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LONG-TERM OUTCOME OF MEDICAL AND SURGICAL THERAPIES FOR GERD: EFFECTS ON GERD SYMPTOMS AND SIGNS.

Stuart Spechler, Edward Lee, Dennis Ahnen, Raj Goyal, Francisco Ramirez, Jean-Pierre Raufman, Richard E. Sampliner, Thomas Schnell, Stephen Sontag, Z. Reno Vlahcevic, Renee Young, William Williford, VA Med Ctr, Dallas, TX; VA Med Ctr, Denver, CO; VA Med Ctr, West Roxbury, MA; VA Med Ctr, Phoenix, AZ; VA Med Ctr, Little Rock, AR; VA Med Ctr, Tucson, AZ; VA Med Ctr, Hines, IL; VA Med Ctr, Richmond, VA; VA Med Ctr, Omaha, NE; VA Med Ctr, Perry Point, MD.

Background: From July 1986 through November 1989, the VA conducted a prospective, randomized trial of medical and surgical antireflux therapies for 248 patients with complicated GERD (N Engl J Med 1992;326:786). We have done a follow-up study of this well-defined cohort to explore the long-term results of GERD therapies. Methods: The whereabouts of the patients were determined with the help of a professional search agency. Patients were asked to: 1) record their GERD symptoms daily in a diary for two weeks (one week on medications, one week with medications discontinued), 2) complete a health history questionnaire, 3) have an endoscopy, and 4) have 24-hour esophageal pH monitoring. GRACI (symptom) scores were calculated using results from the symptom diaries. Results: 79 patients had died; 161 of the 169 survivors were located. Findings are shown in the Table. Conclusions: During a follow-up of 11 to 13 years, patients treated with fundoplication had significantly better symptom control and less frequent use of antireflux medications than medically-treated patients. However, no significant differences between the groups were observed in the grade of esophagitis, duration of esophageal acid exposure, frequency of subsequent antireflux operations, or frequency of treatment for esophageal stricture. The large majority of patients in both groups were satisfied or very satisfied with their therapies.

	Surgical Group	Medical Group	P<0.05
GRACI score on medication *†	78.7±9.5	83.5±14.0	Yes
GRACI score off medication*†	82.6±17.5	96.9±21.6	Yes
Grade of esophagitis *	1.80±0.95	1.88±1.15	No
Total % time esophageal pH<4*	17.1±41.1	30.3±60.9	No
% using antireflux meds regularly‡	46.9%	73.7%	Yes
% having ³1 antireflux operation‡	14.3%	7.9%	No
% having treatment for esophageal stricture‡	13.5%	7.6%	No
% satisfied or very satisfied with therapy‡	89.5%	94.6%	No

*Mean±SD
†Higher scores=more severe symptoms
‡Since the study ended in November 1989

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COMPARISON OF ESOMEPRAZOLE, A NOVEL PPI, VS OMEPRAZOLE IN GERD PATIENTS WITH EROSIVE ESOPHAGITIS (EE).

Peter J. Kahrilas, Gary Falk, James Whipple, Donald D'Amico, Bo Joelsson, Northwestern Univ, Chicago, IL; Cleveland Clin Fdn, Cleveland, OH; AstraZeneca LP, Wayne, PA.

Background: Pharmacologic studies with esomeprazole, an optical isomer of omeprazole, suggest the potential for clinical benefits in acid related disease. The current trial assessed the efficacy of esomeprazole 40 mg (E40) and 20 mg (E20) compared with omeprazole 20 mg (O20) in patients with EE. Methods: In this US, multicenter, randomized, double-blind, parallel group trial, 1960 patients with EGD-confirmed EE (LA Classification grades A-D, *H pylori*-negative by serology) received daily doses of E40(n=654), E20 (n=656), or O20 (n=650) for up to 8 wks. The primary efficacy variable was the proportion of patients healed at wk 8. Secondary variables were the proportion of patients healed at wk 4, heartburn resolution assessed by the investigator (no heartburn episodes) at wk 4, and sustained resolution of heartburn (7 consecutive days without heartburn) assessed by patient diary data. Safety and tolerability were also evaluated. Results: More patients were healed at wks 4 and 8 with E40 and E20 *vs* O20 (cumulative life table estimates, ITT analysis). E40 was also more effective than O20 for heartburn resolution at wk 4. E40 resolved heartburn sooner than O20, and time to sustained resolution of heartburn was significantly shorter for E40 *vs* O20. The 3 most common AEs were headache, abdominal pain, and diarrhea and occurred at similar rates in all treatment groups. Conclusions: This is the first study to demonstrate that a new PPI, esomeprazole, is superior to omeprazole for the healing of EE in GERD patients. Esomeprazole also provides greater heartburn resolution with a safety profile comparable to that of omeprazole. These results have been corroborated in another separate clinical trial.

Healing and Heartburn Resolution at 4 and 8 Weeks

	E40 (n-654)	E20 (n=656)	O20 (n=650)
Week 8 Healing (%)	94.1%*	89.9%*	86.9%
Week 4 Healing (%)	75.9%*	70.5%	64.7%
Investigator Assessment of Heartburn Resolution (Week 4)	64.7%*	61.0%	57.2%
Time to Sustained Resolution of Heartburn (Median # of days)	5*	8	9

* p≤ 0.05 vs. omeprazole

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DETECTION OF HIGH-GRADE DYSPLASIA IN BARRETT'S ESOPHAGUS BY 5-AMINOLEVULINIC ACID (ALA) INDUCED PROTOPORPHYRIN IX (PPIX) FLUORESCENCE SPECTROSCOPY.

Stephan A. Brand, Thomas D. Wang, Kevin T. Schomacker, John M. Poneros, Carolyn C. Compton, Marcos C. Pedrosa, Norman S. Nishioka, MA Gen Hosp, Harvard Med Sch, Boston, MA; VA Boston Med Ctr, Boston Univ Med Sch, Boston, MA.

Background: Previous non-quantitative studies of ALA-induced PpIX fluorescence suggest that this technique may be useful for detecting dysplasia. The purpose of this study was to investigate whether ALA-induced PpIX fluorescence as measured quantitatively by spectroscopy can differentiate between Barrett's mucosa with and without high-grade dysplasia (HGD). Methods: Sixteen patients received 10 mg/kg of ALA (DUSA Pharmaceuticals, Inc., NY) orally three hours prior to endoscopy and underwent conventional white-light endoscopy followed by fluorescence endoscopy using a blue light source (D-light, Storz, Germany) and an intensified fluorescence imaging system (SAFE 1000, Pentax, Japan). Regions suspicious for dysplasia under white light examination (e.g., nodules) or under fluorescence endoscopy (increased fluorescence) were measured spectroscopically using a laser-induced fluorescence system (λ = 400 nm). The 635 nm peak PpIX fluorescence intensity was normalized to the intensity of a fluorescence standard (DCM, Exciton Inc., OH) and compared with the histopathologic results obtained from mucosal biopsies taken immediately following fluorescence measurements. Results: 98 fluorescence spectra were included in the analysis. HGD was distinguished from Barrett's epithelium without dysplasia with a sensitivity of 85.7% and a specificity of 88.5% using a DCM-normalized 635 nm fluorescence intensity of 0.15 as threshold. Conclusion: This study shows for the first time that the mean PpIX peak fluorescence measured quantitatively is higher in HGD than non-dysplastic Barrett's epithelium. ALA-induced fluorescence spectroscopy may be useful for detecting HGD in Barrett's esophagus and guiding biopsy sampling.

Results: PpIX fluorescence intensity peak at 635 nm

Tissue type	Mean ± SE	p vs. HGD	n
HGD	0.71±0.20	-	7
low-grade or indefinite dysplasia	0.18±0.04	0.04	23
non-dysplastic Barrett's	0.11±0.02	0.02	23
gastric mucosa	0.09±0.02	0.02	29
squamous epithelium	0.16±0.03	0.03	16