24 (5), pp. 675-683. Cited 4 times.

ABSTRACT: Background: Staple line leak, although rare, is among the most common postoperative complications after sleeve gastrectomy (SG) and usually occurs in the gastroesophageal (GE) junction. Increased intragastric pressure, regional ischemia, and technical failure of stapling devices have been reported as the main risk factors of postoperative leak. The aim of this study was to evaluate the impact of ischemia and intraluminal pressure in leak appearance. Methods: Landrace swine (n = 12) were subjected to SG and total gastrectomy subsequently. Lactic acid, glycerol, and pyruvate were measured by microdialysis in GE junction and pylorus before and nine times after operation, and lactate/pyruvate (L/P) ratio was calculated as well. Moreover, ex vivo air was insufflated inside the tubularized stomach till a rupture of the staple line occurs. Maximum air pressure reached and location of rupture were recorded. Results: Increase of lactic acid and L/P ratio were demonstrated in GE junction measurements; however, when the measurements between GE junction and pylorus were compared, no statistically significant differences were found, with the exception of a slightly increased lactate concentration in pylorus in the midst of measurements. The maximum air pressure recorded varied from 3 to 75 mmHg (mean 24.5 mmHg) and the majority of ruptures (n = 8) occurred in GE junction. In one of them, clip displacement was noticed. Conclusions: No evidence of increased ischemia in GE junction compared to pylorus was recorded. Increased intraluminal pressure and stapling malfunction may play the most important role in leak appearance. © 2014 Springer Science+Business Media New York.

Kleidi, E.a , Theodorou, D.a , Albanopoulos, K.a , Menenakos, E.a , Karvelis, M.A.b , Papailiou, J.a , Stamou, K.a , Zografos, G.a , Katsaragakis, S.a , Leandros, E.a

The effect of laparoscopic sleeve gastrectomy on the antireflux mechanism: Can it be minimized?

(2013) Surgical Endoscopy and Other Interventional Techniques, 27 (12), pp. 4625-4630. Cited 7 times.

ABSTRACT: Background: Laparoscopic sleeve gastrectomy (LSG) is a promising procedure for the treatment of morbid obesity. The stomach is usually transected near the angle of His; hence, the lower esophageal sphincter (LES) may be affected with consequences on postoperative gastroesophageal reflux disease (GERD). The purpose of this study was to examine the effect of LSG on the LES and postoperative GERD. Methods: Severely obese asymptomatic patients submitted to LSG underwent esophageal manometry and GERD evaluation preoperatively and at least 6 weeks postoperatively. Data reviewed included patient demographics, manometric measurements, GERD symptoms, and pathology. Statistical analysis was performed by SPSS software. Results: Twelve male and eleven female patients participated in the study. Mean age was 38.5 ± 10.9 years, and initial body mass index was 47.9 ± 5.1 kg/m2. At follow-up examination, mean excess body mass index loss was 32.3 ± 12.7 %. The LES total and abdominal length increased significantly postoperatively, whereas the contraction amplitude in the lower esophagus decreased. There was an increase in reflux symptoms postoperatively (p &lt; 0.009). The operating surgeon who mostly approximated the angle of His resulted in an increased abdominal LES length (p &lt; 0.01). The presence of esophageal tissue in the specimen correlated with increased total GERD score (p &lt; 0.05). Conclusions: LSG weakens the contraction amplitude of the lower esophagus, which may contribute to postoperative reflux deterioration. It also increases the total and the abdominal length of the LES, especially when the angle of His is mostly approximated. However, if this approximation leads to esophageal tissue excision, reflux is again aggravated. Thus, stapling too close to the angle of His should be done cautiously. © 2013 Springer Science+Business Media New York.

Tasioudi, K.E.a , Saetta, A.A.a , Sakellariou, S.a , Levidou, G.a , Michalopoulos, N.V.b , Theodorou, D.b , Patsouris, E.a , Korkolopoulou, P.a

PERK activation in esophageal carcinomas: Clinicopathological associations

(2012) Pathology Research and Practice, 208 (7), pp. 398-404. Cited 11 times.

ABSTRACT: MAPK (mitogen-activated protein kinase) pathway is considered a control regulator in various malignant tumors but its role in esophageal carcinomas remains elusive. In our study, we examined the possible prognostic significance of MAPK pathway in human esophageal cancer. We searched for mutations in exons 18-21 of EGFR gene, codons 12 and 13 of K-RAS gene and exon 15 of B-RAF gene by high resolution melting analysis (HRMA) and pyrosequencing in 44 esophageal carcinomas. Immunohistochemistry was performed in 29 cases in order to evaluate expression levels of pERK (extracellular-signal regulated kinase). In one laser microdissected squamous cell carcinoma, a somatic K-RAS mutation at codon 12 was detected, whereas none of the cases displayed mutations in EGFR and B-RAF genes. Elevated nuclear as well as cytoplasmic pERK expression (100% and 62% of cases respectively) was observed independently of EGFR and B-RAF mutational status. Increasing pERK nuclear and cytoplasmic expression as well as the intensity of nuclear staining was found to be significantly correlated with tumor grade in univariate and multivariate statistical analysis. Our findings depict the presence of activated ERK despite the low frequency of upstream alterations, implicating ERK activation in the acquisition of a more aggressive phenotype in esophageal cancer. © 2012 Elsevier GmbH.

Theodorou, D.a , Ayazi, S.a , DeMeester, S.R.a , Zehetner, J.a , Peyre, C.G.a , Grant, K.S.a , Augustin, F.a , Oh, D.S.a , Lipham, J.C.a , Chandrasoma, P.T.b , Hagen, J.A.a , DeMeester, T.R.a c

Intraluminal pH and Goblet Cell Density in Barrett's Esophagus

(2012) Journal of Gastrointestinal Surgery, 16 (3), pp. 469-474. Cited 10 times.

ABSTRACT: Introduction: Goblet cells in Barrett's esophagus (BE) vary in their density within the Barrett's segment. Exposure of Barrett's epithelium to bile acids is a major stimulant for goblet cell formation. The dissociation of bile acids into forms that penetrate Barrett's epithelium is known to be pH dependent. We hypothesized that variations in the esophageal luminal pH environment explains the variability in goblet cell density. The aim of this study was to correlate esophageal luminal pH with goblet cell density in patients with BE. Methods: A customized six-sensor pH catheter was positioned with the most distal sensor in the stomach and the remaining sensors located 1 cm below and 1, 3, 5, and 8 cm above the upper border of the lower esophageal sphincter in five normal subjects and six patients with long-segment BE. The luminal pH was measured by each sensor for 24-h and expressed as median pH. Patients with BE had four quadrant biopsies at levels corresponding to the location of the pH sensors. Goblet cell density was graded from 0 to 3 based on the number per high-power field. Results: In normal subjects, the median pH values recorded in the sensors within the lower esophageal sphincter (LES) and esophageal body were all above 5. In patients with BE, the median pH recorded by the sensor within the LES was 2. 8 and increased progressively to 4. 7 in the sensor at 8 cm above the LES. Goblet cell density was significantly lower in the distal Barrett's segment exposed to a median pH of 2. 2 and increased in the proximal Barrett's segment exposed to a median pH of 4. 4 (p = 0. 003). Conclusion: Patients with BE have a goblet cell gradient that correlates directly with an esophageal luminal pH gradient. This suggests that goblet cell differentiation is pH dependent and likely due to the effect of pH on bile acid dissociation. © 2011 The Society for Surgery of the Alimentary Tract.

Theodorou, D., Doulami, G., Larentzakis, A., Almpanopoulos, K., Stamou, K., Zografos, G., Menenakos, E.

Bougie insertion: A common practice with underestimated dangers

(2012) International Journal of Surgery Case Reports, 3 (2), pp. 74-77. Cited 2 times.

ABSTRACT: INTRODUCTION: Esophageal perforation after bariatric operations is rare. We report two cases of esophageal perforation after bariatric operations indicating the dangers of a common practice - like insertion of esophageal tubes - and we describe our management of that complication. PRESENTATION OF CASE: A 56 year old woman who underwent laparoscopic sleeve gastrectomy and a 41 year old woman who underwent laparoscopic adjustable gastric banding respectively. In both operations a bougie has been used and led to esophageal perforation. DISCUSSION: The insertion of bougie and especially of inflated bougie is a common practice. It is an invasive procedure that in most cases is performed by the anesthesiologist team. CONCLUSION: Bougie insertion is an invasive procedure with risks and should always be attempted under direct supervision of surgical team or should be inserted by a surgeon. © 2011 Published by Elsevier Ltd on behalf of Surgical Associates Ltd.

Karidis, N.P., Theodorou, D.

Esophageal Cancer

(2011) Cancer Surgery in the Elderly, pp. 99-129.

http://www.scopus.com/inward/record.url?eid=2-s2.0-84891977084&partnerID=40&md5=90d1461716efff69d747c15a07470499

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DOCUMENT TYPE: Book Chapter

SOURCE: Scopus

Doulami, G., Theodorou, D.

Reply to: Definitive Chemoradiation for Oesophageal Cancer - A Standard of Care in Patients with Non-metastatic Oesophageal Cancer

(2011) Clinical Oncology, 23 (9), p. 653. Cited 1 time.

http://www.scopus.com/inward/record.url?eid=2-s2.0-80053385311&partnerID=40&md5=bca7df56a1269c2fa2e8d53ec43dacc0

DOI: 10.1016/j.clon.2011.07.004

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DOCUMENT TYPE: Letter

SOURCE: Scopus