Results of antireflux surgery in patients with Barrett's esophagus

A. Csendes

Department of Surgery, University Hospital, University of Chile, Santiago de Chile, Chile

Experten-Meinung Antireflux-Chirurgie bei Barrett-Ösophagus

Zusammenfassung. *Grundlagen:* Barrett-Ösophagus (BÖ) entsteht durch gastroösophagealen Reflux und ist durch den Ersatz des Plattenepithels der Speiseröhre durch intestinale Metaplasie mit Becherzellen definiert. In 0,5–1,0 % der Fälle pro Jahr kann sich aus einem BÖ ein Adenokarzinom der Speiseröhre entwickeln. Diese Arbeit untersuchte die publizierten Ergebnisse zum Stellenwert der chirurgischen Therapie bei kurz- und langstreckigem BÖ.

Methodik: Es wurden 35 zwischen 1980 und 2006 publizierte Arbeiten zur chirurgischen Therapie von Barrett-Ösophagus (BÖ) analysiert. Die untersuchten Parameter waren klinischer Erfolg, Größe des Säure- und Gallerefluxes in den distalen Ösophagus, Endoskopie, Histopathologie sowie Entstehung eines Adenokarzinoms nach Antireflux-Chirurgie. Endoskopische ablative Verfahren wurden nicht in die Analyse inkludiert.

Ergebnisse: Der Großteil der Arbeiten zu langstreckigem BÖ ($\geq$3 cm) inkludierte nur wenige Patienten ($<$50), die Nachsorge war $<$5 Jahre in 80 %. Der klinische Erfolg bei langstreckigem BÖ, weniger als 5 Jahre nach klassischer Antireflux-Chirurgie betrug 81 %, nahm aber über die Zeit weiter ab. Reflux vor und nach Operation wurde nur in 3 Arbeiten untersucht. Die meisten Arbeiten inkludierten nur eine Endoskopie nach der Operation und Regression von BÖ fand sich in 50 % und 5 % bei kurz- bzw. langstreckigem BÖ. Progression zum Adenokarziom fand sich in 0 % und 3,6 % bei kurz-($<$3 cm) bzw. langstreckigem BÖ, auch in asymptomatischen Patienten. Im Gegensatz dazu fand sich bei langstreckigem BÖ nach 8–10 Jahren nach Vagotomie, Antrektomie, Fundoplikatio und Y-Roux-Anastomose (Länge der Y-Roux-Schlinge: 70 cm) in 91% Beschwerdefreiheit sowie permanente Refluxkontrolle, bei 55 % Regression von BÖ zu Kardia-Mukosa und keine Progression zu hochgradiger Dysplasie (= intraepitheliale Neoplasie) und Adenokarzinom. Jene mit kurz-streckigem BÖ ($<$3 cm) zeigten postoperativ klinische, manometrische und pH-metrische Refluxkontrolle nach laparoskopischer Fundoplikatio.

Schlussfolgerungen: Bei langstreckigem BÖ ($\geq$3 cm) kann die Antireflux-Chirurgie die Entstehung eines Adenokarzinoms nicht verhindern. Selektive Vagotomie, Antrektomie, Fundoplikatio und Y-Roux-Anastomose ist eine Alternative bei langstreckigem BÖ, vor allem bei Patienten<60 Jahre. Bei kurzstreckigem BÖ ($<$3 cm) erscheint die laparoskopische Nissen-Fundopikatio als wirksame Therapie der Wahl.

Schlüsselwörter: Barrett-Ösophagus, Fundoplikatio, Kardia-Mukosa, Becherzellen.

Summary. *Background:* Barrett's esophagus (BE) is defined as the presence of intestinal metaplasia with goblet cells, which replace the normal squamous epithelium of the distal esophagus.

Purpose: To review the results of surgical treatment in patients with short- and long-segment BE.

Methods: Between 1980 and 2006, a total of 35 articles published in English literature dealing with surgical treatment of patients with BE were reviewed. Clinical success, stop of acid, and duodenal reflux into the distal esophagus, endoscopic and histologic evaluations and development of adenocarcinoma were the main issues included.

Results: The majority of publications include very few patients (less than 50), the follow-up is less than 5 years in 80% and classic antireflux surgery obtains clinical success before 5 years of follow-up in 81% of the patients, but this success deteriorates with the length of follow-up. Acid reflux before and after surgery was evaluated in few publications and duodeno-esophageal reflux in only 3 papers. The majority of reports include only 1 endoscopic evaluation after surgery while histologic analysis of Barrett's mucosa has shown regression of intestinal metaplasia in only 5%. Progression of adenocarcinoma has been reported in 3.8%, even in asymptomatic patients. On the contrary, the acid suppression and duodenal

Correspondence: Attila Csendes, MD, FACS (Hon), Professor and Chairman, Department of Surgery, University of Chile, Hospital J. J. Aguirre, Santos Dumont 999, Santiago de Chile, Chile.
Fax: ++56-2-7775043
E-mail: acsendes@redclinicauchile.cl

diversion procedure obtained 91% of clinical success at a late follow-up (8 to 10 years), permanent control of acid and duodenal reflux, regression of intestinal metaplasia to cardiac mucosa in 55% of the patients and no progression to high grade dysplasia or adenocarcinoma has been documented. Patients with short-segment BE have shown very good results after laparoscopic fundoplication.

Conclusions: Antireflux surgery in patients with long-segment BE does not prevent the development of adenocarcinoma. Acid suppression and duodenal diversion procedure is an alternative procedure, specially in patients below 60 years of age.

Keywords: Barrett's esophagus, antireflux surgery, adenocarcinoma, acid suppression and duodenal diversion.

Introduction

Barrett's esophagus (BE) can be defined as a condition in which the normal squamous epithelium of the distal esophagus is replaced by an abnormal columnar mucosa, seen by endoscopic approach, and in which this abnormal mucosa contains intestinal metaplasia with goblet cells [1–10]. The pathogenesis of this disease is closely related to the presence of chronic persistent gastroesophageal reflux [11–13], mainly composed of a mixture of gastric and duodenal content, proved both experimentally [14–16] as well as in humans [1–10, 17]. It has been estimated that it is found in approximately 5 to 15% of patients with gastroesophageal reflux undergoing endoscopic evaluation and in 1 to 2% of unselected population undergoing endoscopy [9, 10]. Its clinical importance is related to a significant increase in the development of esophageal adenocarcinoma with a risk of 30- to 120- fold compared to general population [6–10], which means nearly 0.5% to 1% of cancer occurrence per 100 patient-year.

In this review we will only deal with the results of surgical treatment among patients with Barrett's esophagus. All data concerning pathophysiology, clinical features, functional studies, and medical treatment have been extensively analyzed in excellent, previous publications [1–11]. Also there are 3 previous complete reviews dealing with the results of surgical treatment of Barrett's esophagus between 1980 and 2003 [8, 18, 19]. There is a recent review [20], which we consider to be incomplete and inadequate because it excluded several important articles concerning this topic. Also this article will not deal with the treatment of patients with high-grade dysplasia, as well as alternative endoscopic or ablation therapies.

The first important matter related to the surgical treatment of patients with Barrett's esophagus, is whether we are dealing with a short-segment or a long-segment BE. Classically, it was required that at least 3 cm of the distal esophagus should be lined by metaplastic columnar epithelium, which is now denominated as ''long-segment BE'' (Fig. 1). By contrast, the existence of ''short-segment BE'', that is, macroscopic evidence of upward shift of columnar mucosa plus intestinal metaplasia, either a circumferential increase (>1 cm) or one or more tongues (>1 cm) or a combination, but always less than 3 cm of length of the columnar mucosa is increasingly recognized (Figs. 2 and 3). This short-segment BE is at least 4 times more frequent than long-segment BE, provided that routine biopsy samples of the distal esophagus and esophagogastric junction are taken. We will deal separately with both entities. In a previous review, we have defined the main goals of surgical treatment among patients with BE [19] as well as De Meester [21]. The eight goals can be summarized in 2 mains groups:

1. *Clinical goals*
   a. Control of symptoms (clinical questionnaire)
   b. Stop reflux, acid and duodenal (24-h acid and bile monitoring)
   c. Eliminate complications (endoscopic evaluations)
2. *Histological goals*
   a. Prevent increase in length of intestinal metaplasia
   b. Induce regression of intestinal metaplasia to cardiac mucosa
   c. Prevent progression to dysplasia
   d. Induce regression of dysplasia to nondysplastic mucosa
   e. Prevent progression to adenocarcinoma

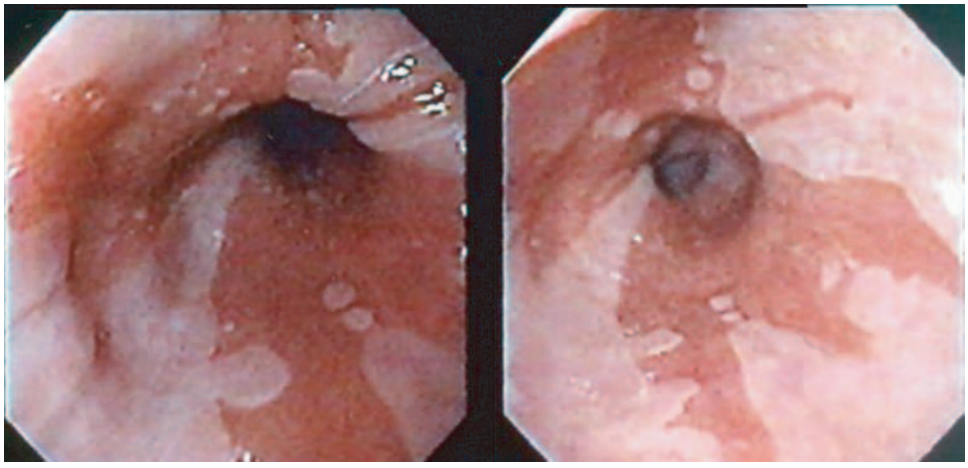

Fig. 1: Long-segment BE with several long tongues of columnar mucosa

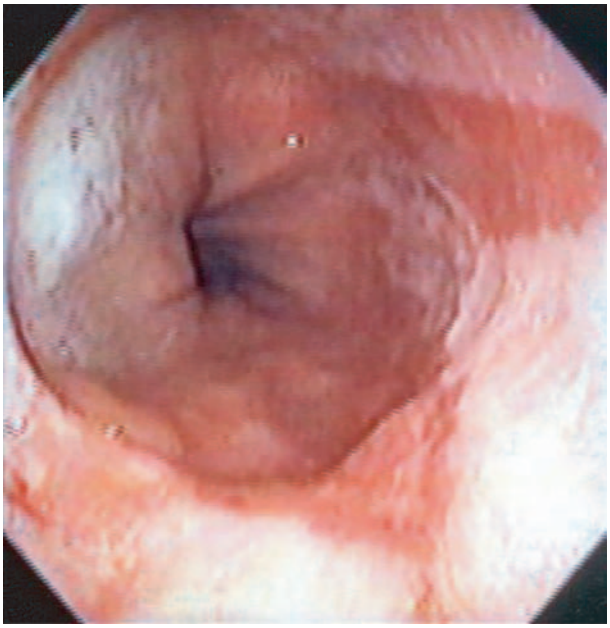

Fig. 2: Short segment BE

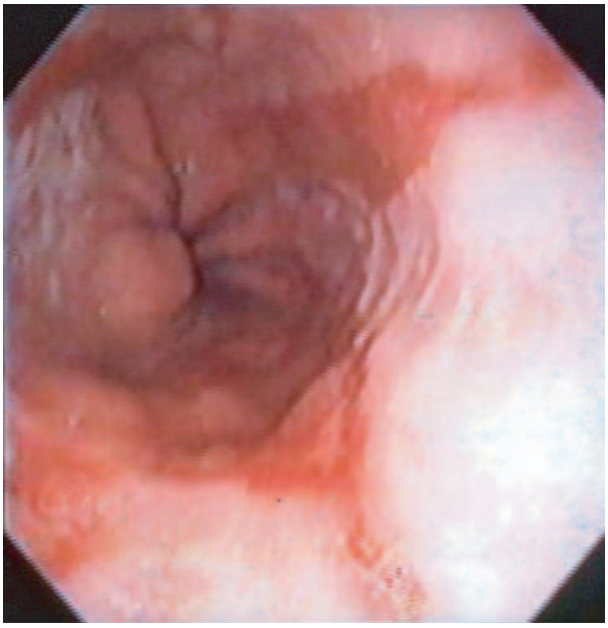

Fig. 3: Short segment BE with tongues and erosions

We will deal separately with the results of surgical treatment among patients with short-segment BE and long-segment BE.

Short-segment Barrett's esophagus

There are only 5 reports mentioning the results of surgical treatment in patients with short- segment BE, as shown in Table 1. Unfortunately the majority of clinical and laboratory data is mixed with patients with long-segment BE, and therefore we can mention only the histological results of these patients. As it can be seen in this table, the number of patients is low (mean 26 patients), with a short follow-up (mean 43 months) all less than 5 years, demonstrating a histological regression of intestinal metaplasia to cardiac mucosa in nearly 54% of the patients. Progression to low grade dysplasia was seen in 1 patient and no progression to high-grade dysplasia or adenocarcinoma has been reported. It is worrying that two articles performed 24-h pH studies after surgery and both report a high rate of abnormal reflux, that is, failure to control acid reflux after surgery, which is the purpose of surgical treatment.

We have recently submitted for publication a study of 125 patients with short-segment BE subjected to 3 different antireflux techniques:

A. Laparoscopic fundoplication (28 patients),
B. Open antireflux procedure plus duodenal switch [28],
C. Open antireflux surgery, selective vagotomy, antrectomy and Roux-en-Y gastrojejunostomy [29].

Tab. 1: Results of surgical treatment in patients with short-segment Barrett's esophagus

Author	No. of patients	Antireflux procedure	Follow-up (months)	Regression of IM	Time for regression (months)	No. of postop. endoscopies	Postoperative abnormal 24-h pH studies
Bowers (2002)	22	Lap. Nissen	60	13 (59%)	?	1	?
Gurski (2003)	33	Lap. Nissen	50	11 (33%)	50	2	?
Oelschlager (2003)	54	Lap. Nissen	30	30 (56%)	30	1	32%
O'Riordan (2004)	9	Lap. Nissen-Rossetti and Open	45	6 (67%)	45	2	42%
Zaninotto (2005)	11	Lap. Nissen	28	6 (55%)	28	2	?
Csendes (2008) Santiago	22	Duodenal switch	106	14 (63.6%)	54	4	18%
	52	Acid suppression Duodenal diversion	76	34 (65.4%)	38	3	14%
	23	Lap. Nissen	54	14 (60.8%)	48	3	25%

A careful follow-up of all 125 patients submitted to these 3 procedures, assessing subjective and objective variables, showed that the results of the 3 techniques were entirely similar when compared, measured as symptomatic evaluations (Visick grading), functional studies (Manometric tests, 24-h pH monitoring and 24-h bile monitoring) and histologic evaluations expressing the percentage of loss of intestinal metaplasia to cardiac or to oxyntocardiac mucosa.

Besides, the less aggressive surgical approach has finally shown that Nissen laparoscopic fundoplication is the treatment of choice when dealing with the surgical management of patients with short-segment Barrett's esophagus.

Long-segment Barrett's esophagus

There are 35 articles published in English literature between 1980 and 2006 dealing with the results of surgical treatment of patients with BE [22–27, 30–59].

There are 3 articles published by us, which were grouped together. Tables 2 to 5 summarize all these reports. In Table 2 we show the authors, the year of publication, number of patients treated, the mean follow-up, the clinical success achieved after surgery, and the functional studies (manometry, 24-h pH and 24-h bile monitoring), measuring the magnitude of acid and duodenal reflux into the distal esophagus before and after surgery. Table 3 presents the summary of clinical results, Table 4

Tab. 2: Results of classic antireflux surgery in patients with Barrett's esophagus from 25 studies (1980–2003)

Study	No. of patients	Mean follow (months) (%)	Clinical success (%)	Postop. plain radiography	Manometry (LESP) (in mmHg)	24-h pH studies (% positive)	Bilitec
Brand (9) 1980	10	48	40	No	No	60	No
Ranson (10) 1982	10	36	66	No	7 → 12	40	No
Skinner (11) 1983	10	48	90	+	4 → 12	20	No
Iascone (12) (1983	13	36	85			No	No
Starnes (13) 1984	8	24	75	–	–	No	No
DeMeester (14) 1998	35	36	77	No	No	No	No
Williamson (15) 1990	37	60	81	No	8 → 15	28	No
McEntee (16) 1991	21	22	90	No	10 → 16	(39 → 8)	No
Mc Callum (17) 1991	29	60	?	No	No		No
Attwood (18) 1992	19	36	79	No	No	No	No
Sagar (19) 1995	56	66	75	No	8 → 17	39 (16.0 → 3.7)	No
Ortiz (20) 1996	28	60	90	No	8 → 16	37 (17.0 → 1.0)	No
McDonald (21) 1996	113	66	82	+	No	No	No
DeMeester (22) 1990	45	24	?	No	No	No	No
Low (23) 1999	14	24	90	No	11.9 → 27.4	(48.5 → 6.7)	No
Patti (24) 1999	38	24	92	No	6.0 → 14	No	No
Farrell (25) 1999	20	24	90	No	No	No	No
Chen (26) 1999	45	36	93	+	20.0 → 23.0	22.7	No
Yau (27) 2000	69	24	84	No	3.3 → 16.7	9.5 (17.5 → 3.3)	No
Hofstetter (28) 2001	85	60	74	+	No	19 (11.0 → 2.8)	No
Spechler (29) 2001	63	108	38	No	No	23.0 → 17.1	No
Bamehriz (20) 2002	21	39	?	No	3.7 → 12.3	(26.5–2.1)	No
Bowers 2002	33	54	73	–	–	–	–
Mabrit (31) 2003	13	46	77	+	No	12.5	No
Csendes (32–34) 1998–2002	161	108	42	+	7.6 → 15.0	44% (28.5 → 18.1)	+30/31 (97%) (5.3% to 30.9%)
Parrilla (35) 2003	58	72	91	–	7.0 → 15.0	15% (19.0 → 6.0)	36.0–15.4
Desai 2003	68	30	88	–	–	–	No
Gurski 2003	44	60	?	–	–	–	No
Oelshgen 2003	38	40	96	–	–	26%	No
O'Riordan 2004	47	45	98	–	–	42%	No
Ablas 2004	26	29	88	–	–	–	No
Zaninotto 2005	24	28	82		8 → 11	18%	3.7% → 0
Cowgill 2006	80	30	71	–	–	–	No

Tab. 3: Summary of clinical evaluation after antireflux surgery in patients with long-segment Barrett's esophagus (1980–2006)

1. Number of publications	35
2. Number of patients	1381
	42 pt/article
3. Mean follow-up	45 months
	>61 = 7 articles (20%)
4. Clinical success	78%
	<60 months: 81%
	>61 months: 59%

Tab. 4: Summary of functional studies after antireflux surgery in patients with long-segment Barrett's esophagus

1. 24-h intraesophageal pH monitoring
19 articles mention it (57%)
a. 12 articles mention % of abnormal acid reflux test = all with positive values (15–60%)
b. 7 articles mention reduction of acid reflux test compared to preoperative values = all with abnormally high results
2. 24-h intraesophageal bile monitoring
3 articles (9%) mention it

the summary of functional results and Table 5 the progression to dysplasia or adenocarcinoma.

Control of symptoms or clinical success

There are a total of 1381 patients submitted to antireflux surgery: 2 authors have performed Hill's antireflux procedure, 3 authors performed Belsey technique, 4 authors have performed in some patients a Nissen-Collis procedure, but in the great majority, Nissen fundoplication, either open or laparoscopic, has been the surgical technique employed. The numbers of patients per publication is 42 and the mean follow-up was 45 months. However, only 7 articles (20%) report a follow-up longer than 61 months. Clinical success defined by some authors as ''excellent and good results'' or as Visick I and II gradation by others, was obtained in 78% of the patients. This success was closely related to the length of follow-up: When it was less than 60 months, the mean success was 81%, while if the follow-up was longer, the mean success fall to 58%. As conclusions of this table, we can observe that:

- in the majority of publications (23 out of 33) very few patients (less than 50) were included and evaluated;
- the follow-up in a benign disease, that has potentially carcinogenetic effect, is too short, less than 5 years, in the great majority of studies (80%);
- the clinical success, that is, free of reflux symptoms or some occasional reflux symptoms, is inversely correlated with the length of the follow-up: the longer the follow-up, the less the clinical success deteriorates.

Objective measurement of control of acid and duodenal reflux into the distal esophagus after the so called ''antireflux surgery''

It is difficult to understand why in such an end-stage disease of gastroesophageal reflux disease such as Barrett's esophagus, objective measurements of the effect of antireflux surgery in controlling acid and/or duodenal reflux into the esophagus are missing in several surgical reports. If the final effect of surgery is to stop or to abolish pathological reflux, why is it not measured and reported after antireflux surgery in patients with BE? Table 4 shows the main conclusions after reviewing one by one each article of table 2 concerning measurements of 24-h pH monitoring and 24-h bile monitoring. Acid reflux determinations are only mentioned in 57% of the papers. Seven of these reports mean preoperative and postoperative values, which are the most correct way to express it. In all articles postoperative values are higher than normal values. Twelve articles only mention the percentage of acid reflux test after surgery. In all of them high abnormal values can be seen. Again, similar to what happens with clinical success, the percentage of positive abnormal values increases parallel to the length of the follow-up.

Only 3 groups have reported some studies concerning the measurements of duodeno-esophageal reflux before and after surgery. Our studies [53–55] have shown that 8 to 10 years after surgery, even in patients with Visick I or II gradation, a small amount of duodeno-esophageal reflux is present. This value increases significantly among patients with Visick III or IV gradation. Parrilla et al. [56] reported a significant decrease after surgery, measured in 12 patients. Zaninotto et al. [26] also mentioned this determination in some patients before and after surgery. As conclusions from this review, we can observe that

- few studies have evaluated acid reflux before and after ''antireflux surgery'',
- very few studies have measured duodeno-esophageal reflux,
- pathologic reflux increases as the follow-up is longer, parallel to clinical deterioration.

Concerning manometric studies evaluating lower esophageal sphincter pressure and the amplitude of the distal esophageal waves, there are only 14 publications reporting some of these results. Manometric evaluation is not only important in order to measure the changes in resting sphincter pressure before and after surgery, but also it is essential to perform it before the 24-h pH studies, in order to determine precisely the location of the lower esophageal sphincter and therefore place the electrode 5 cms proximal. This is specially relevant in patients with BE, who frequently have also a hiatal hernia. Therefore, there are several studies, which are only performed 24-h pH studies without manometry before. The final summary of all manometric studies is that there is an increase in resting sphincter pressure after surgery, which does not correlate with the presence or absense of an abnormal acid reflux and therefore, is not a good index of surgical success. There is only one study which has performed

Tab. 5: Results of classic antireflux surgery in patients with Barrett's esophagus from 25 studies (1980–2003)

Study	No. of patients	Mean follow-up (months)	Appearance of dysplasia	Appearance of adenocarcinoma	Regression of L-G dysplasia	Regression of IM
Brand (1980)	10	48	No	1 (10%) 4 years	–	3/10
Ranson (1982)	10	36	No	No	?	?
Skinner (1983)	10	48	2 (10%)	No	1/5: 4 years: 3 cm	1/10
Iascone (1983)	13	36	?	?	?	?
DeMeester (1998)	8	36	No	No	No	No
Starnes (1984)	35	24	No	1 (13%): 2 years	?	?
Williamson (1990)	37	60	4 (11%)	3 (8%): 1,6,10 years asymptomatic	?	?
McEntee (1991)	21	22	1 (5%)	–	4/10: B 3 cm	1/21
McCallum (1991)	29	60	1 (3.4%)	0	?	?
Attwood (1992)	19	36	?	1 (5%): 3 years	?	?
Sagar (1995)	56	66	2 (3.6%)	1 (18%): 9 years asymptomatic	?	5/56
Ortiz (1996)	28	60	1 (3%)	1 (3%): 7 years symptomatic	?	8/28
McDonald (1996)	113	66	?	3 (2.7%): 1, 2, 3 years	?	?
DeMeester (1990)	45	24	4 (11%)	No	6/9 (3 cm)	4.4%
Low (1999)	14	24	No	No	4/7 (6 cm)	–
Patti (1999)	38	24	No	No	?	?
Farrel (1999)	20	24	?	?	?	?
Chen (1999)	45	36	No	No	No	No
Yau (2000)	69	24	1 (1.5%)	3 (4.3%): 2–4 years	?	?
Hofstetter (2001)	85	60	4/63 (6%)	No	7/16 (44%)	9/63 (14%)
Spechler (2001)	63	108	?	1 (1.6%): 7 years	?	?
Bamehriz (2002)	21	39	?	?	?	?
Bowers (2002)	33	54	–	–	–	10(33%)
Csendes (1998–2002)	161	108	17 (10.5%)	6 (4%):4, 5, 7, 9, 17, 18 years	No	No
Mabrit (2003)	13	46	1/13 (7.7%)	No	2/2	–
Parrilla (2003)	58	72	5 (6%)	2 (3.4%)	5	No
Desai (2003)	68	30	1 (1.5%)	0	66%	14%
Gurski (2003)	44	60	8%	0	9%	0
Oelschalger (2003)	38	40	2 (5.2%)	1 (2.6%)	–	0
O'Riordan (2004)	47	59	2 (4.2%)	2 (4.2%)	0	2 (4.2%)
Abbas (2004)	26	29	–	1 (3.8%)	–	–
Zaninotto (2005)	24	28	4 (17%)	–	5 (21%)	0
Total	1301	45	1.5–17%	1.6–10%	9 years	4–35%

more than one manometric evaluation after surgery. It was published by our group [54], performing 3 postoperative manometric evaluations. In this study, it is clearly demonstrated how lower esophageal sphincter pressure deteriorates with time, parallel to clinical results and 24-h acid reflux determination.

Endoscopic and histologic evaluations

These objective measurements are essential when evaluation of surgical results in patients with BE is reported. However, it is noteworthy that 2 reports [34, 46] do not mention them as part of surgical evaluation. Histological analysis of biopsy samples are not reported in 5 articles [33–36, 46]. There are mainly 4 points that should be reported when performing endoscopic and histological analysis:

1. Regression of intestinal metaplasia to cardiac mucosa: Only 16 reports have specifically mentioned this very important aspect. In 7 of them no regression was observed. In 9 articles regression of IM was reported in some patients. As mean results, from 719 patients evaluated,

regression of IM to cardiac mucosa was documented in only 35 patients (4.8%), which is quite different to what has been observed in patients with short-segment BE.

2. Regression of low-grade dysplasia to non-dysplastic mucosa: There are only 10 articles that mention regression of low-grade dysplasia usually 2 to 4 years after surgery to intestinal metaplasia or even to cardiac mucosa. This has occurred in a mean of 45% of patients with low-grade dysplasia.

3. Progression from IM to low or high grade dysplasia: There are 19 articles which have reported progression from IM to low or high grade dysplasia in 1.5–17% of the operated patients, with a mean of 7.5%. On the contrary, there are 7 articles that have denied this progression.

4. Preventing the development of Adenocarcinoma: This is one of the most important and controversial issues in patients with BE who undergo surgical treatment. We have published two previous articles concerning this particular topic [50, 60] in which a complete analysis of this complication is presented. Besides, there are some other review articles concerning this subject. Ye et al. from Sweden [61] made a retrospective analysis of 6046 men who underwent antireflux surgery, followed by 96 months. During the years of observations, a clear risk for developing adenocarcinoma was demonstrated. Later Corey et al. [62] in a meta-analysis demonstrated that the risk of adenocarcinoma in BE is low and not decreased by surgical antireflux procedure. Therefore, antireflux surgery should not be recommended as an antineoplastic measure. Finally, the paper of Chang et al. [20] also suggested that antireflux surgery in patients with BE does not prevent the development of adenocarcinoma appreciably more than medical therapy. The careful review concerning this special topic of all articles has shown that 18 articles (Table 6) did not mention the appearance of esophageal adenocarcinoma after classical antireflux surgery. As it can be seen, the mean number of patients is 31 per article, but what is

Tab. 6: Absence of adenocarcinoma after antireflux surgery in patients with Barrett's esophagus (*n* = 14)

Reference	*n*	Mean follow-up (months)	% good results
Ranson 1982	10	36	66
Skinner 1983	10	48	90
Lascone 1983	13	36	85
DeMeester 1990	35	36	77
McEntee 1991	21	22	90
McCallum 1991	29	60	?
DeMeester 1998	45	24	?
Low 1999	14	24	90
Patti 1999	38	24	92
Farrell 1999	20	24	90
Chen 1999	45	36	93
Hofstetter 2001	85	60	74
Bamehriz 2002	21	39	2
Bowers 2002	33	54	73
Mabrit 2003	13	46	77
Desai 2003	68	30	88
Gurski 2003	44	60	?
Zaninotto 2005	24	28	82

Tab. 7: Adenocarcinoma appearing after antireflux surgery in patients with Barrett's esophagus (*n* = 11)

References	*n*	Mean follow-up (months)	% Good results	Adenocarcinoma	Years after operation
Brand 1980	9	60	40	1 (10%)	4 symptomatic
Starned 1984	8	26	75	1 (13%)	2 mean asymptomatic
Williamson 1996	37	60	81	3 (8%)	1–6–10 asymptomatic
					Adequate antireflux
Attwood 1992	19	36	79	1 (5%)	3
Sagar 1995	56	66	75	1 (1.8%)	9 asymptomatic (men)
Ortiz 1996	28	60	90	1 (3%)	7 sympomatic
McDonald 1996	112	66	82	3 (2.7%)	1–2–3 asymptomatic
Yau 2000	75	24	84	3 (4.3%)	2–4
Spechler 1992–2001	38	108	38	1 (2.6%)	7
Csendes 1998–2002	161	108	42	6 (4%)	4–5–6–9–17–18 4 symptomatic (5 men)
					2 asymptomatic (1 women)
Parrilla 2003	58	72	91	2 (3%)	4–6 sympatomatic 2 men
Oelschlager 2003	38	40	96	1 (2.6%)	1 year
O'Riordan 2004	47	59	90	2 (4.2%)	4–7 years symptomatic
Abbas 2004	26	29	88	1 (3.8%)	
Total	712	57	75	27 (18%)	

more troubling is the fact that the mean follow-up in these publications is 38 months and *none* has more than 61 months of follow-up. Table 7 shows the 16 articles that reported the development of adenocarcinoma of the esophagus after antireflux surgery. A total of 712 patients have been followed much longer, for a mean of 57 months (almost 20 months more than the previous group), demonstrating the appearance of adenocarcinoma in 27 patients (3.8%). In 13 of these patients, adenocarcinoma developed before 5 years of the operation, whereas 14 patients showed the appearance of adenocarcinoma between 5 to 18 years after surgery. Twelve patients were symptomatic, that is, had recurrence of reflux symptoms before the appearance of adenocarcinoma. On the contrary, 10 patients were asymptomatic and with apparently adequate antireflux surgery. In 5 patients no data are given.

The most important point is to determine whether patients with adenocarcinoma had previously an abnormal acid reflux test or not, which would be the most objective way to demonstrate recurrence of pathologic reflux after antireflux surgery. Unfortunately, only 3 articles have mentioned this assessment. Parrilla et al. [56] suggested that adenocarcinoma can only be present in patients with recurrence of abnormal reflux, as occurred in both patients. Csendes et al. observed that [60] among 6 patients with adenocarcinoma, two had 24-h pH monitoring and both were abnormal. O'Riordan et al. [25] also described that both patients with adenocarcinoma had pathologic acid reflux. However, it is worrying that the publication of Hakansson et al. [63] in which they report the malignant transformation in Barrett's esophagus in 4 patients after successful antireflux surgery, assessed by endoscopy and 24-h pH monitoring. Table 8 summarizes the main points in the appearance of adenocarcinoma after antireflux surgery. Considering only the 14 articles that reported the development of adenocarcinoma after antireflux surgery, the incidence is 1 per 132 patient-year. In the whole group, this incidence is 1 per 179 patient-year.

Therefore, we can conclude that antireflux surgery does not prevent the development of adenocarcinoma in patients with Barrett's esophagus. In the majority of patients, this transformation occurs in the presence of recurrent pathologic acid reflux. However, there are several points which are questionable:

a. the low number of patients studied,
b. the *very short* (3 years) follow-up in the ''absent group'',
c. absence of symptoms does not necessarily mean absence of reflux,
d. the need to perform objective endoscopic and histologic evaluation,
e. the need to inform the truly late results after at least 10 years from surgery, as Richter has stated ''let the truth be told''.

Tab. 8: Appearance of adenocarcinoma after antireflux surgery

	Adenocarcinoma		
	Absent	Present	Total
No. of publication	18	14	32
No. of patients operated	568	712	1280
Patients/publication	31.5	51	42
Mean follow up (months)	38	57	45
≥60 months	3/18 = 17%	8/14 = 57%	34%
Development of adenocarcinoma	0	27	27
Ca/patient year	–	1/132	1/179

Why are the poorer results after antireflux surgery in patients with BE compared to GERD patients without BE?

In patients with chronic reflux without BE, the physiological and structural damage of the lower esophageal sphincter is not so pronounced [65]. Besides, they have mainly acid reflux into the distal esophagus, which can be controlled and diminished by restoring the function of the lower esophageal sphincter. This was clearly demonstrated by us [54] in a study performing 3 manometric evaluations after surgery, specifically between 2 and 90 months after surgery. However, in patients with long-segment BE, there is a severe structural damage of the lower esophageal sphincter, with presence of hiatal hernia and a very dilated esophagogastric junction [65, 66], with no intra-abdominal portion and a very incompetent sphincter, due to alterations of the clasps and sling fibers at this level [67]. This is why, as time goes by and objective late follow-up is performed [53, 54] the rate of failure after antireflux surgery increases progressively, the percentage of patients taking antisecretory drugs in greatly increased [50] and adenocarcinoma may appear. The functional alteration of the lower esophageal sphincter in patients with BE has been clearly documented by us [54] performing 3 manometric studies after surgery in patients with BE. Besides, these patients with long-segment BE have an important acid and duodenal reflux into the distal esophagus [10]. Although initially, the first 2 to 3 years after surgery, pathologic reflux is controlled, after 8 to 10 years of follow-up, the percentage of patients with abnormal reflux increases [50, 53].

In summary, although antireflux surgery effectively alleviates GERD symptoms, in patients with long-segment BE, surgical outcome is less optimal than that encountered in patients with GERD without BE. Complete regression of columnar mucosa is extremely uncommon, regression of intestinal metaplasia to cardiac mucosa is rare, and the long durability of antireflux surgery is an open, not answered question. The reported results of antireflux surgery suggest that it does not influence the natural history of Barrett's esophagus, especially concerning the development of adenocarcinoma.

Based on the high recurrence rate of antireflux surgery in these patients, we started to employ a procedure that should suppress acid secretion permanently and should abolish the duodeno-esophageal reflux. This oper-

Tab. 9: Results of acid suppression and duodenal diversion, in patients with long-segment Barrrett's esophagus ($n = 245$)

Control of symptoms	91%
Decrease of maximal gastric acid output (PAO)	90%
Percent patients with absence of pathologic acid reflux	85%
Percent patients with absence of duodenal reflux	95%
Regression of intestinal metaplasia to cardiac mucosa	55%
Regression of low grade dysplasia to non-dysplastic mucosa	62%
Progression to low grade dysplasia	1%
Progression to adenocarcinoma	0

ation is based on performing an antireflux surgery, selective vagotomy, partial distal gastrectomy and Roux-en-Y anastomosis, with a loop of 70 cm-long [68, 69]. The final late results of 245 patients reported are shown in Table 9. Symptoms of chronic GE reflux are controlled in 91% of the patients at the late follow-up (8 to 10 years). Gastric acid output is reduced in 90% compared to preoperative values, due to vagotomy and partial gastrectomy. Therefore, there is a very low volume of gastric acid secretion to reflux. Duodeno-esophageal reflux is completely abolished due to the presence of a Roux-en-Y loop. The rate of loss of intestinal metaplasia or regression to cardiac mucosa is 10 times higher than with classic antireflux surgery [71]. Regression of low grade dysplasia is very high, depending on the length of the columnar mucosa [70]. The most important aspect of this operation is that there is no progression to high-grade dysplasia or to adenocarcinoma, up to 20 years of follow-up, which is the longest time of this procedure.

At a first glance, it seems that this operation is too aggressive to be performed for patients with benign disease. However, it is an old operation from the 50s and 60's, when patients with a much more benign disease than Barrett's esophagus, that is, duodenal ulcer, were submitted to this procedure. The results reported were excellent. Also, there is a prospective randomized study performed by a British group in 1984 [72] in which antrectomy and Roux-en-Y anastomosis had significantly better results at 5 years of follow-up compared to Nissen fundoplication (95 vs 65%).

Patients with low-grade dysplasia enter into a special protocol. They should be treated with PPI's for 1 year and endoscopy with multiple biopsy samples are repeated. If low-grade dysplasia persists and functional studies demonstrate pathologic acid and/or duodenal reflux, surgical treatment is indicated. If the patient has a short-segment BE, laparoscopic fundoplication can be performed with a mean of 50% of regression to non-dysplastic mucosa. However, with the acid suppression and duodenal diversion procedure this regression is 90%. If a long- segment BE is present, we perform the duodenal diversion operation, with 60% of regression to non-dysplastic mucosa [70].

As was commented in the introduction, high-grade dysplasia is not included in this review, because it deserves a completely different approach.

In conclusion, classic antireflux surgery, either laparotomic or laparoscopic in patients with long-segment BE, obtains a clinical success, which is inversely related to the length of the follow-up. The control of acid reflux into the distal esophagus is not so adequate compared to patients without BE. Regression of intestinal metaplasia to cardiac mucosa is very uncommon and does not prevent the development of adenocarcinoma, even after ''successful'' surgery, and therefore, does not influence the natural history of this condition. On the contrary, acid suppression and duodenal diversion procedure, abolishes permanently acid and duodenal reflux into the esophagus, the loss of intestinal metaplasia is 10 times greater than after antireflux surgery alone and no progression to high grade dysplasia or adenocarcinoma has been documented. This operation seems to influence the below 60 years of age, with long-segment BE. In patients with short-segment BE, laparoscopic fundoplication is the procedure of choice.

References

[1] Spechler SJ, Goyal RK. Barrett's esophagus. New Engl J Med 1986;315:362–71.
[2] Cameron AJ, Lomboy CT. Barrett's esophagus: age, prevalence and extent of columnar epithelium. Gastroenterology 1992;103:1241–5.
[3] Spechler SJ. Barrett's esophagus. Semin Oncol 1994;21:431–7.
[4] Spechler SJ, Goyal RK. The columnar lined esophagus, intestinal metaplasia and Norman Barrett. Gastroenterology 1996;110:614–21.
[5] Spechler SJ. The columnar lined esophagus. Gastroent Clin N Am 1997;26:455–66.
[6] Navaraman RM, Wristel MC. Barrett's esophagus. Postgrad Reed I. 1998;74:655–7.
[7] Cameron AJ. Management of Barrett's esophagus. Mayo Clin Proceed 1998;73:457–61.
[8] DeMeester TR, Peters JH, DeMeester TR. Barrett's esophagus. Curr Probl Surg 2001;38:549–640.
[9] Falk GW. Barrett's esophagus. Gastroenterology 2002;122:1569–79.
[10] Csendes A, Smok G, Quiroz J, Burdiles P, Rojas J, Castro C, Henríquez A. Clinical, endoscopic and functional studies in 408 patients with Barrett's esophagus compared to 174 cases with intestinal metaplasia of the cardia. Am J Gastroent 2002;97:574–60.
[11] Lagergen J, Bergstrom R, Lindberg A, Nyren O. Symptomatic gastroesophageal reflux as a risk factor for esophageal adenocarcinoma. New Eng J Med 1999;340:825–30.
[12] Solaymani-Dodaran M, Logan RIA, West J, Card T, Coupland C. Risk of oesophageal cancer in Barrett's oesophagus and gastro-oesophageal reflux. Gut 2004;53:1070–4.
[13] Eisen GM, Sandler RS, Murray S, Gottfried M. The relationship between gastroesophageal reflux disease and its complications with Barrett's esophagus. Am J Gastroent 1997;92:27–31.
[14] Attwood SEA, Smyrk TC, DeMeester TR, Mirvish SS, Stein HJ, Hinder RA. Duodenoesophageal reflux and the development of esophageal carcinoma in rats. Surgery 1992;111:503–10.
[15] Fein M, Peter JH, Chandrasoma P, Ireland AP, Oberg S, Ritter MP, Bremner CG, Hagen JA, DeMeester TR. Duodenoesophageal reflux induces esophageal adenocarcinoma without exogenous carcinogen. J Gastrointest Surg 1998;2:260–8.
[16] Nishijima K, Miwa K, Miyoshita T, Kirani S, Ninomiya I, Fushida S, Fujimira R, Hattori T. Impact of the biliary diversion procedure on carcinogenesis in Barrett's esophagus surgically induced by duodenoesophageal reflux in rats. Ann Surg 2004;240:57–67.
[17] Sarela AJ, Hick DG, Verbeke CS, Casey JF, Guillou PJ, Clark GNB. Persistent acid and bile reflux in asymptomatic patients with Barrett's esophagus receiving proton pump inhibitor therapy. Arch Surg 2004;139:547–51.

[18] DeMeester SR, DeMeester TR. Columnar mucosa and intestinal metaplasia: fifty years of controversy. Ann Surg 2000;231:303–21.
[19] Csendes A. Surgical treatment of Barrett's esophagus: 1980–2003. World J Surg 2004;28:225–31.
[20] Chang EY, Morris CD, Seltman AK, O'Rourke RW, Chan BK, Hunter JG, Jobe BA. The effect of antireflux surgery on esophageal carcinogenesis in patients with Barrett's esophagus. Ann Surg 2007;246:11–21.
[21] DeMeester TR. Surgical therapy for Barrett's esophagus: prevention, protection and excision. Dis Esoph 2002;15:109–16.
[22] Bowers SP, Mattar SG, Smith CD, Waring JP, Hunter JG. Clinical and histologic follow-up after antireflux surgery for Barrett's esophagus. J Gastrointest Surg 2002;6:532–9.
[23] Gurski RR, Peters JH, Hagen JA, DeMeester SR, Bremne CG, Chandrasoma PT, DeMeester TR. Barrett's esophagus can dand does regress after antireflux surgery: a study of prevalence and prediction features. J Am Coll Surg 2003;196:706–13.
[24] Oelschlager DK, Baneca M, Chay L, Oleynikow O, Pellegrini CA. Clinical and pathologic response of Barrett's esophagus to laparoscopic antireflux surgery. Ann Surg 2003;238:458–66.
[25] O'Riordan JM, Byrne N, Rari N, Keeling PW, Reynolds JV. Long-term clinical and pathologic response of Barrett's esophagus after antireflux surgery. Am J Surg 2004;188:27–33.
[26] Zaninotto G, Cassano M, Pennelli G, Battaglice G, Farinati F, Ceolin M, Constantini M, et al. Barrett's epithelium after antireflux surgery. J Gastrointest Surg 2005;9:1253–6.
[27] Csendes A, Burdiles P, Korn O. Laparoscopic Nissen fundoplication: the right posterior approach. J Gastrointest Surg 2005;9:985–91.
[28] Csendes A, Braghetto I, Burdiles P, Díaz JC, Maluenda F, Korn O. A new physiological approach for surgical treatment of patients with Barrett's esophagus. Ann Surg 1997;226:123–33.
[29] Csendes A, Burdiles P, Braghetto I, Korn O, Díaz JC, Rojas J. Early and late results of the acid suppression and duodenal diversion operation in patients with Barrett's esophagus: analysis of 210 patients. World J Surg 2002;26:566–76.
[30] Brand DL, Ylvisaker JT, Gelfand M, et al. Regression of columnar esophageal epithelium after antireflux surgery. N Engl J Med 1980;10:844–8.
[31] Ranson JM, Patel GK, Clefts SA, et al. Extended and limited types of Barrett's esophagus in the adult. Ann Thorac Surg 1982;33:19–27.
[32] Skinner DB, Walter BC, Riddell RM. Barrett's esophagus: comparison of benign and malignant cases. Ann Surg 1983;198:554–66.
[33] Iascone C, DeMeester T, Little G, et al. Barrett's esophagus: functional assessment, proposed pathogenesis, and surgical therapy. Arch Surg 1983;118:534–49.
[34] Starnes VA, Adkins RB, Ballinger JF, et al. Barrett's esophagus: a surgical entity. Arch Surg 1984;119:563–7.
[35] DeMeester SR, Campos GM, DeMeester TR, et al. The impact of an antireflux procedure on intestinal metaplasia of the cardia. Ann Surg 1998;228:547–56.
[36] Williamson WA, Ellis FH, Gibb SP, et al. Effect of antireflux operation on Barretts mucosa. Ann Thorac Surg 1990;4:523–4.
[37] McEntee GP, Stuart RG, Byrne PS, et al. An evaluation of surgical and medical treatment of Barretts esophagus. Gullet 1991;1:169–72.
[38] Mc Callum RW, Polepalle S, Davensport K, et al. Role of antireflux surgery against dysplasia in Barretts esophagus. Gastroenterology 1991;100:A121.
[39] Attwood SE, Barlow AP, Norris TL, et al. Barretts esophagus; effect of antireflux surgery on symptom control and development of complications. Br J Surg 1992;79:1050–3.
[40] Sagar PM, Ackroyd R, Hosie KB, et al. Regression and progression of Barrett's esophagus after antireflux surgery. Br J Surg 1995;82:806–10.
[41] Ortiz A, Martínez de Haro LF, Parrilla P, et al. Conservative treatment versus antireflux surgery in Barrett's esophagus: long term results of a prospective study. Br J Surg 1996;83:1013.
[42] McDonald ML, Trastek VF, Allen MS, et al. Barrett's esophagus: does an antireflux procedure reduce the need for endoscopic surveillance? J Thorac Cardiovasc Surg 1996;111:1135–8.
[43] DeMeester TR, Attwood SE, Smyrk TC, et al. Surgical therapy in Barrett's esophagus. Ann Surg 1990;212:528–40.
[44] Low DE, Levine DS, Dail DH, et al. Histologic and anatomic changes in Barrett's esophagus after antireflux surgery. Am J Gastroenterol 1999;94:11–12.
[45] Patti MG, Arcerito M, Feo CV, et al. Barrett's esophagus: a surgical disease. J Gastrointest Surg 1999;3:397–403.
[46] Farrell TM, Smith D, Metreveli RE, et al. Fundoplication provides effective and durable symptoms relief in patients with Barrett's esophagus. Am J Surg 1999;178:18–21.
[47] Chen LQ, Nastos D, Hu CY, et al. Results of the Collis-Nissen gastroplasty in patients with Barrett's esophagus. Ann Thorac Surg 1999;68:1014–20.
[48] Yau P, Watson DI, Devitt PG, et al. Laparoscopic antireflux surgery in the treatment of gastroesophageal reflux in patients with Barrett's esophagus. Arch Surg 2000;135:801–5.
[49] Hofstetter WL, Peters JH, DeMeester T, et al. Long term outcome of antireflux surgery in patients with Barrett's esophagus. Ann Surg 2001;234:532–8.
[50] Spechler SJ. Long term outcome of medical and surgical therapies for gastroesophageal reflux disease: follow-up of a randomized controlled trial. JAMA 2001;285:2331–8.
[51] Bamehriz F, Dutta S, Pottruff CG, et al. Does laparoscopic Nissen funcoplication case regression of Barrett's esophagus? In: Proceedings of the SSAT meeting 2002;43.
[52] Mabrit JY, Baulieux J, Adham M, et al. Impact of antireflux operation on columnar lined esophagus. J Am Coll Surg 2003;196:60–7.
[53] Csendes A, Braghetto I, Burdiles P, et al. Long term results of classic antireflux surgery in 152 patients with Barrett's esophagus: clinical, radiologic, endoscopic, Manometric and acid reflux test analysis before and late after operation. Surgery 1998;26:645–65.
[54] Csendes A, Burdiles P, Korn O, et al. Late results of a randomized clinical trial comparing total fundoplication versus calibration of the cardia with posterior gastropexy. Br J Surg 2000;87:289–97.
[55] Csendes A, Burdiles P, Braghetto I, et al. Dysplasia and adenocarcinoma after classic antireflux surgery in patients with Barrett's esophagus: the need for long term subjective and objective follow-up. Ann Surg 2002;235:178–85.
[56] Parrilla P, Martínez de Haro LF, Ortiz A, et al. Long term results of a randomised prospective study comparing medical and surgical treatment of Barrett's esophagus. Ann Surg 2003;237:29–98.
[57] Desai KM, Soper NJ, Frisella MM, Quasebarth MA, Dunnegar DL, Brent LM. Efficacy of laparoscoic antireflux surgery in patients with Barrett's esophagus. Am J Surg 2003;186:652–9.
[58] Abbas AE, Deschamps C, Cassivi SD, Allen MS, Nichols FC 3rd, Miller DL, Pairolero PC. Barrett's esophagus: the role of laparoscopic fundoplication. Ann Thorac Surg 2004;77:393–6.
[59] Cowgill SM, Al-Saadi S, Villadolid D, Zervos EE, Rosemurgy AG. Does Barrett's esophagus impact outcome alter laparoscopic Nissen fundoplication? Am J Surg 2006;192:622–6.
[60] Csendes A, Burdiles P, Braghetto I, Korn O. Adenocarcinoma appearing very late after antireflux surgery for Barrett's esophagus: long term follow-up review of the literature and addition of 6 patients. J Gastrointest Surg 2004;8:434–41.
[61] Ye W, Clow W, Lagergen J, Yin L, Nyren O. Risk of adenocarcinoma of the esophagus and gastric cardia in patients with gastroesophageal reflux disease and after antireflux surgery. Gastroenterology 2001;121:1286–93.
[62] Corey KE, Schmitz SM, Shaheen NJ. Does a surgical antireflux procedure decrease the incidence of Esophageal adenocarcinoma in Barrett's esophagus? A meta-analysis. Am J Gastroent 2003;98:2390–4.
[63] Hakansson NO, Johnsson F, Johansson J, Kjellen G, Walther B. Development of adenocarcinoma in Barrett's esophagus after antireflux surgery. Eur J Surg 1996;163:469–71.
[64] Richter JE. Antireflux surgery and adenocarcinoma of the esophagus: Let the truth be told. Gastroenterology 2001;1211:1506–7.
[65] Korn O, Csendes A, Burdiles P, Braghetto I, Stein H. Anatomic dilatation of the cardia and competence of the lower esophageal sphincter: a clinical and experimental study. J Gastrointest Surg 2000;4:398–406.
[66] Csendes A, Maluenda F, Baghetto I, Csendes P, Henríquez A, Quesada S. Location of the lower esophageal sphincter and the squamous columnar mucosal junction in 109 healthy controls and 778 patients with different degrees of endoscopic esophagitis. Gut 1993;34:21–7.

[67] Korn O, Richter TH, Stein HJ, Feussner H, Liebermann-Meffert D, Siewert JR. The gastroesophageal sphincter: a model. Dis Esophagus 1997;10:105–9.
[68] Csendes A, Burdiles P, Braghetto I, Korn O, Díaz JC, Rojas J. Early and late results of the acid suppression and duodenal diversion operation in patients with Barrett's esophagus: analysis of 210 cases. World J Surg 2002;26:566–76.
[69] Csendes A, Braghetto I, Burdiles P. Roux-en-Y long limb diversion as the first option for patients who have Barrett's esophagus. Chest Surg Clin N Am 2002;12:157–84.
[70] Csendes A, Smok G, Burdiles P, Braghetto I, Castro C, Korn O. Effect of duodenal diversion on low grade dysplasia in patients with Barrett's esophagus: analysis of 37 patients. J Gastrointest Surg 2002;6:645–54.
[71] Csendes A, Braghetto I, Burdiles P, Smok G, Henríquez A, Parada F. Regression of intestinal metaplasia to cardiac or fundic mucosa in patients with Barrett's esophagus submitted to vagotomy, partial gastrectomy and duodenal diversion. A prospective study of 78 patients with more than 5 years of follow-up. Surgery 2006;139:46–53.
[72] Washer GF, Gear MWL, Dawling BL, Spencer J. Randomized prospective trial of Roux-en-Y duodenal diversion versus fundoplication for severe reflux esophagitis. Br J Surg 1984;71:181–4.