

Modern trends in oesophageal surgery

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Changes in the practice of oesophageal surgery have paralleled the increased incidence of gastro-oesophageal reflux disease (GORD), the introduction of minimally invasive techniques, a better understanding of the pathophysiology of oesophageal disease, advances in instrumentation and the surge of molecular biological interests. The recent explosion of bariatric surgery in the USA has also opened new dimensions for investigation of the effects of bariatric procedures on oesophageal function.

Pathophysiology of gastro-oesophageal reflux disease

There is evidence that the biomechanical alterations of the lower oesophageal sphincter are related to gastric distension resulting in an unfolding of the sphincter which in turn allows gastric content to damage the mucosa of the lower oesophagus.¹ There is now evidence to support the concept that 'cardiac' mucosa at the interface of the squamous and columnar epithelia is an acquired sequel to acid-induced squamous mucosal injury, and is not a normal epithelium.² Our present interpretation after exhaustive studies is that cardiac-type mucosa is a normal sequel to squamous mucosal injury and is an early sign of GORD. Cardiac-type mucosa nearly always shows inflammatory and reactive changes referred to as 'carditis'. This inflamed cardiac-type mucosa is the only mucosa that progresses to intestinal metaplasia, the hallmark of Barrett's mucosa.

As the lower oesophageal sphincter weakens in response to continued reflux, cardiac-type mucosa develops in the distal oesophagus from squamous mucosa. This metaplastic process in which the squamous epithelium actually changes to cardiac and then columnar epithelium replaces the old 'creeping substitution' theory.³ As the process progresses the length of this segment of mucosa becomes intestinalised, characterised by the appearance of goblet cells. The process of intestinalisation is related to three conditions, viz.: (i) the length of the oesophagus that has become lined by columnar epithelium; (ii) the number of years that gastric juice has refluxed into the oesophagus; and (iii) the presence of bile in the refluxed gastric juice.⁴

Fitzgerald *et al.*⁵ showed that exposure of columnar mucosal cell lines to a pH of 3 - 5 (acid-pulsed exposure) enhanced cell proliferation, whereas continuous acid exposure blocked cell proliferation. These studies suggest that intermittent control of reflux may result in cell proliferation and possibly cancer, and that it is better to stop all reflux than to allow only partial control. From these studies and previous animal models,^{6,8} we believe that columnarisation of the oesophagus results from acid reflux, and that bile is responsible for intestinalisation and carcinogenesis. These recent studies suggest that intestinalisation of the cardiac-type mucosa is initiated by exposure to a pH of 3 - 5, result-

ing from the interaction of gastric juice, duodenal juice and saliva at the squamo-columnar interface. As the length of the intestinalised epithelium increases the more distal portion is exposed to more acid and less saliva (and consequently less exposure to a pH of 3 - 5); it then reverts to cardiac-type mucosa by losing its intestinal characteristics and may eventually become fundic mucosa. This would also explain why intestinal metaplasia is found consistently in the proximal portion of a long segment of Barrett's metaplasia.¹

The epithelial changes from squamous to cardiac to columnar with intestinalisation, dysplasia and ultimately carcinoma are accompanied by many molecular changes. Molecular biology laboratories are processing tissue from resected malignant specimens in an attempt to match the results with chemotherapeutic agents that will specifically target the cancer. 'Targeting' has become a key word in the realms of cancer chemotherapy.

Investigation

Surgical interest in oesophageal function has increased since the explosion of laparoscopic antireflux procedures. Three hundred surgeons registered for a motility course held for surgeons at the Surgical Association of Gastro-Esophageal Surgeons 3 years ago. The American College of Surgeons offered a motility course at the annual meeting 2 years ago and it was fully subscribed. Of course the threat of litigation also plays a role in the desire to avoid mismanagement of patients.

Motility recording is now fully computerised, and in the USA Medtronic and the Sandhill Corporation have near perfected the apparatus to give meaningful results. pH monitoring is now tubeless and the 'Bravo' probe (Medtronic, Minn., USA) gives equal results without much of the discomfort of a trans-nasal tube. Sandhill Corporation has added 'impedance monitoring' to its equipment. Impedance monitoring has the advantage of being able to assess bolus transport within the oesophagus at the same time as measuring motility and pH. The bolus movement in a prograde or retrograde direction can be assessed and the pH of the bolus determined. This has advantages in deciding whether an antireflux procedure will be tolerated or not. Manometry is unable to detect bolus transport; patients with abnormal manometry that suggests a contraindication to a 360° antireflux operation, may be shown to have complete bolus transit by impedance criteria. Motility disorders have also been more clearly defined. Leite *et al.*⁹ introduced the term 'ineffective esophageal motility' (IEM) to define a group of oesophageal disorders with mean pressures of less than 30 mmHg in more than 30% of swallow responses and/or more than 30% of non-transmitted swallows. This definition embraces scleroderma and endstage reflux disease. We now also pay more attention to the measurement of intra-bolus

pressures and incomplete relaxation of the lower oesophageal sphincter, particularly in patients who have post-Nissen fundoplication dysphagia. A raised intra-bolus pressure and incomplete relaxation of the lower oesophageal sphincter have also been detected in studies of many patients with hypertensive lower oesophageal sphincter.¹⁰ The latter condition can only be diagnosed by manometry, and without this assessment the cause of dysphagia or chest pain in these patients cannot be adequately assessed or treated.

More detailed study methods of the cricopharyngeal sphincter have also given direction as to which patients will benefit from a cricopharyngeal myotomy. A raised intrabolus pressure and incomplete relaxation are highly suggestive of outflow obstruction, and dysphagic patients with these motility disorders are likely to get relief from a crico-pharyngeal myotomy.¹¹

Advances in surgical approaches and techniques

Minimally invasive techniques have opened a Pandora's box for the innovative surgeon. Antireflux surgery, achalasia, Zenker's and epiphrenic diverticula, and oesophagectomy have all tested the skills of the modern minimally invasive surgeon.

Endoscopic antireflux procedures

Several new ingenious techniques and devices have been introduced.¹² These are all performed under conscious sedation and as day cases.

Radiofrequency (RF) energy (the Stretta procedure) (Curon Medical, USA) is used in a controlled fashion to cause a thermal lesion which results in scarring of the lower oesophageal sphincter area. In so doing it helps to control the sphincter, preventing inappropriate opening due to gastric distension. The procedure is safe, increases the lower oesophageal pressure by about 60% and reduces pH reflux scores. The use of proton pump inhibitors (PPIs) also decreases and patient quality-of-life scores improve. However, it was found that acid reflux scores do not return to normal. This is the most tested of all the endoscopic procedures, and long-term follow-up will be necessary. At the present time the procedure would appear to be inappropriate for patients with a very poor lower oesophageal sphincter.

Bard Endocinch. This is an endoscopic suturing device which plicates the gastric mucosa at the gastro-oesophageal junction (C. R. Bard Inc., Boston). It also decreases heartburn and improves the lower oesophageal sphincter, but the results suggest that the technique also falls far short of surgical procedures.

Plicator. An endoscopic full-thickness plicating device (ndo surgical, Mass., USA) is still being tested and appears to be safe and effective, improving heartburn and regurgitation scores by 50% at 3 months. However, at 3 months, only 40% of patients were completely off medications.

Medigus SRS is another endoluminal device (SRS system, Israel) under investigation, and this forms an anterior fundoplication.

Bulking agents. Intraluminal bulking agents include 'Enteryx' (Boston Scientific) and 'Gatekeeper' (Medtronic, Minn.). Enteryx is a biocompatible polymer, which when injected forms an inert spongy mass. Symptom improvement has been reported but again pH values have not normalised in follow-up studies. Longer follow-up is required to assess the value of the method. The 'Gatekeeper' is an implantable prosthesis which can be removed if necessary. Trials are underway to evaluate the impact on reflux of this

procedure. Plexiglass microspheres have also been injected into the oesophageal submucosa to form a barrier at the gastro-oesophageal junction. Further studies are underway to assess the efficacy of the method.

These methods are clearly not nearly as effective in the control of gastro-oesophageal reflux as surgical fundoplication, but have the advantage of being outpatient procedures. At present they are inappropriate for the control of reflux in patients with Barrett's oesophagus, especially as there is now some evidence that complete control may prevent cancer in these patients.^{13,14} It is of interest to note the enthusiasm of gastro-enterologists in the performance of these techniques despite the remarkable results published on the use of PPI medication.

Endoscopic mucosal resection (EMR)

Inoue *et al.*¹⁵ have reported on extensive use of this simple technique. In our centre it has been used to remove small segments of Barrett's oesophageal mucosa with high-grade dysplasia, so that histological assessment of the depth of invasion may be made more accurately. This has assisted in planning either a vagal-sparing procedure (depth of invasion confined to the mucosa) or an *en bloc* resection (depth of invasion beyond the muscularis mucosa). Secondly it has been used to resect early cancer in patients otherwise unfit for surgery. Inoue *et al.*¹⁵ have resected segments of oesophageal mucosa by multiple resections, but also report on oesophageal stricture with such practice.

Antireflux surgery

Laparoscopic antireflux surgery and PPI medication were introduced in the late 1980s. Against all expectations there was nevertheless a surge in the number of surgical procedures performed. The easier approach for the patient, short hospital stay, high cost of medication, industry interest and support all contributed to this explosion of surgical correction of reflux. The debate as to which treatment is preferable continues. The Nissen fundoplication operation has stood the test of time. The Belsey Mark IV and Hill operations are rarely practised. The Toupet and Dor procedures do not control reflux sufficiently to be of value to the regular refluxer with satisfactory motility. They are used mostly to decrease reflux following myotomy for achalasia.

Achalasia

Laparoscopic myotomy with a Dor procedure is the current procedure of choice.¹⁶ Surgery still gives better results than pneumatic dilation. The Toupet antireflux procedure is preferred in some circles, but requires mobilisation of the oesophagus and take-down of the short gastric vessels. Several large series report excellent results after laparoscopic myotomy and the Dor procedure, with control of pH-proven gastro-oesophageal reflux in more than 90% of patients tested. The control of reflux is therefore better in post-myotomy achalasia patients than in regular gastro-oesophageal reflux patients, although the reason for this discrepancy remains unexplained. Assessment of the results of surgery for achalasia must now include objective testing to qualify for publication. 'Timed barium swallow' and pH tests will assess the adequacy of the myotomy and the control of reflux.¹⁷

Zenker diverticulum

Diverticula that are 3 cm or more in length are best treated with per-oral cricopharyngeal bar division and stapling. To

accomplish this the Wierda mouth gag is used, and the GIA stapler is modified by sawing off the half inch of protruding backplate so as to give sufficient stapling length. The procedure also has to be performed under general anaesthesia.¹⁸

Unfortunately the open technique is still required for smaller diverticula.¹⁹ The morbidity for this procedure in reported series is about 30 - 40%. Botox injection has been used in some centres but the recurrent laryngeal nerve proximity poses a potential problem. Division of the cricopharyngeal bar with argon beam coagulation under endoscopic guidance can be done under conscious sedation. This technique includes a potential hazard, viz. opening the oesophagus into the neck and mediastinum, but the actual reported morbidity is low, despite the fact that many patients have crepitus in the neck following the procedure. Antibiotic coverage obviously protects these patients from disaster.

Epiphrenic diverticulum

Epiphrenic diverticula are pulsion diverticula resulting from an outflow obstruction. Achalasia and hypertensive lower oesophageal sphincter are common causes. The 'triple treat' (myotomy, diverticulectomy and an antireflux procedure) has been described for this condition.²⁰ The conventional approach is via a left thoracotomy, but it has recently also been accomplished laparoscopically in a few centres.²¹ Thirteen patients were treated laparoscopically without mortality and at long-term follow-up all patients were symptom-free.

Hypertensive lower oesophageal sphincter

This condition can only be diagnosed by manometry. Dysphagia and chest pain are the most common symptoms.¹⁰ Surprisingly, 26% of these patients also have pH-proven gastro-oesophageal reflux.²² Symptomatic patients with a hypertensive lower oesophageal sphincter and reflux respond well to antireflux measures alone. If reflux is absent, treatment is essentially the same as for achalasia, and myotomy with a Dor antireflux procedure is currently the procedure of choice.²³

Oesophagectomy for carcinoma of the oesophagus

Worldwide the most common approach is still either a transhiatal or transthoracic pull-up of a tubularised oesophagus. The 5-year survival does not exceed about 20%. A few centres in the USA have persisted with *en bloc* oesophagectomy. Survival of patients with adenocarcinoma at the cardia is related to the number of metastatic nodes and the ratio of involved to total number removed. Patients with no nodes involved had an 85% 5-year survival following *en bloc* resection.²⁴ Patients with more than four nodes involved or a ratio of involved to metastatic nodes greater than 0.1 had a likelihood of recurrence and death. Japanese surgeons²⁵ are very vigorous with two and three-field oesophagectomy and have repeatedly reported longer survival rates. A controlled trial of the different approaches is still lacking.

A recent study²⁶ of a large series of patients from our centre who underwent oesophagectomy reported that 10% of patients developed conduit ischaemia or an anastomotic leak, and 22% an anastomotic stricture. Leaks and strictures are more common, and strictures are more severe after gastric pull-up compared with colon interposition. Dilatation of these strictures is safe and effective.

Vagal sparing oesophagectomy

Originally reported by Akiyama, this technique was not used in the USA until it was introduced by DeMeester. His series was presented recently, and the results have been very rewarding in relation to function of the stomach. Tests have confirmed the integrity of the vagal nerves after the procedure, and patients were free of dumping and diarrhoea. It is best used for replacement of benign conditions such as endstage achalasia and a burned-out oesophagus from long-standing gastro-oesophageal reflux, but is also used in patients with high-grade dysplasia in a Barrett's oesophagus. The technique is fully described in the *Annals of Surgery*.²⁷

Laparoscopic and thorascopic oesophagectomy

Oesophagectomy via a combined laparoscopic and thorascopic approach is both feasible and safe. With practice and increasing expertise the procedure can be done in about 5 hours, and may offer the usual advantages of minimally invasive procedures.²⁸ Robot-assisted oesophagectomy is also being tested, but comparisons with other techniques are not yet available.

Robotic surgery

The Federal Drug Administration in the USA sanctioned the use of the 'Da Vinci' robot for cardiac valve replacement therapy some years ago. Since then the use of the apparatus has been extended to include oesophagectomy, Nissen fundoplication, mediastinal tumours, and a variety of other uses. An extended learning curve and longer operating room schedules have been inhibitory in many centres. There are two such robots at the University of Southern California and one is dedicated for training. Time will tell whether this technique will be cost effective and in the patients' interests.

The short oesophagus

Recent reports on series of laparoscopic antireflux surgery refute the entity of the short oesophagus, and articles on 'The myth of the short oesophagus' have been published. The fact that such surgeons have not experienced the entity is probably a manifestation of the effect that early treatment is having on the disease. Nowadays it is uncommon to see a serious oesophageal stricture because of earlier and more effective treatment with over-the-counter medications and PPIs.

There is no doubt that the short oesophagus is a serious complication of GORD. A hernia larger than 5 cm that does not reduce on radiological studies or endoscopy has a 50% chance of being short. Laparoscopic mobilisation may be possible if the surgeon has the expertise to mobilise the oesophagus well into the chest.²⁹ Collis lengthening procedures via a thorascopic or laparoscopic approach have also been described for these cases.^{30,31}

In conclusion, oesophageal surgery has rightfully become a specialised subject, and many institutions have dedicated units that practise this surgery exclusively. The subject has posed many challenges to the young surgeon, and this alone has made the specialty attractive to the surgeons' intellect. The trend to less invasive procedures will undoubtedly grow, and the desire to improve results will keep surgery in the forefront of oesophageal research.

REFERENCES

1. DeMeester TR, Peters JH, Bremner CG, Chandrasoma P. Biology of gastroesophageal reflux disease; pathophysiology relating to medical and surgical treatment. *Annu Rev Med* 1999; 50: 469-506.

2. Chandrasoma P, Lokuhetty PT, DeMeester TR, *et al.*, Definition of histopathologic changes in gastroesophageal reflux disease. *Am J Surg Pathol* 2000; **24**: 344-351.
3. Bremner CG, Lynch VP, Ellis FH, jun. Barrett's esophagus: congenital or acquired? An experimental study of esophageal mucosal regeneration in the dog. *Surgery* 1970; **68**: 209-216.
3. Campos GM, DeMeester SR, Peters JH, *et al.* Predictive factors of Barrett esophagus: multivariate analysis of 502 patients with gastroesophageal reflux disease. *Arch Surg* 2001; **136**:1267-1273.
5. Fitzgerald RC, Omar MD, Triadafilopoulos G. Dynamic effects of acid on Barrett's esophagus. *J Clin Invest* 1996; **98**: 2120-2128.
6. Pollara WM, Zilberstein B, Cecconello I, Filho UL, Pinotti HW. Regeneration of esophageal epithelium in the presence of gastroesophageal reflux. In: DeMeester TR, Skinner DB, eds. *Esophageal Disorders: Pathophysiology and Therapy*. New York: Raven Press, 1985: 225-231.
7. Narbona-Arnau B, Argente-Narvarro P, Miguel Lloris-Carsi J, Calvo-Bermúdez MA, Cejalvo-Lapeña D. Experimental endobrachyoesophagus in dogs. A model without mucosectomy. *Dis Esophagus* 1994; **7**: 112-117.
8. Martin C. In: Bremner CG, DeMeester TR. Proceedings from an international conference on ablation therapy for Barrett's mucosa. *Dis Esophagus* 1998; **11**: 1-27.
9. Leite LP, Johnson BT, Barnett J, Castell JA, Castell DO. Ineffective esophageal motility (I.E.M). The primary finding in patients with non-specific esophageal motor disorders. *Dig Dis Sci* 1997; **42**: 1859-1865.
10. Gockel I, Lord RVN, Bremner CG, *et al.* The hypertensive lower esophageal sphincter: A motility disorder with manometric features of out-flow obstruction. *J Gastrointestinal Surgery* 2003; **7**: 692-700.
11. Mason RJ, Bremner CG, DeMeester TR, *et al.* Pharyngeal swallowing disorders: selection for and outcome after myotomy. *Ann Surg* 1998; **228**: 598-608.
12. Behm B, Stollman N. Endoluminal therapies for gastroesophageal reflux disease. *J Clin Gastroenterol* 2004; **38**: 209-217.
13. Gurski RR, Peters JH, Hagen JA, *et al.* Barrett's esophagus can and does regress after antireflux surgery: a study of prevalence and predictive features. *J Am Coll Surg* 2003; **196**: 706-712.
14. DeMeester SR, Campos GM, DeMeester TR, *et al.* The impact of an antireflux procedure on intestinal metaplasia of the cardia. *Ann Surg* 1998; **228**: 547-556.
15. Inoue H, Sato Y, Sugaya S, *et al.* Review of endoscopic surgery for esophageal cancer. *Japanese Journal of Cancer & Chemotherapy*. 2003; **30**: 920-922.
16. Finley RJ, Clifton JC, Stewart KC, Graham AJ, Worsley DF. Laparoscopic Heller myotomy improves esophageal emptying and the symptoms of achalasia. *Arch Surg* 2001; **136**: 892-896.
17. Vaezi MF, Baker ME, Achkar E, Richter JE. Timed barium oesophagram: better predictor of long term success after pneumatic dilation in achalasia than symptom assessment (see comment). *Gut* 2002; **50**: 765-770.
18. Narne S, Cutrone C, Bonavina L, Chella B, Peracchia A. Endoscopic diverticulotomy for the treatment of Zenker's diverticulum: results in 102 patients with staple-assisted endoscopy. *Ann Otol Rhinol Laryngol* 1999; **108**: 810-815.
19. Bremner CG. Zenker diverticulum. *Arch Surg* 1998; **133**: 1131-1133.
20. Nehra D, Lord R, De Meester TR, *et al.* Physiologic basis for the treatment of epiphrenic diverticulum. *Ann Surg* 2002; **253**: 346-354.
21. DelGenio A, Rossetti G, Maffetone A, *et al.* Laparoscopic approach in the treatment of epiphrenic diverticula: long-term results. *Surg Endosc* 2004; **18**: 741-745.
22. Katzka DA, Sidhu M, Castell DO. Hypertensive lower esophageal pressures and reflux: An apparent paradox which is not unusual. *Am J Gastroenterol* 1995; **90**: 280-284.
23. Tamhankar AP, Almogy G, Arain MA, *et al.* Surgical management of hypertensive lower esophageal sphincter with dysphagia or chest pain. *Journal of Gastrointestinal Surgery* 2003; **7**: 990-996.
24. Hagen JA, DeMeester SR, Peters JH. Curative resection for esophageal adenocarcinoma: analysis of 100 *en bloc* esophagectomies. *Ann Surg* 2001; **234**: 520-530.
25. Noguchi T, Wada S, Takeno S, Hashimoto T, Moriyama H, Uchida Y. Two-step three-field lymph node dissection is beneficial for thoracic esophageal carcinoma. *Dis Esophagus* 2004; **17**: 27-31.
26. Briel JW, Tamhankar AP, Hagen JA, *et al.* Prevalence and risk factors for ischemia, leak, and stricture of esophageal anastomosis: Gastric pull-up versus colon interposition. *J Am Coll Surg* 2004; **198**: 536-542.
27. Banki F, Mason RJ, DeMeester SR *et al.* Vagal-sparing esophagectomy: A more physiologic alternative. *Ann Surg* 2002; **236**: 324-336.
28. Nguyen NT, Roberts P, Follette DM, Rivers R, Wolfe BM. Thoracoscopic and laparoscopic esophagectomy for benign and malignant disease: lessons learned from 46 consecutive procedures. *J Am Coll Surg* 2003; **197**: 902-13.
29. O'Rourke RW, Khajanchee YS, Urbach DR, *et al.* Extended transmediastinal dissection: an alternative to gastroplasty for short esophagus. *Arch Surg* 2003; **138**: 735-740.
30. Swanstrom LL, Marcus DR, Galloway GQ. Laparoscopic Collis gastroplasty is the treatment of choice for the shortened esophagus. (see comment). *Am J Surg* 1996; **171**: 477-481.
31. Hunter JG. Laparoscopic Collis gastroplasty and Nissen fundoplication. A new technique for the management of esophageal foreshortening. *Surg Endosc* 1998; **12**: 1055-1060.