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Perspectives of Surgery for Benign Esophageal Diseases

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1.1. Introduction

We are definitely living in the age of innovation. Unfortunately, primarily due to lack of judgment, innovation has become synonymous with renouncing any type of precursor, generally termed old or outdated. At first glance, due to lack of judgment, typical of inexperienced youth, but in fact because of scientific illiteracy, many health innovations are adopted without being adequately compared with real-world use, which often precedes them in many years.

This practice is also present in surgery, and given the methodological challenges of producing consistent studies, this becomes even more difficult, and consequently discouraging and demoralizing, which justifies for many the disincentive to do so, or for some the opportunity to generate information full of biases and conflicts of interest [1, 3]. Critically dealing with the evidence [1], on the other hand, establishes the image of a ferocious grunt that rejects all things and a theoretical world far removed from practice.

All of this is the consequence of lack of knowledge and skill to establish a harmonious relationship between the best available evidence, the experience gathered by the surgeon, and the values of his or her patients, the inability to translate knowledge into strong and sound decision making, and to demonstrate how much increase in benefits and reduction of harm can be produced by replacing current practice with new and generally more expensive alternatives [1]. But what are the biases present and inherent in surgical research that, although acknowledged and used, can be minimized but not overcome, and will always introduce a level of uncertainty that needs to be considered in the results, conclusions, and decision making [2, 4]?

1.2. Patient Related [2, 4]

a. Strict and homogeneous eligibility criteria tend to reduce the sample, especially when only one research center is involved, and small samples have no power of generalization.
b. Who is the patient studied and who is the patient in daily practice? Surgery research, in comparison with clinical or non-invasive treatment, tends to involve patients without surgical indication, who would not be operated on, or patients whose only option is surgery, and who would never be treated conservatively.
c. Although the allocation of patients randomly and in a blindfolded fashion is a simple and easy process to perform, observational cohort studies are preferred because of the ease of obtaining patients to be compared.
d. The experimental cohort studies (controlled and randomized clinical trials), where the day-to-day service is slightly modified with inclusion of more flexible patients, are seldom used and would be an alternative to weak observational studies.

1.3. Related to Intervention [2, 4]

a. The impossibility of double blindness (patient and surgeon) is the most serious limitation of surgical research. Once the curtains are lifted up, the surgeon can take greater care of a patient in the group, which might give better results.

b. An attenuator used is the blindness of evaluators, in addition to the patient's whenever possible. But this is insufficient, especially when outcomes analyzed are not subjected to being protected from the influence of the patient and often from the evaluator.
c. Another limitation related to surgery is the difference in surgical skill among groups, especially in multicenter studies and also differences among surgeons within the studies and those in the practice who will use the results.
d. The use of comparison models between techniques according to the practice already used by surgeons could attenuate the differences, favoring the execution of multicenter clinical trials.

1.4. Related to Comparison [2, 4]

a. The need for comparison in surgery could sound like an ineffective and unnecessary waste of time because after all the results speak for themselves. But the question is: Could we have better results? Will it be more effective and unharmful? How can one know without comparing?
b. In the past, with the absence of options to provide for the patient, comparing might seem unnecessary, but with the increasing emergence of non-operative or non-invasive treatments, comparing seemed an obvious obligation.
c. But this obviousness turned into immediate present, in regard to "the least damage is always better than the greatest harm," and the medical community, forgetting to consider the results concerning time and efficacy, just like before, began to deem it ineffective and unnecessary to compare.
d. Industry moved aggressively with funding, which flooded literature with low-level, biased research that satisfies marketing. In addition, health community is unprepared to deal with, understand, and communicate to patients the level of uncertainty and risks of using such weak evidence.

1.5. Related to Outcomes [2, 4]

a. Appropriate and relevant outcomes are not always considered, given the benefits are based on intermediary results like reduction in acid

exposure, or on results including solid details assuming, but not demonstrating, improved quality of life of patients, such as recurrence or efficacy rates.

b. Measurement of outcomes is usually done using subjective instruments, such as analog scales, or using instruments like patient satisfaction and quality of life, which are not replicable across other populations.
c. Through randomized controlled trials (RCT), short-term follow-up (weeks or months) establishes advantages of one procedure over another, as if patients would only live within such timeframes. Long-term observational studies are discarded, and "upgrading" of concepts are unknown.
d. To make chaos within the literature even worse, clinical research (even when based on RCT) reports similar outcomes with diverging, incomplete, and often missing measurements, or different outcomes across similar comparisons, impeding meta-analysis in systematic reviews.

The literature profile (evidence) in esophageal surgery is no different from other surgery specialties in regard to bias and strength, and level of uncertainty. Some topics can clearly illustrate these limitations and weaknesses, such as achalasia, gastroesophageal reflux disease (GERD), and Barrett's esophagus.

Fundoplication has been considered as an important tool for surgical treatment of these diseases. For GERD and Barrett's esophagus, the following can be stated:

a. At short and medium follow-up, surgical treatment is more effective than medical management [5]; on the other hand, open anti-reflux surgery or the use of proton pump inhibitors (PPIs) are both effective in normalizing reflux into the esophagus in a follow-up of 10 years. Lower esophageal sphincter pressure is repaired and maintained after fundoplication [6].
b. In general, long-term follow-up outcomes of laparoscopic total (Nissen) and partial (Toupet-270°) fundoplication give similar results for treatment of GERD [7]. In the short term, dysphagia symptoms and the inability to belch may be higher in the Nissen procedure, but decreases with time. For patients with moderate to severe GERD, including Barrett's esophagus, total fundoplication is recommended.

c. Considering the effectiveness of partial and total fundoplication for treatment of extra esophageal manifestations of GERD, both are recommended for patients with atypical symptoms refractory to medical treatment, although Nissen fundoplication is better for asthma patients [8].
d. Randomized clinical trial showed better results for fundoplication than for medical treatment in Barrett's esophagus [9].
e. Satisfaction results in a long follow-up (6–9 years) showed better results for patients submitted to surgery, including those who needed PPI, after the surgery compared with the medical treatment only group [10].
f. Anti-reflux surgery probably minimizes the risk of esophageal carcinoma after fundoplication [11].

Robot-assisted laparoscopic fundoplication had emerged as a promising technical innovation [12–14]. It is a possible and safe alternative for the surgical treatment of GERD, but in comparison to laparoscopic procedures, it didn't show advantages in terms of operating time, hospital stay, and results [15]. The principal disadvantage is the high costs. On the other hand, comparisons should not be restricted only to common procedures, but to more demanding operations such as redo hiatal hernia and anti-reflux surgery or achalasia, when robotic support could be really beneficial [16].

New procedures are being introduced in the treatment of GERD, reducing surgical aggression and also for treating patients with small or without hiatal hernias. The focus is also to avoid or diminish the long-term use of PPI. These include endoscopic fundoplications [17–20], the Linx magnetic esophageal sphincter augmentation [21], and electric stimulation of the lower esophageal sphincter [22]. More data are needed in order to establish the best use for each procedure.

For achalasia, non-operative treatment generally provides only temporary relief of dysphagia.

Cardiomyotomy is the main form of treatment, specially associated with partial fundoplication. Motility studies confirm a significant decrease of lower esophageal sphincter pressure after both types of operation, open or laparoscopic. Occurrence of gastroesophageal reflux is much more usual when the fundoplication is not performed [23, 24].

After anatomic studies of the esophagogastric junction, Curti [25] proposed to realize the myotomy in the right lateral wall, extending from the

esophagus to the upper stomach. His belief was that avoiding manipulating the fibers of the His muscles, reflux would be lower. Based on these remarks, Chaib [26] studied 76 patients submitted to a long myotomy (6 cm in the esophagus and 3 cm in the stomach) in the right lateral wall of the esophagogastric junction. Patients were studied in a mean follow-up of 8 years by endoscopy. Reflux esophagitis was found in 42.1% of the patients.

These comments are presented here due to the increasing use of peroral endoscopic myotomy (POEM) procedure, which still needs a long follow-up evaluation to be validated [27]. Will continuous use of lifelong PPI be able to control reflux in these patients? Further, considering the three main causes of recurrence of symptoms after cardiomyotomy — scarring, evolution to dolichomegaesophagus, and reflux esophagitis — the last condition will be the most difficult to treat.

Partial anterior (Dor) or partial posterior fundoplication (Toupet) in transabdominal cardiomyotomy for achalasia gives similar results [24, 28] with prevention of reflux in 80–90% of the patients. Csendes *et al.* [29] demonstrated that gastroesophageal reflux increases with time, after cardiomyotomy and Dor fundoplication (35% after 20 years). Ortiz *et al.* [30] observed 13.9% of heartburn, 11.1% of dysphagia, and 23% of pathological pH studies after more than 15 years of follow-up after posterior partial fundoplication.

Cardiomyotomy with posterior, left lateral, and anterior partial fundoplication [31, 32] was employed for the treatment of achalasia in 1753 patients (open in 1011 and laparoscopic in 782) in our service. Dysphagia or gastroesophageal reflux was observed in 14.9% of them in a follow-up of 18 years. A total of 169 patients were submitted to esophagectomy due to dolichomegaesophagus. Mortality in this group was 2.3%. Robotic myotomy for achalasia showed better results in terms of morbidity and mortality when compared to open and laparoscopic surgery [33].

Finally, old and new procedures must be studied according to the principles referred to in the beginning of this chapter. We believe that this book, written by the leading esophageal surgeons of today, will certainly throw more light on the surgery for benign esophageal disorders.

References

[1] Evidence-Based Medicine Working Group. Evidence-based medicine. A new approach to teaching the practice of medicine. *J Am Med Assoc.* 1992;**268**:2420–2425.

[2] Paradis C. Bias in surgical research. *Ann Surg.* 2008;**248**(2):180–188.

[3] Probst P, Knebel P, Grummich K, Tenckhoff S, Ulrich A, Büchler MW, Diener MK. Industry bias in randomized controlled trials in general and abdominal surgery: An empirical study. *Ann Surg.* 2016;**264**(1):87–92.

[4] Gurusamy KS, Gluud C, Nikolova D, Davidson BR. Assessment of risk of bias in randomized clinical trials in surgery. *Br J Surg.* 2009;**96**(4):342–349.

[5] Rickenbacher N, Kötter T, Kochen MM, Scherer M, Blozik E. Fundoplication versus medical management of gastroesophageal reflux disease: Systematic review and meta-analysis. *Surg Endosc.* 2014;**28**(1):143–155.

[6] Emken BG, Lundell LR, Wallin L, Myrvold HE, Engström C, Montgomery M, Malm AR, Lind T, Hatlebakk JG; SOPRAN Study Group. Effects of omeprazole or anti-reflux surgery on lower oesophageal sphincter characteristics and oesophageal acid exposure over 10 years. *Scand J Gastroenterol.* 2017;**52**(1):11–17.

[7] Du X, Hu Z, Yan C, Zhang C, Wang Z, Wu J. A meta-analysis of long follow-up outcomes of laparoscopic Nissen (total) versus Toupet (270°) fundoplication for gastro-esophageal reflux disease based on randomized controlled trials in adults. *BMC Gastroenterol.* 2016;**16**(1):88.

[8] Koch OO, Antoniou SA, Kaindlstorfer A, Asche KU, Granderath FA, Pointner R. Effectiveness of laparoscopic total and partial fundoplication on extraesophageal manifestations of gastroesophageal reflux disease: A randomized study. *Surg Laparosc Endosc Percutan Tech.* 2012;**22**(5):387–391.

[9] Parrilla P, Martínez de Haro LF, Ortiz A, Munitiz V, Molina J, Bermejo J, Canteras M. Long-term results of a randomized prospective study comparing medical and surgical treatment of Barrett's esophagus. *Ann Surg.* 2003;**237**(3):291–298.

[10] Mehta S, Bennett J, Mahon D, Rhodes M. Prospective trial of laparoscopic nissen fundoplication versus proton pump inhibitor therapy for gastroesophageal reflux disease: Seven-year follow-up. *J Gastrointest Surg.* 2006;**10**(9):1312–1316.

[11] Maret-Ouda J, Konings P, Lagergren J, Brusselaers N. Antireflux Surgery and Risk of Esophageal Adenocarcinoma: A Systematic Review and Meta-analysis. *Ann Surg.* 2016; **263**(2):251–257.

[12] Wykypiel H, Bodner J, Wetscher G, Schmid T. Robot-assisted versus conventional laparoscopic fundoplication: Short-term outcome of a pilot randomized controlled study. *Surg Endosc.* 2008;**22**(5):1407.

[13] Müller-Stich BP, Reiter MA, Wente MN, Bintintan VV, Köninger J, Büchler MW, Gutt CN. Robot-assisted versus conventional laparoscopic fundoplication: Short-term outcome of a pilot randomized controlled trial. *Surg Endosc.* 2007;**21**(10):1800–1805.

[14] Morino M, Pellegrino L, Giaccone C, Garrone C, Rebecchi F. Randomized clinical trial of robot-assisted versus laparoscopic Nissen fundoplication. *Br J Surg.* 2006;**93**(5):553–558.

[15] Mi J, Kang Y, Chen X, Wang B, Wang Z. Whether robot-assisted laparoscopic fundoplication is better for gastroesophageal reflux disease in adults: A systematic review and meta-analysis. *Surg Endosc.* 2010;**24**(8):1803–1814.

[16] Tolboom RC, Draaisma WA, Broeders IA. Evaluation of conventional laparoscopic versus robot-assisted laparoscopic redo hiatal hernia and antireflux surgery: A cohort study. *J Robot Surg.* 2016;**10**(1):33–39.

[17] Kaindlstorfer A, Koch OO, Antoniou SA, Asche KU, Granderath FA, Pointner R. A randomized trial on endoscopic full-thickness gastroplication versus laparoscopic antireflux surgery in GERD patients without hiatal hernias. *Surg Laparosc Endosc Percutan Tech.* 2013;**23**(2):212–222.

[18] Hunter JG, Kahrilas PJ, Bell RC, Wilson EB, Trad KS, Dolan JP, Perry KA, Oelschlager BK, Soper NJ, Snyder BE, Burch MA, Melvin WS, Reavis KM, Turgeon DG, Hungness ES, Diggs BS. Efficacy of transoral fundoplication vs omeprazole for treatment of regurgitation in a randomized controlled trial. *Gastroenterology* 2015;**148**(2):324–333.e5.

[19] Witteman BP, Conchillo JM, Rinsma NF, Betzel B, Peeters A, Koek GH, Stassen LP, Bouvy ND. Randomized controlled trial of transoral incisionless fundoplication vs. proton pump inhibitors for treatment of gastroesophageal reflux disease. *Am J Gastroenterol.* 2015;**110**(4):531–542.

[20] Huang X, Chen S, Zhao H, Zeng X, Lian J, Tseng Y, Chen J. Efficacy of transoral incisionless fundoplication (TIF) for the treatment of GERD: A systematic review with meta-analysis. *Surg Endosc.* 2017;**31**(3):1032–1044.

[21] Bonavina L, De Meester T, Fockens P, Dunn D, Saino G, Bona D, Lipham J, Bemelman W, Ganz RA. Laparoscopic sphincter augmentation device eliminates reflux symptoms and normalizes esophageal acid exposure: One- and 2-year results of a feasibility trial. *Ann Surg.* 2010;**252**(5):857–862.

[22] Rodríguez L, Rodriguez P, Gómez B, Ayala JC, Oksenberg D, Perez-Castilla A, Netto MG, Soffer E, Crowell MD. Long-term results of electrical stimulation of the lower esophageal sphincter for the treatment of gastroesophageal reflux disease. *Endoscopy* 2013;**45**(8):595–604.

[23] Campos GM, Vittinghoff E, Rabl C, Takata M, Gadenstätter M, Lin F, Ciovica R. Endoscopic and surgical treatments for achalasia: A systematic review and meta-analysis. *Ann Surg.* 2009;**249**(1):45–57.

[24] Kurian AA, Bhayani N, Sharata A, Reavis K, Dunst CM, Swanström LL. Partial anterior vs partial posterior fundoplication following transabdominal

esophagocardiomyotomy for achalasia of the esophagus: Meta-regression of objective post-operative gastroesophageal reflux and dysphagia. *J Am Med Assoc Surg.* 2013;**148**(1):85–90.

[25] Curti P. Esfincter esôfago-gástrico: Estudo anatômico e importância cirúrgica do componente muscular [tese]. São Paulo: Faculdade de Medicina, Universidade de São Paulo, 1955.

[26] Chaib SA. Tratamento cirúrgico do megaesôfago [livre docente]. São Paulo: Faculdade de Medicina, Universidade de São Paulo, 1968.

[27] Tantau M, Crisan D. Peroral endoscopic myotomy: Time to change our opinion regarding the treatment of achalasia? *World J Gastrointest Endosc.* 2015;**7**(3):237–246.

[28] Rawlings A, Soper NJ, Oelschlager B, Swanstrom L, Matthews BD, Pellegrini C, Pierce RA, Pryor A, Martin V, Frisella MM, Cassera M, Brunt LM. Laparoscopic Dor versus Toupet fundoplication following Heller myotomy for achalasia: Results of a multicenter, prospective, randomized-controlled trial. *Surg Endosc.* 2012;**26**(1):18–26.

[29] Csendes A, Braghetto I, Burdiles P, Korn O, Csendes P, Henríquez A. Very late results of esophagomyotomy for patients with achalasia: Clinical, endoscopic, histologic, manometric, and acid reflux studies in 67 patients for a mean follow-up of 190 months. *Ann Surg.* 2006;**243**(2):196–203.

[30] Ortiz A, de Haro LF, Parrilla P, Lage A, Perez D, Munitiz V, Ruiz D, Molina J. Very long-term objective evaluation of heller myotomy plus posterior partial fundoplication in patients with achalasia of the cardia. *Ann Surg.* 2008;**247**(2):258–264.

[31] Pinotti HW, Gama-Rodrigues JJ, Ellenbogen G, Arab-Fadul R, Raia A. Novas bases para o tratamento cirúrgico do megaesôfago: Esofagocardiomiotomia com esofagofundogastropexia. *AMB Rev Assoc Med Bras.* 1974;**20**(9):331–334.

[32] Pinotti HW, Cecconello I, Zilberstein B, Pollara WM. Surgical Management of the megaesophagus. In: Siewert JR, Holscher AH, (Eds.). *Diseases of the Esophagus*, Springer-Verlag, Berlin, 1988:942–946.

[33] Shaligram A, Unnirevi J, Simorov A, Kothari VM, Oleynikov D. How does the robot affect outcomes? A retrospective review of open, laparoscopic, and robotic Heller myotomy for achalasia. *Surg Endosc.* 2012;**26**(4):1047–1050.