

DOI: <https://doi.org/10.56936/18290825-2022.16.4-64>**COMPLETE VERSUS NON-COMPLETE FUNDOPLICATION IN SURGICAL TREATMENT OF GASTROESOPHAGEAL REFLUX DISEASE****STEPANYAN S.A.<sup>1,2\*</sup>, HAKOBYAN V.M.<sup>1,2</sup>, PETROSYAN A.A.<sup>1,2</sup>, YEGHIAZARYAN H.H.<sup>1,2</sup>,  
PAPAZYAN K.T.<sup>1,2</sup>, BATIKYAN H.KH.<sup>1,2</sup>, ALEKSANYAN A.YU.<sup>1,2</sup>, SAFARYAN H.H.<sup>1,2</sup>,  
SHMAVONYAN H.H.<sup>1,2</sup>, BABAYAN A.M.<sup>1,2</sup>**<sup>1</sup> Department of Surgery 1, Yerevan State Medical University after M. Heratsi, Yerevan, Armenia<sup>2</sup> Clinic of Surgery, Mikaelyan Institute of Surgery, Yerevan, Armenia

Received 26.05.2022; accepted for printing 18.08.2022

**ABSTRACT**

*Gastroesophageal reflux disease is a common disorder accounting for approximately 75% of esophageal pathology. It seriously compromises quality of life. It develops when the reflux of gastric content causes troublesome symptoms or complications. During the last decades significant changes have occurred in the role of surgery for gastroesophageal reflux disease. Initially antireflux surgery was reserved only for patients who had failed any kind of medical therapy. Now the range of indications for antireflux procedures is wide. Operations for gastroesophageal reflux disease are now well established and have good short- and long-term results, but no unique laparoscopic antireflux technique has been accepted so far, and a number of different antireflux procedures with numerous modifications have been reported. A total of 102 consecutive patients with gastroesophageal reflux disease were operated in the clinic of Republican Medical Center "Armenia" (Yerevan, Armenia) and Mikaelyan Institute of Surgery (Yerevan, Armenia) from 2010 to 2021. In all cases the esophagogram showed hiatal hernia. Nissen, Nissen-Rossetti and Toupet funduplications were performed as antireflux procedures. In all cases of combination of hiatal hernia and Gastroesophageal reflux disease mesh reinforcement was performed. The results of follow-up assessment of the operated patients were compared. The results in early postoperative period were assessed with contrast X-ray examination and 24-hour pH-metry on the 5-th to 7-th days after surgery. The quality-of-life evaluation by the questionnaire showed a significant difference between the two groups, improvement of results in the laparoscopy group with complete fundoplication in comparison with not complete fundoplication. Complete fundoplication is a more reliable method of antireflux procedures for surgical treatment of gastroesophageal reflux disease. The division of short gastric vessels helps to prevent persistent dysphagia. The repair of esophageal hiatus of diaphragm is mandatory in antireflux procedures.*

**KEYWORDS:** GERD, FUNDOPLICATION, HIATAL HERNIA, ANTIREFLUX PROCEDURES, RECURRENCE OF REFLUX**INTRODUCTION**

Gastroesophageal reflux disease (GERD) is a common disorder of the gastrointestinal tract, with a prevalence of 10–20% in Western countries [Triadafilopoulos G, 2004; Huttel TP et al.,

2005]. It is currently big medical and social-economic problem. The estimated direct and indirect costs of treatment and lost productivity due to GERD was annually 10 billion USD in the USA,

**CITE THIS ARTICLE AS:**

Stepanyan S.A., Hakobyan V.M., Petrosyan A.A., Yeghiazaryan H.H., Papazyan K.T., Batikyan H.Kh., Aleksanyan A. Yu., Safaryan H.H., Shmavonyan H.H., Babayan A.M. (2022). Complete versus non-complete fundoplication in surgical treatment of gastroesophageal reflux disease. The New Armenian Medical Journal, 16(4): 64-73, <https://doi.org/10.56936/18290825-2022.16.4-64>

**ADDRESS FOR CORRESPONDENCE:**

Suren A. Stepanyan, PhD, Professor of Surgery  
Mikaelyan Institute of Surgery  
9 Hasratyan Street, Yerevan 0052, Armenia  
Tel.: (+374 93) 50-35-40  
E-mail: [sastepanyan5@gmail.com](mailto:sastepanyan5@gmail.com)

9.3 billion EUR in Germany, 2.9 billion EUR in Italy, and 1.9 billion EUR in Spain [DeMeester TR, Stein HJ, 1992; Fuchs KH, 2014; Garg SK, Gurusamy KS, 2015].

The first and main method of treatment for GERD is medical therapy, but often it includes escalating dosages, which can be a big financial burden on patients and insurance companies [Hetzl DJ et al., 1988; Sataloff DM et al., 1997; Iqbal A et al., 2006].

Usually prolonged and not effective medical therapy is indication for surgery. A controlled randomized study of patients with GERD has demonstrated that surgery is superior to medical therapy. Surgery is currently a common and regular part of the treatment algorithm. Generally, the treatment of GERD has changed from a more conservative to a more aggressive approach for better prevention of complications [Donahue PE et al., 1985; DeMeester TR et al., 1986; Stirling MC, Orringer MB, 1986; Granderath FA et al., 2002].

Many modifications of antireflux procedures were suggested for surgical treatment of GERD. The Nissen fundoplication and its various modifications are widely used in the surgical treatment of patients with severe GERD and its associated complications [Dallemagne B et al., 1991; Hinder RA et al., 1994; Dallemagne B et al., 1998]. Now these procedures are performed mainly laparoscopically. Since the first description of laparoscopic fundoplication by Dallemagne B et al. in 1991, the minimally invasive approach has gained popularity among surgeons. Good to excellent functional and symptomatic outcomes after laparoscopic procedures with lower mortality and morbidity rates than in open antireflux surgery have been reported [Soricelli E et al., 2009]. The choice of modification depends on the surgeons' preference. 64% of German surgeons prefer 360° procedures (Nissen 16%; Nissen-Rosetti 27%; Floppy-Nissen 21%). Partial fundoplications are used in 10% of the hospitals (Toupet 5%; Dore 5%). 9% of surgeons reported both 360° fundoplication and a Toupet procedure as standard operations [Huttl TP et al., 2005].

Surgical complications after antireflux procedures have two main groups: failure of wrap with

subsequent reflux recurrence and tight wrap with subsequent dysphagia. The overall complication rate for laparoscopic antireflux operations is 7.7% (5.7% surgical and 2% nonsurgical complications) [Huttl TP et al., 2005]. The published failure rates of laparoscopic Nissen fundoplication are 2% to 17% [Cuschieri A et al., 1993; Jamieson GG et al., 1994; Peters JH et al., 1995; Hunter JG et al., 1996]. In majority of cases dysphagia is associated with 360° fundoplication (Nissen, Nissen-Rosetti), recurrence of reflux is associated with not complete fundoplication (Toupet, Dore).

Another problem of antireflux procedures is association of GERD and esophageal hiatal hernia. In GERD hiatal hernia is a very frequent finding, found in up to 80-90 % of the surgical patient population [Fuchs KH et al., 2014]. It is the “Achilles heel” of antireflux surgery [Granderath FA et al., 2005; Juhasz A et al., 2012].

Despite many studies in this field nowadays no unique antireflux procedure has been accepted [Huttl TP et al., 2005]. The perfect method of the esophageal hiatus reconstruction has not yet been determined too [Gryska PV et al., 2005].

Many studies have not suggested the method of procedure which can reliably prevent postoperative dysphagia, recurrence of GERD and hiatal hernia. Complications of antireflux operations and recurrence of hiatal hernia are big problems in foregut surgery. The aim of our study was chosen the method of antireflux surgery reliably preventing mentioned above complications.

#### MATERIALS AND METHODS

A total of 102 consecutive patients with GERD were operated on in the clinic of Republican Medical Center “Armenia” (Yerevan, Armenia) from 2010 to 2017 and Mickaelyan Institute of Surgery (Yerevan, Armenia) from 2018 to 2021.

*To overcome it is possible, due to the uniting the knowledge and will of all doctors in the world*



The male-to-female ratio was 1:1,7 (38 male, 64 female). The mean age was 51,5 years (range 21-81) years.

In 62 cases were performed laparoscopic, in 40 – open procedures, in 2 cases operation had started laparoscopically, then it was converted to open, these patients are included in open procedure group. Nissen and Nissen-Rossetti methods were performed in group of complete fundoplication, Toupet procedure – in group of not complete fundoplication. Perioperative patient risk was assessed using the American Society of Anesthesiology (ASA) Scoring System. In the laparoscopy group were included only ASA I and ASA II patients. The demographic data for all the groups are shown in Table 1-1 and Table 1.

Patient's demographics did not differ significantly between the groups with complete and not complete fundoplication (Table 1).

The preoperative evaluation included upper endoscopy (Fig. 1), x-ray with barium contrast (Fig. 2) in all patients. Final confirmation of a paraesophageal involvement by the hernia was accomplished intraoperatively.

24-hour pH monitoring in preoperative period was performed in 68 patients with the portative pH meter in inpatient order. Postoperative pH-metry was performed in 32 cases.

Preoperative medical therapy had 76 patients, the duration of the therapy in the study group was 6-120 months.

### Surgical technique

Preoperative intravenous administration of an antibiotic was done an hour before the procedure. The patient was placed in a combined reversed Trendelenburg and French position.

Capnoperitoneum was created with Veress needle inserting above the umbilicus. An intra-abdominal pressure of 12–14 mm Hg was achieved and maintained. Five trocars were placed in the anterior abdominal wall at the follow sites: 10mm trocar in the left mesogastrium for the scope, 10mm trocar above the umbilicus for Bebbcock grasper, 5mm trocar in upper epigastrium for liver retractor, 5mm trocar in the right subcostal area and 5-12mm trocar in left subcostal area for working instruments.

A careful reposition of the stomach and a circular mobilization of the esophagogastric junction were performed. In case of hiatal hernia (Fig. 3) complete reduction of the hernia content was done. The first step was dissection of the phrenogastric and hepatogastric attachments. The vagus nerves were identified and left attached to the esophagus. The hepatic branch of the vagus nerve was carefully preserved.

After the mobilization of the hepatogastric ligament the right diaphragmatic crus was exposed.

The short gastric vessels and gastro-diaphragmatic ligament were divided to release the gastric fundus. After the mobilization of the gastric fundus the left crus was exposed. The esophagus was mobilized from the medial margins of the left and

Patient's demographics and clinical characteristics

TABLE 1.

	Operations with		P-value	Open procedures (n = 40; 39.2%)	Laparoscopic procedures (n = 62; 60.8%)	P-value
	complete fundoplication (n = 42; 41.2%)	not complete fundoplication (n = 60; 58.8%)				
Male/female	16/26	22/38	0.44	14/26	24/38	0.75
Age (years)	49 (21–73)	53 (26–81)	0.098	57.5 (21-81)	47.5 (26-73)	<0.001
Laparoscopic procedures	25	37	0.38			
Open procedures	17	23				
Presence of Barrett's esophagus	8	7	0.76	9	3	0.074
ASA I	17	15	0.173	3	36	<0.001
ASA II	21	41		4	42	
ASA III	4	4		9	2	

**Notes:** Patient's demographics did not differ significantly between the groups with complete and not complete fundoplication.



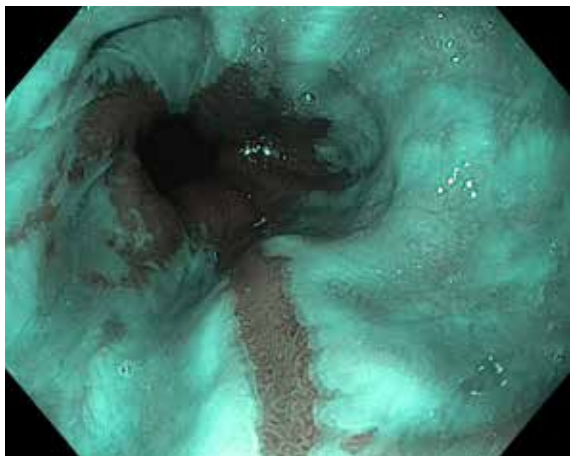


FIGURE 1. The endoscopic picture of Barrett's esophagus



FIGURE 2. X-ray examination with barium meal: revealed the combination of hiatal hernia and gastroesophageal reflux. The arrow shows cardiofundal region of stomach moved into mediastinum in sliding hiatal hernia

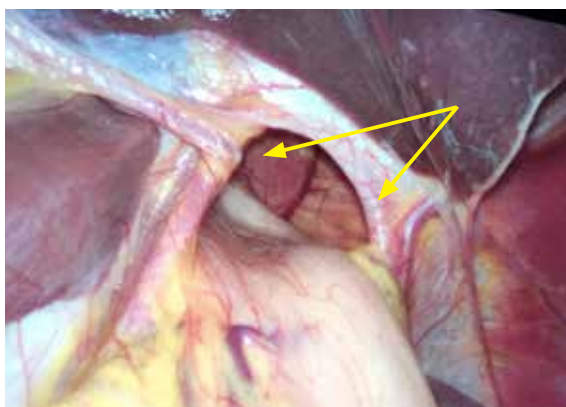


FIGURE 3. The wide esophageal hiatus in case of GERD and hiatal hernia combination. The upper part of stomach is fixed in the mediastinum. The arrows show the enlarged esophageal hiatus of diaphragm

right crura and it provided a wide posterior window behind the esophagus.

The hiatal orifice was estimated after complete mobilization using the opening jaws of a atraumatic grasper (Karl Storz, Tübingen, Germany) as a reference.

The hernia sac was completely dissected in case of small hiatal hernia. For subtotal or total hiatal hernia complete dissection of the sac was not performed due to the risk of intrathoracic structures injury. After the mobilization of the esophagogastric junction at least 4 cm of the esophagus was brought into the abdomen (Fig. 4).

In the group of hiatoplasty without mesh reinforcement posterior crurorrhaphy was routinely performed with the application of two to three nonabsorbable sutures (2-0 Ethibond; Ethicon, Spreitenbach, Switzerland) (Fig. 5). In all cases of hiatal hernia mesh reinforcement was performed. Prostesis was fixed around the esophagus in addition to the suture repair of the hiatus (Fig. 6). A polypropylene mesh was fixed by nonabsorbable stitches (2-0 Ethibond; (Ethicon, Spreitenbach, Switzerland) or 3-0 PremiCron (B.Braun, Barcelona, Spain)) on the both cruras and diaphragm only.

The internal edges of the mesh were stitched to the diaphragm to avoid the contact of free edges of the mesh and esophagus, erosion of the organ wall. We took a special care to avoid wrinkles and free flaps. Fundoplication was performed as the antireflux procedure (Fig. 7).

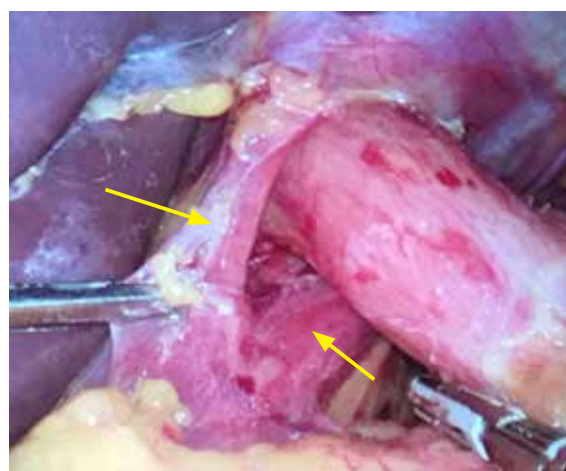
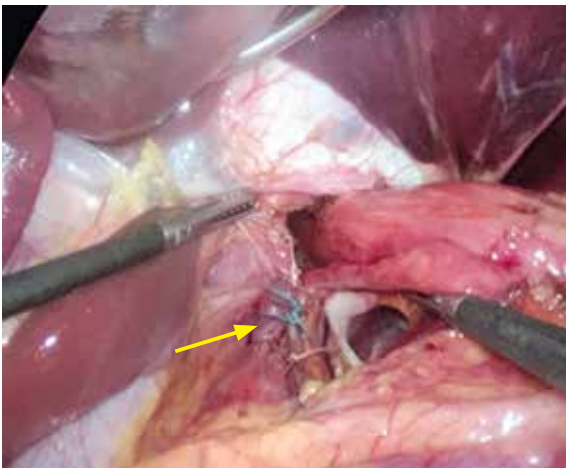


Figure 4. Mobilization of the abdominal part of the esophagus and cruras of the diaphragm. Arrows show right and left cruras of the diaphragm

The antireflux wrap was formed with two or three 3-0 Ethibond (Ethicon, Spreitenbach, Switzerland) or 3-0 PremiCron (B.Braun, Barcelona, Spain) stitches fixed to the anterior wall of the esophagus.

During the crurorrhaphy and wrap formation 36Fr gastric probe was inserted into the cardia.



**FIGURE 5.** The crurorrhaphy is performed. Arrow shows stitches on diaphragmatic cruras



**FIGURE 6.** Mesh is fixed around esophagus



**FIGURE 7.** Complete 360° fundoplication is performed. The arrow shows the antireflux wrap

### The Postoperative period

Oral feeding was started on the 1<sup>st</sup> day after surgery, beginning with liquid food and a soft diet.

Patients without complications were discharged on the second or third postoperative day and were invited for follow-up examination on the 7th day, in the second month and in the 6th month. They were instructed to take soft food for 2 months.

The results in early postoperative period were assessed with contrast X-ray examination and 24-hour pH-metry on the 5-th to the 7-th days after surgery. A barium contrast examination was performed for all patients to rule out an anatomic recurrence. Recurrence was defined as the presence of gastroesophageal reflux or/and any migration of the wrap to the chest level or/and evidence of a new paraesophageal sac.

Postoperative complications were considered as a major failure when a second operation or medical therapy longer than 6 months was required. All other complications were considered minor.

### Quality-of-life assessment

After a 6-month follow-up, patients were interviewed in the outpatient clinic or over the phone. Patients were specifically asked about their symptoms, and Short Form-36 [SF-36] quality-of-life questionnaire was implemented.

They were also called via telephone and questioned about their complaints (heartburn, belching, dysphagia, gas-bloating syndrome, diarrhea, etc.). Functional outcomes were considered “excellent” when a patient was asymptomatic and did not need any medication; “good” when a patient had symptoms not severe enough to require medications; “moderately good” when a patient’s symptoms could be controlled with medication; and “poor” when a patient’s symptoms were not eliminated by the operation.

This study was approved by the Ethics Committee of Yerevan State Medical University.

### Statistical analysis

The results were analyzed using both the Chi-square test and the Student t-test. A p-value less than 0.05 was considered statistically significant.



**RESULTS**

The mean period from the onset of the symptoms to operation was 46 (10-120) months. No patient had a history of previous operation for hiatal hernia or GERD. Common complaints in preoperative period were heartburn and regurgitation. Preoperative and postoperative symptoms are presented in Table 2.

There is a combination of GERD and hiatal hernia in 94 cases. In all the mentioned cases the esophagogram showed hiatal hernia. There were no cases of short esophagus in the study group.

Endoscopic evaluation revealed no esophagitis in 65 patients (63.7%), grade A-B esophagitis - in 29 patients (28.4%) and grade C-D esophagitis in 8 patients (7.9%).

Esophageal pH-metry showed acid exposure in 58 cases (56.9%). The mean pH<4 and the median pH<3.5 were in 32 patients (31.4%). Nonacid refluxes were registered in 12 cases (11.8%). DeMeester Score were >14,7 in 54 cases (52.9%). An interesting fact has been observed: nonacid pH in stomach was often in patients with subtotal or total hiatal hernia.

In all cases operations were performed from a planned elective list after the regular admission. The conversion to open surgery was performed in 2 cases due to adhesions in the upper abdomen after the previous operation – open cholecystectomy. The mean operative time was significantly shorter in the group without mesh.

The perioperative data is presented in Table 3.

In the postoperative period 2 patients had transient subcutaneous emphysema in the neck that resolved spontaneously within 24 hours.

**TABLE 2.**

Preoperative and postoperative symptoms		
	Preoperative (cases)	Postoperative (cases)
Heartburn	86	4
Regurgitation	27	0
Respiratory symptoms	17	1
Dysphagia/post-prandial chest pain	2/10	3/1
Abdominal pain	4	0
Chronic bleeding	2	-
Gas-bloating syndrome	8	4

Gas-bloating syndrome (4 cases) occurred after both complete and non-complete funduplications and disappeared during 3-4 weeks.

In all 3 cases of postoperative dysphagia the problem occurred after the complete fundoplication and was solved spontaneously during 5-6 weeks. Difficulties of swallowing in the first 3-4 postoperative days had 21 patients after surgery with a complete wrap. There were no cases of persistent dysphagia, that require endoscopic balloon dilation or reoperation.

All 4 cases of gastroesophageal reflux recurrence happened after non-complete fundoplication, in all cases patients required medical treatment with proton pump inhibitors and prokinetics for the symptom relief. In one case medical therapy was not effective and refundoplication was done.

In our study we had 3 cases of hernia recurrence, 2 patients underwent reoperation with mesh reinforcement and complete fundoplication.

No deaths and no intraoperative complications were detected in both groups. There was no one in-hospital mortality. No mesh-related complica-

**TABLE 3.**

Perioperative characteristics					
	Operations with complete fundoplication (n = 42)		Operations with not complete fundoplication (n = 60)		P Value
	Laparoscopic procedures (n = 25)	Open procedures (n = 17)	Laparoscopic procedures (n = 37)	Open procedures (n = 23)	
Mean operative time (min)	170 (range 120-200)	169 (range 130-210)	162 (range 110-200)	175 (range 120-210)	0.24
Postoperative overall hospital stay (days)	5.6 (range 3-7)	7.3 (range 5-8)	5 (range 3-7)	7.4 (range 5-9)	< 0.001
Hernia recurrence	1	1	1	0	-
Recurrence of reflux	0	1	0	2	-

tion was in mesh reinforcement group.

Perioperative data were collected retrospectively. The mean follow-up period was 58 months (range, 12–120 months). Complete follow-up assessment was obtained for 26 (25.5%) patients, follow-up evaluation only by the telephone interview – for 52 (51%), there were no contacts with 24 (23.5%) the other patients, they were considered dropouts. The GERD recurrence rate was investigated via a barium contrast swallow and esophagoscopy. The results of the follow-up assessment of 78 patients are presented in Table 4.

The quality-of-life evaluation by the questionnaire showed a significant difference between two groups, improvement of the results in the laparoscopic group with complete fundoplication.

#### DISCUSSION

GERD is a common disorder accounting for approximately 75% of esophageal pathology [DeMeester TR, Stein HJ, 1992; Kamolz T et al., 2003; Fuchs KH et al., 2014]. Dysfunction of the antireflux barrier is recognized as the main cause of this disease [Triadafilopoulos G, 2004; Huttel TP et al., 2005].

Generally the disease severity ranges from mild to severe symptomatic perception and several different gradings of esophagitis, which may result in complications such as Barrett's esophagus or ultimately as adenocarcinoma of the esophagus, as well as upper respiratory symptoms [Kamolz T et al., 2003].

The major problem in the treatment of GERD is the duration of medical therapy and the time of indication for surgery. Despite the tendency of more aggressive approach and wide indications for anti-

reflux surgery [Granderath FA et al., 2002], many patients continue to avoid any procedure. In our study 76 patients (74.5%) had previous non effective prolonged medical therapy, 5 of them had 10 years use of proton pump inhibitors. In our opinion, not regular use of medical therapy was the main cause of high incidence of esophagitis in study group.

In the operative treatment of GERD open procedures currently are performed in few cases. The laparoscopic approach has been a standard and the main operative method in this field since the 1990s. Functional results of laparoscopic antireflux operations are equal to that of open surgery and is associated with low morbidity and mortality, significantly less postoperative morbidity, and a shorter hospital stay [Geagea T 1991; Frantzides CT et al., 1997; Hinder R.A et al., 1997; Laine S et al 1997; Peters MJ et al., 2009; Fuchs KH et al., 2014]. But there is no unique reliable method of antireflux surgery, surgeons use various modifications. Another problem of antireflux surgery are high complication and recurrence rates. Poor results of fundoplication (recurrent reflux, disabling dysphagia, or long-term discomfort) occur in 2-10% of patients [Huttel TP et al., 2005].

After some experience of open antireflux surgery laparoscopic operations were performed in our clinic. In the first part of this period Nissen-Rossetti method without short gastric vessels division was used. In the second period of the investigation short gastric vessels division with complete and not complete wrap formation was done.

Some authors have reported a significant decrease in postoperative dysphagia after routine division of

TABLE 4.

Results of follow-up assessment of operated patients

	Operations with complete fundoplication (n = 35)		Operations with not complete fundoplication (n = 43)		
	Laparoscopic procedures (n = 21)	Open procedures (n = 14)	Laparoscopic procedures (n = 25)	Open procedures (n = 18)	
“Excellent” functional outcome	17	12	19	15	0.938
“Good” functional outcome	3	1	4	1	
“Moderately good” functional outcome	1	-	1	1	
“Poor” functional outcome	-	1	1	1	

the short gastric vessels [Hunter JG et al., 1995].

We had the same result in our study - all cases of postoperative dysphagia refer to the first period of our investigation when we didn't perform division of short gastric vessels. We consider the division of short gastric vessels decreases the tonus of gastric wall in fundus resulting in less compression of the esophagus and cardia by the wrap. Complete fundoplication with tight wrap and without short gastric vessel's division has a high risk of dysphagia. But the complete mobilization of the gastric fundus has an advantage, it provides sufficient material for fundoplication wrap formation. Fundoplication over the bougie prevents tight wrap formation and various deformities, but it doesn't solve all problems. It is important to note that in majority of cases the problem of dysphagia is solved within 6 weeks after the procedure.

Recurrence of symptoms like heartburn and belching are common after not complete fundoplication. In late postoperative period there is high risk of reflux recurrence. We consider the cause of recurrence is associated with loose wrap and large mobilization of greater curvature of stomach, it results in low tonus of gastric wall included in the wrap.

Another point of discussion are follow technical aspects of antireflux procedures: to create a functional antireflux barrier and perform hiatal repair. The reconstruction of the antireflux barrier consists of three fundamental components: (1) proper length of the intra-abdominal esophagus, (2) crural repair, and (3) fundoplication [Fuchs KH et al., 2014]. In cases of the combination of GERD and hiatal hernia operation includes also hernia sac excision [Oelschlager BK, Pellegrini CA, 2001; Taragona EM et al., 2004].

In our study we followed the mentioned above principles, but in cases of giant hiatal hernias the hernia sac was not removed for the prevention of

injuries of intrathoracic organs and structures. After a proper mobilization of the abdominal part of the esophagus we performed crural repair and mesh reinforcement, procedures completed with fundoplication. Fundoplication wrap in our study is always fixed to the wall of esophagus and cardia, it is never fixed to the diaphragmatic cruras and surround tissues. In our opinion fixation of the wrap to the surround tissues impairs the mobility of the esophagus and stomach and can cause pain in the upper abdomen. We always use mesh reinforcement in cases of hiatal hernia. We do it in a similar way as in cases of external abdominal hernias. In our study there was no case of erosion of organs walls by mesh.

Different antireflux procedures with numerous modifications have been reported, but no unique open or laparoscopic antireflux technique has been accepted. The best surgical technique for GERD, however, remains a subject of debate, and should be assessed with prospective randomized clinical studies [Huttl TP et al., 2005]. Adherence to principles of antireflux procedures, complete wrap formation with the division of short gastric vessels and hiatal repair seem reliable and effective method for surgical treatment of GERD. Subsequent investigations are needed for this problem solution.

#### CONCLUSION

Complete fundoplication is a more reliable method of antireflux procedures for surgical treatment of gastroesophageal reflux disease. Division of short gastric vessels helps to prevent the persistent dysphagia. Repair of esophageal hiatus of diaphragm is mandatory in antireflux procedures. In cases of subtotal or total hiatal hernias is efficient to avoid removal of hernia sac for prevention of intrathoracic structures injury.

#### REFERENCES

1. Cuschieri A, Hunter J, Wolfe B (1993). Multi-center prospective evaluation of laparoscopic antireflux surgery: preliminary report. Surg Endosc. 7: 505-510
2. Dallemagne B, Weerts JM, Jeahes C (1998). Results of laparoscopic Nissen fundoplication. Hepatogastroenterology. 45: 1338-1343



3. *Dallemagne B, Weerts JM, Jehaes C (1991)*. Laparoscopic Nissen fundoplication: preliminary report. *Surg Laparosc Endosc*. 1: 138-143
4. *DeMeester TR, Bonavina L, Albertucci M (1968)*. Nissen fundoplication for gastroesophageal reflux disease: evaluation of primary repair in 100 consecutive patients. *Ann Surg*. 204: 9-20
5. *DeMeester TR, Stein HJ (1992)*. Surgical treatment of gastroesophageal reflux disease. In: Castell DO, ed. *The Esophagus*. Boston: Little, Brown. 579-626
6. *Donahue PE, Samelson S, Nyhus LM (1985)*. The floppy Nissen fundoplication: effective long-term control of pathologic reflux. *Arch Surg*. 120: 663-668
7. *Frantzides CT, Carlson MA (1997)*. Laparoscopic redo Nissen fundoplication. *Laparosc Adv Surg Tech*. 7: 235-239
8. *Fuchs KH, Babic B, Breithaupt W, Dallemagne B, Fingerhut A., et al (2014)*. EAES recommendations for the management of gastroesophageal reflux disease. *Surg Endosc*. DOI: 10.1007/s00464-014-3431-z
9. *Garg SK, Gurusamy KS (2015)*. Laparoscopic fundoplication surgery versus medical management for gastro-oesophageal reflux disease (GORD) in adults. *Cochrane Database of Systematic Reviews*. 11: CD003243 DOI: 10.1002/14651858.CD003243.pub3.
10. *Geagea T (1991)*. Nissen fundoplication by laparoscopy. *L'unionmédicale du Canada*. 120: 417
11. *Granderath FA, Kamolz T (2002)*. Quality of life, surgical outcome and patients' satisfaction three years after laparoscopic Nissen fundoplication. *World J Surg*. 26: 1234-1238
12. *Granderath FA, Kamolz T, Schweiger UM, Pasiut M, Wykypiel H, Pointner R (2002)*. Surgical outcome and analysis of failure after 500 laparoscopic antireflux procedures. *Surg Endosc*. 16: 753-757
13. *Granderath FA, Schweiger UM, Kamolz T, Pointner R (2005)*. Dysphagia after laparoscopic antireflux surgery: a problem of hiatal closure more than a problem of the wrap. *Surg Endosc*. 19: 1439-1446
14. *Granderath FA, Schweiger UM, Kamolz T, Pointner R (2005)*. Laparoscopic Nissen fundoplication in patients with nonerosive reflux disease. *Surg Endosc*. 19: 494-500
15. *Gryska PV, Vernon JK (2005)*. Tension-free repair of hiatal hernia during laparoscopic fundoplication: a ten-year experience. *Hernia*. 9: 150-155
16. *Hetzel DJ, Dent J, Reed WD (1998)*. Healing and relapse of severe peptic esophagitis after treatment with omeprazole. *Gastroenterology*. 95: 903912
17. *Hinder RA, Filipi CJ, Wetscher G (1994)*. Laparoscopic Nissen fundoplication is an effective treatment for gastroesophageal reflux disease. *Ann Surg*. 220: 472-481
18. *Hinder RA, Perdakis G, Klinger PJ (1997)*. The surgical option for gastroesophageal reflux disease. *Am J Med*. 103: 144-148
19. *Hunter JG, Swanstrom L, Waring JP (1995)*. Dysphagia after laparoscopic antireflux surgery: the impact of operative technique. *Ann Surg*. 224: 51-57
20. *Hunter JG, Trus TL, Branum GD (1996)*. A physiologic approach to laparoscopic fundoplication for gastroesophageal reflux disease. *Ann Surg*. 223: 673-685
21. *Huttl TP, Hohle M, Wichmann MW, Jauch KW, Meyer G (2005)*. Techniques and results of laparoscopic antireflux surgery in Germany. *Surg Endosc*. 19: 1579-1587
22. *Iqbal A, Awad Z, Simkins J, Shah R, Haider M., et al (2006)*. Repair of 104 Failed Anti-Reflux Operations. *Annals of Surgery*. 244(1): 42-51
23. *Jamieson GG, Watson DI, Britten-Jones R (1994)*. Laparoscopic Nissen fundoplication. *Ann Surg*. 220: 137-145
24. *Juhasz A, Sundaram A, Hoshino M, Lee TH, Mittal SK (2012)*. Outcomes of surgical management of symptomatic large recurrent hiatal hernia. *Surg Endosc*. 26: 1501-1508 DOI: 10.1007/s00464-011-2072-8

25. Kamolz T, Granderath F, Pointner R (2003). Laparoscopic antireflux surgery. Disease-related quality-of-life assessment before and after surgery in GERD patients with and without Barrett's esophagus. *Surg Endosc.* 17: 880-885 DOI: 10.1007/s00464-002-9158-2
26. Laine S, Rantala A, Gullichsen R (1997). Laparoscopic vs conventional Nissen fundoplication: a prospective randomized study. *Surg Endosc.* 11: 441-444
27. Oelschlager BK, Pellegrini CA (2001). Paraesophageal hernias: open, laparoscopic or thoracic repair. *Chest Surg Clinic of North Am.* 11: 589-603
28. Peters JH, Heimbucher J, Kauer WK (1995). Clinical and physiologic comparison of laparoscopic and open Nissen fundoplication. *J Am CollSurg.* 180: 385-393
29. Peters MJ, Mukhtar A, Yunus RM (2009). Meta-analysis of randomized clinical trials comparing open and laparoscopic anti-reflux surgery. *Am J Gastroenterol.* 104: 1548-1561
30. Sataloff DM, Pursnani K, Hoyo S (1997). An objective assessment of laparoscopic antireflux surgery. *Am J Surg.* 174: 63-67
31. Soricelli E, Basso N, Genco A, Cipriano M (2009). Long-term results of hiatal hernia mesh repair and antireflux laparoscopic surgery. *Surg Endosc.* 23: 2499-2504 DOI: 10.1007/s00464-009-0425-3
32. Stirling MC, Orringer MB (1986). Surgical treatment after the failed antireflux operation. *J Thorac Cardiovasc Surg.* 92: 667-672
33. Taragona EM, Novell J, Vela S (2004). Mid-term analysis of safety and quality of life after the laparoscopic repair of paraesophageal hiatal hernia. *Surg Endosc.* 18: 1045-1050
34. Triadafilopoulos G (2004). Changes in GERD symptom scores correlate with improvement in esophageal acid exposure after the Stretta procedure. *Surg Endosc.* 18: 1038-1044 DOI: 10.1007/s00464-003-8243-5



**CONTENTS**

- 6. MURADYAN A.A., ZILFYAN A.V., AVAGYAN S.A.**  
REGIONAL MELATONIN AND SOMATOSTATIN DEPENDENT MECHANISMS IN PANCREATIC INCRETORY ACTIVITY AND IN INTESTINAL BACTERIAL HOMEOSTASIS
- 14. KHUDAVERDYAN D.N., HASRATYAN H.A., MELKUMYAN K.V., GHAMBARYAN H.K., ABOVYAN L.A.**  
THE ROLE OF CALCIUM AND CALCIUM REGULATING HORMONAL SYSTEM IN THE MECHANISMS OF COVID-19 CONTAGIOUSNESS AND SEVERITY
- 23. KESOYAN A.A., ARAKELYAN N. L., ALOYAN D.A., KARAPETYAN A.A., MANVELYAN H.M.**  
CIGARETTE SMOKING, NICOTINE AND PARKINSON'S DISEASE: CONTROVERSIES IN CLINICAL TRIALS DATA AND MEDICAL PRACTICE
- 31. HOVHANNISYAN A.H., ASOYAN V.A., SHMAVONYAN M.V., HARUTYUNYAN L.A., TOROSYAN M.H., AYVAZYAN T.V., GHAZARYAN A.A., BARSEGHYAN E.S., MURADYAN A.A.**  
ACHIEVEMENTS AND CHALLENGES OF MANAGEMENT OF COVID-19 PATIENTS AT MIKAELYAN UNIVERSITY HOSPITAL
- 36. STEPANYAN N.A., BADALYAN S.H., ALEKSANYAN V.A., NAZINYAN R.A., ZAQARYAN A.V., KALASHYAN M.V., FANARJYAN R.V.**  
MICRODISCECTOMY: AN OBSERVATIONAL STUDY
- 41. AVAGYAN S.A., ZILFYAN A.V., MURADYAN A.A., GAZARYAN H.V.**  
POTENTIAL SIGNIFICANCE OF ALIPHATIC POLYAMINES,  $\alpha$ -SYNUCLEINS AND HELICOBACTER PYLORI IN DIAGNOSTICS AND PROGNOSIS OF SOME MALIGNANT TUMORS
- 54. HARUTYUNYAN K.R., MELKUMYAN K.V., ABRAHAMYAN H.T., ADAMYAN S.H., KHUDAVERDYAN D.N., TER-MARKOSYAN A.S.**  
CALCIUM-REGULATING HORMONAL SYSTEM IN CARDIAC FUNCTIONAL ACTIVITY
- 64. STEPANYAN S.A., HAKOBYAN V.M., PETROSYAN A.A., YEGHIAZARYAN H.H., PAPAZYAN K.T., BATIKYAN H.Kh., ALEKSANYAN A.Yu., SAFARYAN H.H., SHMAVONYAN H.H., BABAYAN A.M.**  
COMPLETE VERSUS NON-COMPLETE FUNDOPLICATION IN SURGICAL TREATMENT OF GASTROESOPHAGEAL REFLUX DISEASE
- 74. MINASYAN A.H., MINASYAN H.L., ARAZYAN D.R., ALEKSANYAN A.B., HARUTUNYAN E.A.**  
FEATURES OF ABDOMINAL SURGERY IN COMBAT INJURIES, OUR EXPERIENCE
- 79. AZATYAN V.Yu., YESSAYAN L.K., SHMAVONYAN M.V., PORKSHEYAN K.A.**  
THE CHARACTERISTICS OF MICROBIAL LANDSCAPE OF THE ORAL CAVITY IN PATIENTS WITH VIRAL HEPATITIS B, VIRAL HEPATITIS C AND HIV INFECTION
- 89. ADAMYAN N.H., SHAMILYAN Q.M., ZHAMHARYAN A.G., TOPCHYAN H.V., BALASANYAN M.G.**  
INVESTIGATION OF CEREBROVASCULAR ACTIVITY OF NEW GABA-DERIVED SHORT PEPTIDES
- 96. GHAZARYAN N.L., KHACHATRYAN A.H., ADAMYAN M.Yu., HOVAKIMYAN T.B.**  
CARDIAC IMPLANTABLE ELECTRONIC DEVICE INFECTION: PREVALENCE AND RISK FACTORS (A single center experience)
- 102. SAHAKYAN G.G., ORDUYAN M.H., BABAYAN A.G., MANVELYAN H.M.**  
CLINICAL OUTCOMES OF REPERFUSION THERAPIES IN ELDERLY PATIENTS WITH ACUTE ISCHEMIC STROKE
- 107. AZNAURYAN A.V., NAVASARDYAN G.A., AVAGIMYAN A.A.**  
PERIVASCULAR ADIPOSE TISSUE – ORCHESTRATOR OF CARDIOVASCULAR DISTURBANCES SEQUEL





The Journal is founded by  
Yerevan State Medical  
University after M. Heratsi.

## Rector of YSMU

Armen A. Muradyan

## Address for correspondence:

Yerevan State Medical University  
2 Koryun Street, Yerevan 0025,  
Republic of Armenia

## Phones:

(+37410) 582532 YSMU

(+37493 588697 Editor-in-Chief

**Fax:** (+37410) 582532

**E-mail:** namj.ysmu@gmail.com, ysmiu@mail.ru

**URL:** <http://www.ysmu.am>

*Our journal is registered in the databases of Scopus,  
EBSCO and Thomson Reuters (in the registration process)*



SCOPUS



EBSCO

REUTERS

**Copy editor: Tatevik R. Movsisyan**

Printed in "VARM" LLC  
Director: Ruzanna Arakelyan  
Armenia, 0018, Yerevan,  
Tigran Mec 48, 43  
Phone: (+374 91) 19 29 00,  
E-mail: armana6@mail.ru

## Editor-in-Chief

Arto V. Zilfyan (Yerevan, Armenia)

## Deputy Editors

Hovhannes M. Manvelyan (Yerevan, Armenia)

Hamayak S. Sisakyan (Yerevan, Armenia)

## Executive Secretary

Stepan A. Avagyan (Yerevan, Armenia)

## Editorial Board

Armen A. Muradyan (Yerevan, Armenia)

Drastamat N. Khudaverdyan (Yerevan, Armenia)

Levon M. Mkrtchyan (Yerevan, Armenia)

## Foregin Members of the Editorial Board

Carsten N. GUTT (Memmingen, Germany)

Muhammad MIFTAHUSSURUR (Indonesia)

Alexander WOODMAN (Dharhan, Saudi Arabia)

Hesam Adin Atashi (Tehran, Iran)

## Coordinating Editor (for this number)

Drastamat N. Khudaverdyan (Yerevan, Armenia)

## Editorial Advisory Council

Ara S. Babloyan (Yerevan, Armenia)

Aram Chobanian (Boston, USA)

Luciana Dini (Lecce, Italy)

Azat A. Engibaryan (Yerevan, Armenia)

Ruben V. Fanarjyan (Yerevan, Armenia)

Gerasimos Filippatos (Athens, Greece)

Gabriele Fragasso (Milan, Italy)

Samvel G. Galstyan (Yerevan, Armenia)

Arthur A. Grigorian (Macon, Georgia, USA)

Armen Dz. Hambardzumyan (Yerevan, Armenia)

Seyran P. Kocharyan (Yerevan, Armenia)

Aleksandr S. Malayan (Yerevan, Armenia)

Mikhail Z. Narimanyan (Yerevan, Armenia)

Levon N. Nazarian (Philadelphia, USA)

Yumei Niu (Harbin, China)

Linda F. Noble-Haeusslein (San Francisco, USA)

Arthur K. Shukuryan (Yerevan, Armenia)

Suren A. Stepanyan (Yerevan, Armenia)

Gevorg N. Tamamyanyan (Yerevan, Armenia)

Hakob V. Topchyan (Yerevan, Armenia)

Alexander Tsiskaridze (Tbilisi, Georgia)

Konstantin B. Yenkovyan (Yerevan, Armenia)

Peijun Wang (Harbin, China)