



Review Article

The evolution of oesophageal function testing and its clinical applications in the management of patients with oesophageal disorders

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ABSTRACT

The last decade has brought significant technical advances in laparoscopic surgery. In this constantly evolving technological climate, less told is the story of the evolution of diagnostic technology that improved the clinical management of patients with oesophageal disorders. The successful outcome of the laparoscopic treatment of oesophageal disorders is due to a combination of three different factors: the skills and the ability of the foregut surgeon, the high volume of referral, the expertise in the critical evaluation of the oesophageal function tests. This is an art *per se*, and it is rarely acknowledged in the achievement of the excellent results of surgery. Oesophageal function testing provides the clinician with information that cannot be obtained by the clinical, endoscopic, and radiological evaluation of patients. This expertise, intimately coupled with the other factors, allows the surgeon to better understand the pathophysiology of these diseases and to provide the optimal management. Therefore, it is essential to understand the evolution that this technology is currently undergoing, and how these changes are expanding the current indications for antireflux surgery by identifying additional predictors of successful outcome.

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The last decade has brought significant technical advances in laparoscopic surgery. A widespread partnership between the biomedical industry and academic institutions has boosted progress with several technical improvements, from laparoscopic instruments to high definition optic systems. This technological evolution has also affected the laparoscopic treatment of patients with oesophageal disorders. The laparoscopic treatment of these disorders is nowadays considered the standard of care and the long-term results for diseases, such as GERD and achalasia, have proven to be excellent. Recent reports confirm that GERD could be controlled effectively by an operation whose effects last for many years. For instance, Dallemagne et al. followed for 10 years 100 consecutive patients operated on in 1993 and showed that 5 and 10 years later more than 90% of patients were free of symptoms of GERD [1]. Smith and co-workers showed that laparoscopic Heller myotomy and Dor fundoplication for achalasia relieves dysphagia in 94% of patients for 10 years [2].

However, these results were achieved in the 1990s, during a time when laparoscopic surgery was still in the midst of its continuous evolution. For instance, the non-selective approach that involved performing a total fundoplication regardless of the peristaltic function of the oesophagus has resulted in a better control of reflux

with a minimal incidence of *de novo* dysphagia [3]. Therefore, we argue that another 10 years from now the reported results of this laparoscopic operation might be better than those reported thus far.

In this constantly evolving technological climate, less told is the story of the evolution of the diagnostic technology that allowed laparoscopic surgeons to achieve such excellent results, and on how this technology has improved over time the management of patients with oesophageal disorders. The successful outcome of the laparoscopic treatment of oesophageal disorders is due to a combination of three different factors. Like a three-legged chair cannot stand without each of its legs, the success of laparoscopic foregut surgery would not be possible if one of these factors were missing. The skills and the ability of the foregut surgeon are one of these factors, maybe the most evident. The volume of referral and the collaboration with other departments, such as gastroenterology and radiology, play also a very important role. Lastly, the expertise in the critical evaluation of the oesophageal function tests is the third factor. This is an art *per se* that is rarely acknowledged in the achievement of the excellent results of surgery. This art provides the clinician with information that cannot be obtained by the clinical, endoscopic, and radiological evaluation of patients. It is this expertise, intimately coupled with the other factors, that allows the surgeon to better understand the pathophysiology of these diseases and allows him to provide the optimal management. Therefore, it is essential to understand how this technology has improved the man-

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agement of patient with oesophageal disorders, the evolution that this technology is currently undergoing, and how these changes are expanding the current indications for antireflux surgery by identifying additional predictors of successful outcome.

Oesophageal function testing (oesophageal manometry and 24 h pH monitoring) has been based on the same technology for decades up until these very last years, when several technical improvements transformed the field of oesophageal diagnostic testing. Prolonged (up to 48 h) monitoring of the oesophageal pH is now possible with the wireless pH capsule monitoring and more detailed pressure topography of the oesophagus has been achieved by the recent development of the high-resolution manometry.

Oesophageal manometry and ambulatory pH monitoring were developed in the 1970s. With time, the relevance of these techniques in clinical practice became evident. Johnston et al. in 1993 showed how oesophageal manometry changed the management of 20% of patients with non-cardiac chest pain and GERD and of 60% of those with dysphagia [4]. Eckardt, followed by Netzer, reported in 1999 that the introduction of pH monitoring in their clinical practice changed management in 42–66% of the patients [5,6]. Since that time, many research investigations have enhanced our understanding of the utility of this diagnostic modality in the pathogenesis and in the management of patients with GERD and primary oesophageal motility disorders (PEMDs). The results of these studies allowed the characterization of the central role of oesophageal function tests in diagnosing GERD objectively. A study on 822 consecutive patients referred for oesophageal function tests with a clinical diagnosis of GERD based on symptoms and endoscopic finding, showed that only 70% had abnormal reflux on pH monitoring [7]. Symptoms such as heartburn and regurgitation were also no more frequent in patients who had genuine reflux than in those who did not [7]. Thus, symptomatic evaluation, by itself, could not distinguish between the two groups. In addition, endoscopy could not confirm a diagnosis of GERD based on symptoms, because abnormalities in the oesophageal mucosa were absent in about half of patients with GERD and a significant interobserver variation between endoscopists is common, particularly for low-grade oesophagitis [7,8]. This finding is important because oesophageal function tests would obviate the prescription of inappropriate acid suppression medications or the performance of an antireflux operation.

Ambulatory pH monitoring also establishes a temporal correlation between symptoms and episodes of reflux. Such a correlation is particularly important when atypical symptoms of gastro-oesophageal reflux disease, such as cough, are present, as it identifies patients most likely to benefit from antireflux surgery. For instance, Patti et al. have showed that following laparoscopic fundoplication, typical symptoms resolved in 90% of patients, and respiratory symptoms resolved in 83% of patients when a strong temporal correlation between cough and reflux was found on pH monitoring [9]. Moreover, ambulatory pH monitoring allows stratifying patients with GERD on the basis of its severity. Specifically, pH monitoring identifies a subgroup of patients characterized by a worse reflux profile because of more acid reflux in the distal and proximal oesophagus, and slower acid clearance. These patients more frequently develop Barrett's metaplasia and thus might benefit from early antireflux surgery [10]. Lastly, ambulatory pH monitoring provides baseline data that may prove useful postoperatively if symptoms persist or recur postoperatively. For instance, when a patient has heartburn postoperatively it is assumed that the fundoplication has failed and acid-reducing medications are prescribed. However, when ambulatory pH monitoring is performed, it shows that about two-third of patients who are taking acid-reducing medications postoperatively have a normal reflux status [11–13].

The invaluable role of oesophageal function tests in clinical practice has also been proven in the management of patients

with PEMDs, such as achalasia, nutcracker oesophagus, diffuse oesophageal spasm, and hypertensive lower oesophageal sphincter. The application of these diagnostic tools in clinical practice has yielded helpful information about the pathophysiology of PEMD and the implications for their treatment. Symptoms alone do not distinguish PEMD from GERD, because a clinical diagnosis of PEMD, when validated by ambulatory pH monitoring, was correct in only 42% of the patients, while 25% had been treated with acid-suppressing medications on the wrong assumption that they had GERD [14]. In addition, a large number of untreated patients with achalasia have been incorrectly diagnosed with GERD. We reported that 63% of these patients were on acid-suppressing medications at the time of their preoperative evaluation [15]. The heartburn reported by all these patients with PEMD was probably caused by stasis and fermentation of food in the oesophagus, not GERD. Therefore, ambulatory pH monitoring had allowed us to distinguish GERD from PEMD and oesophageal manometry discriminated the type of PEMD. A barium swallow has also shown to be unreliable, as it suggested achalasia in 60% of the patients and it added little to the diagnosis of other PEMDs [14]. The findings of oesophageal function tests had helped also planning optimal treatment. The manometric findings of diffuse oesophageal spasm or nutcracker oesophagus often occur in the presence of GERD. In these cases, optimal management consists in correcting the reflux first, because the dysmotility is secondary. Only in the absence of reflux on pH monitoring can dysmotility be considered a primary disease. Therefore, oesophageal function tests are crucial in making the correct the diagnosis, as treatment of GERD is completely different from PEMD and performing a laparoscopic fundoplication in a patient without reflux but with achalasia can have catastrophic consequences.

This technology has also improved our ability of predicting the outcome of laparoscopic antireflux surgery. In a multivariate analysis, Campos et al. in 1999 have shown that an abnormal ambulatory pH monitoring, together with a good response to acid suppression therapy and the presence of typical symptoms, such as heartburn, are important in predicting a successful outcome of laparoscopic antireflux surgery [16]. The findings of this work influenced the practice of gastroenterologists and surgeons, for almost 10 years. This work, however, left some questions unanswered. It was not clear how to treat patients who still experienced typical or atypical symptoms while receiving optimal medical therapy and specifically it was not clear if another disease was responsible or if a non-acid form of reflux was still present. A suggestion that reflux was not always acid in nature had come by Dr. DeMeester's group. In 1995 Kauer et al., using spectrophotometric bilirubin detection as a marker of duodeno-gastro-oesophageal reflux, showed that in 59% of patients a mixed form of reflux was present in the oesophagus [17]. The breakthrough came with the development of oesophageal impedance, which detects the flow of liquids and gas through hollow viscera, such as the oesophagus. When used in combination with oesophageal pH monitoring, this technique is able to detect both the transit of the refluxate and its pH throughout the oesophagus. In 2004, Tamhankar et al. showed that in normal subjects, medical therapy did not affect the number of reflux episodes or their duration, but that it just altered the pH of the refluxate [18]. They clearly showed that the oesophagus can still be bathed by gastric refluxate with only less acidic properties and they also speculated that the reflux itself more than its pH might be responsible for the refractory symptoms of GERD [18]. This was the first objective clue that explained why symptoms could be refractory to medical therapy. This observation has led to important clinical implications: that GERD cannot be excluded in patients with weakly acidic reflux and that in some of these selected patients surgery can be effective. Mainie et al. have shown that patients with persistent symptoms on acid suppressive therapy can be successfully treated surgically when multichannel intraluminal impedance

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