Review Article

Secrets for successful laparoscopic antireflux surgery: patients with collagen diseases

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Abstract: Gastroesophageal reflux disease (GERD) in patients with connective tissue disorders (CTDs) is often severe, and complications such as erosive esophagitis, strictures, and Barrett's metaplasia may worsen the patient's clinical course. Medical treatment is effective in most cases; however, symptoms often do not improve. In addition, PPIs reduce the pH of refluxate but have almost no effect on the backflow of gastroesophageal contents into the esophagus. Hence, medical therapy should give way to surgical correction of reflux in selected cases. Even though worsening of dysphagia after a fundoplication remains a concern in these patients, as their esophageal body motility is often severely compromised, laparoscopic antireflux surgery (LARS) should be considered as an effective treatment, as outcomes have been proven good in selected patients.

Keywords: Gastroesophageal reflux disease (GERD); fundoplication; upper endoscopy; barium esophagram; esophageal manometry; ambulatory 24-hour pH monitoring; connective tissue disorders (CTDs)

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Introduction

Systemic sclerosis (scleroderma) and other collagen diseases (mixed connective tissue disease, dermatomyositis, polymyositis, etc.) are connective tissue disorders (CTDs) that involve the esophagus resulting in esophageal hypomotility. Studies on the pathogenesis of gastroesophageal reflux disease (GERD) in patients with CTDs suggest that decreased esophageal clearance is a central pathophysiologic factor for the development of GERD (1,2). Shoenut *et al.* demonstrated higher amounts of acid refluxate in both the distal and proximal esophagus in those with aperistalsis than in those with intact peristalsis (3). Gyger *et al.* and Spechler *et al.* also showed that patients with CDTs are frequently found to have absent esophageal peristalsis and an incompetent lower esophageal sphincter (LES) (4,5). Therefore, GERD in these patients may be severe, leading to major complications such as Barrett's metaplasia, erosive esophagitis, and strictures. Medical treatment for GERD in patients with CTDs is effective in most cases (6,7). However, some patients do not improve and symptoms worsen over time. In addition, pharmacological therapy does not stop the backflow of gastroesophageal contents into the esophagus and may not prevent aspiration, with consequent damage to the lungs from pepsin and bile acids (8-12). Hence, medical therapy should give way to surgical correction of reflux in selected cases: those refractory to PPIs and those who

aspirate. Surgical correction of reflux in those with CTDs after lung transplantation is still matter of debate in the transplant community. Even if worsening of dysphagia after a laparoscopic fundoplication remains a concern in those with severely impaired esophageal clearance, laparoscopic antireflux surgery (LARS) should be considered as an effective treatment, as outcomes have been proven satisfactory in selected patients (13,14).

Diagnostic evaluation

The diagnostic evaluation of GERD in patients with CTDs should include endoscopy, barium swallow, high-resolution impedance manometry (HRIM), and ambulatory pH monitoring.

Upper endoscopy

Esophagogastroduodenoscopy could confirm the diagnosis of GERD or can identify other pathologies; in fact, it is usually the initial evaluation modality of patients with reflux symptoms. The presence of severe erosive esophagitis or Barrett's esophagus can indirectly support the diagnosis of GERD and, in some cases it can be therapeutic (e.g., dilation of a peptic stricture) (15,16). Despite the long-term medical treatment of these patients, Marie *et al.* showed that the incidence of esophagitis and Barrett's esophagus in patients with scleroderma was 32% and 7%, respectively (17).

Barium swallow

The barium swallow has no diagnostic role, as the presence of reflux during the test does not correlate with the pH monitoring data (18). The diagnostic value of barium swallow in the evaluation of GERD is therefore limited to the identification of anatomical problems, like a hiatal hernia, the presence of a Schatzki ring, or an esophageal stricture. More recently, a modified barium swallow has been increasingly used to detect aspiration in those with worsening lung function.

HRIM

HRIM has a central role in the evaluation of patients with CTDs. Typically, CTDs present with ineffective or absent esophageal motility and hypotensive LES (1,19). Roman *et al.* studied the esophageal peristalsis of 51 patients with scleroderma and the results showed that that 83% had hypotensive LES, 47% and 20% had absent or weak peristalsis, respectively (20). In particular, in the group of patients with Barrett's esophagus or esophagitis, they all had absent peristalsis and a hypotensive LES. Conversely, Dantas *et al.* showed that only 6% of patients with systemic sclerosis had a deterioration of the esophageal motility, at a median follow-up of 40 months (21). Hence, esophageal peristalsis does not always worsen.

Ambulatory pH monitoring

Ambulatory pH monitoring is an essential test in all patients undergoing LARS, especially in the presence of extra-esophageal manifestations or in patients unresponsive to PPIs because it confirms the diagnosis of GERD, ruling out other potential pathologies causing the symptoms (22,23). Impedance measures the intra-esophageal contents and when combined with the pH probe, can detect acid and non-acid refluxate. Since PPIs increase gastric pH, the impedance pH monitoring help to detect reflux episodes while on PPIs, and might provide prognostic information in patients with CTDs and interstitial lung disease (ILD) (24). In a prospective study by Savarino *et al.*, 40 patients with scleroderma underwent pulmonary high-resolution computed tomography (HRCT) and 24-hour impedance pH monitoring. The results showed that the refluxate (acid and non-acid) reached more often the proximal esophagus in patients with ILD compared to patients with normal lungs, and that the total number of reflux episodes correlated with the degree of pulmonary fibrosis (25). In addition, Fisichella *et al.*, in retrospective study of 10 patients with severe scleroderma who underwent esophageal functional testing for lung transplant evaluation, found that severe reflux was a better predictor of survival than pulmonary function testing values (24).

Surgical indications and treatment

LARS is often indicated for patients with refractory GERD, for patients who opt out long-term medical treatment, or in those with side effects of PPIs or who aspirate. However, in patients with CTDs a fundoplication has been considered with suspicion because of the risk of worsening dysphagia in those with severely impaired esophageal peristalsis (6,26,27). For this reason, PPIs are considered the treatment of choice. Unfortunately, the pharmacological approach has downsides that must be taken into account. PPIs in patients with CTDs are not always able to heal esophagitis (26)

and do not prevent nocturnal refluxate (27). Acid-reducing medications also only affect acid production and raise the pH of the gastric content, while reflux into the esophagus still occurs (28-30) thus potentially leading to aspiration and deterioration of the lung function with resultant pulmonary fibrosis (2,9,10,13,31). Furthermore, although esophageal manometry is often abnormal (32), the classical depiction of aperistalsis and hypotensive LES is not always present. Patti *et al.* (33) showed that in 20 patients with CTDs their LES pressure and esophageal motility were not different from the control group. Conversely, esophageal peristalsis was most often lacking in patients with end-stage lung disease secondary to CTDs. Based on these data, one may speculate that an early screening would increase the chance to detect GERD in patients with effective esophageal peristalsis, reducing the risk of postoperative dysphagia in case a fundoplication is performed.

Few authors have reported the outcomes of LARS in patients with CTDs. Poirier *et al.* and Kent *et al.* have shown that a fundoplication reduces reflux symptoms and improve esophageal acid exposure in the majority of cases. Postoperatively, the incidence of dysphagia was 71% in both studies; however, Poirier *et al.* reported that dysphagia was already present in 86% of patients before the operation, and that a postoperative radionuclide transit study showed no significant decrease in esophageal emptying. Similarly, Kent *et al.* showed the incidence of preoperative dysphagia was already high (61%), and that the average postoperative dysphagia score was 1.8, on a scale from 0 to 5 (34,35). In addition to the small number of patients, another limitation of these studies is that a total fundoplication was performed in all patients, even in those with absent peristalsis.

Conversely, Patti *et al.* demonstrated that a tailored approach for patients with CTDs was effective in improving reflux while it was associated to a low incidence of post-operative dysphagia. Only one patient out of ten presented with dysphagia, but it improved with two Savary dilatations. They performed a total fundoplication in all patients with normal esophageal motility and a partial 240° fundoplication in those with weak (distal esophageal amplitude ≤40 mmHg) or absent peristalsis (33). Similarly, Watson *et al.* performed LARS (4 total and 22 partial anterior fundoplication) in 26 patients with GERD (six had scleroderma, while the remaining 20 had no evidence of CTDs) in whom manometry showed complete aperistalsis. At a 5- to 12-year follow-up, good outcomes were recorded in 93% of patients (36). Many believe that these results can be attributed to a properly constructed fundoplication, tailored to the patient's esophageal motility (37,38).

Scleroderma and other CTDs have long been considered a strict contraindication for lung transplantation. In addition, 50% to 80% of these patients have some form of esophageal dysfunction, leading to GERD (39). The incumbent risk of aspiration following transplantation is the main area of concern, as GERD-induced aspiration has been linked to the development of bronchiolitis obliterans syndrome (BOS), which has limited the transplant options for these patients. In support of these data, Fisichella *et al.* demonstrated that pH monitoring could predict survival status in patients with scleroderma awaiting lung transplantation, as the severity of reflux seemed to have a direct correlation with the survival rate (24). In the most recent updated guidelines for the selection of transplant candidates, the International Society for Heart and Lung Transplantation (ISHLT) stated that carefully selected candidates with scleroderma can undergo lung transplantation; however, in the "relative contraindication" section they state that "*Other medical conditions…such as… gastroesophageal reflux*, *should be optimally treated before transplantation*" (40). In addition, LARS has been shown to preserve lung function in these patients, before and after the transplant (41), reducing the risk of rejection (13,42). The available evidence seems to suggest that a pH monitoring must be performed early in these patients, as this test can identify those who will benefit from LARS, preventing GERD and its harmful effects on the allograft.

Finally, a laparoscopic Roux-en-Y gastric bypass (RYGB) has been recently proposed as an alternative to control GERD in patients with CTDs (35,43,44). In a series of patients with CTDs who underwent RYGB (35), Kent *et al.* showed better outcomes for dysphagia, bloating, diarrhea, and GERD score than in those who underwent a fundoplication. However, the authors performed a total fundoplication in all patients, including those with absent esophageal peristalsis.

Conclusions

The management of GERD in patients with CTDs is challenging. It is based on the evaluation of clinical features, objective evidence of reflux, manometric patterns, likelihood of aspiration, and lung function. Regardless of the medical treatment efficacy, these patients need to be screened early and a careful assessment of the esophageal motility is essential. In the setting of a significant esophageal dysfunction, the role of fundoplication has

been controversial given the potential for dysphagia. However, the few data available support the thought that these patients should be evaluated for a tailored antireflux procedure. Although the literature on LARS and CTDs is scant and all series have a small number of patients and short follow-up, evidence seems to suggest that the success of the operation relies in the proper patient selection. Patients refractory to PPIs and those with suspected aspiration should be referred to LARS early enough before the progression of the disease precludes any meaningful surgical intervention.

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