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Clinical Application of Layered Anastomosis During Esophagogastrostomy

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Abstract The aim of this study was to compare the operative results in regard to reducing anastomotic leakage and stricture formation using a newly designed layered manual esophagogastric anastomosis versus a stapler esophagogastrostomy versus the conventional hand-sewn whole-layer anastomosis after resection for esophageal or gastric cardiac carcinoma. From January 2004 to September 2006, a total of 1024 patients with esophageal or gastric cardia carcinoma underwent a layered esophagogastric anastomosis with the assistance of a three-leaf clipper in a single university medical center. The mucosal layers of the esophagus and stomach were sutured continuously with 4/0 Vicryl plus antibacterial suture (polyglyconate). From May 2002 to December 2003, there were also 170 patients and 69 patients who underwent stapler and conventional whole-layer anastomosis, respectively; they served as control groups. The results were analyzed retrospectively. The operative mortality rate was 0.7% in the layered group compared to 5.9% and 7.2% for the stapler group and the whole-layer group ($p < 0.01$), The anastomotic leakage rates were 0%, 3.5%, and 5.8% for the layered group, stapler group, and whole-layer group, respectively ($p < 0.01$). All patients were followed postoperatively. Six patients in the layered group (0.6%) developed mild stricture formation compared to 16 patients in stapled group (9.9%) and 5 patients in the conventional whole-layer group (7.8%) ($p < 0.01$). The application of layered esophagogastric anastomosis could reduce the incidence of anastomotic leakage and stricture after esophagectomy compared with the stapler and whole-layer manual anastomoses. It is easy to apply and could be used as an alternative for esophagogastric anastomosis after resection for esophageal or cardiac carcinoma.

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Anastomotic leakage and stricture formation following esophagogastrectomy continue to be major challenges after resection of esophageal carcinoma. They are the main causes of postoperative mortality and poor quality of life (QOL), especially in patients with leakage in the chest cavity [1, 2]. Anastomotic leakage is the direct consequence of poor healing. Primary intention healing of the anastomotic stoma has no complications, but anastomotic stricture during secondary intention healing often results from increased fibroplasia. Moreover, the unhealed anastomotic stoma tends to become leakage. Automated stapler instruments seem to be advantageous during esophageal surgery. However, some studies have revealed that stapled and hand-sewn anastomotic techniques had similar anastomotic leakage rates, although strictures were more common after a stapled anastomosis. The incidence rates of anastomotic leakage and stricture were 1% and 5%, respectively, following hand-sewn anastomosis versus 5% and 10% with stapled intrathoracic anastomosis [3, 4]. Anastomotic leakage and stricture with cervical anastomosis could be as high as 22% and 10% in the hand-sewn

group versus 14% and 18% in the stapler group [5]. Finding effective methods to promote smooth healing of the anastomosis and prevent anastomotic leakage or stricture is still a hot area in esophageal surgery. As esophageal carcinoma is prevalent in this part of China, we designed a technique using a three-leaf clipper-assisted layered anastomosis with the mucosa layer sewed continuously with 4/0 Vicryl plus antibacterial suture (polyglyconate) during esophagogastrostomy. After successful utilization of the technique in animal experiments designed to observe and analyze the healing effect of the anastomosis in 2004 [6], it was applied consecutively on 1024 clinical cases from January 2004 to September 2006. The results were compared to those after use of the stapler and whole-layer manual anastomosis techniques from May 2002 to December 2003 in our center. The technique details and clinical results are reported.

Materials and Methods

Clinical Data

A total of 1024 patients were enrolled in the layered group in this study from January 2004 to September 2006. The group included 928 patients with esophageal carcinoma and 96 with gastric cardia carcinoma. There were 170 patients enrolled in the stapler anastomosis group and 69 patients in the whole-layer hand-sewn anastomosis group from May 2002 to December 2003 who served as controls. The patients in control groups were consecutively admitted and assigned to the surgeons by the registration nurse (M. Zhang) without any known research-related information of the patients considered. They were operated on by two other surgeons (Z.W., L.X.L), who favored the other anastomotic method. All of these surgeons were similarly experienced in esophageal surgery. In the stapler group, there were 145 patients with esophageal carcinoma and 25 with gastric cardia carcinoma. In the hand-sewn whole-layer group, there were 64 patients with esophageal carcinoma and 5 with gastric cardia carcinoma. The pathologic staging was done according to the UICC-TNM classification (2002). The detailed demographic data for the three groups are given in Table 1.

The diagnosis was established by initial barium esophagography followed by endoscopic biopsies with documented carcinoma as histologic evidence. Preoperative chemotherapy and/or radiotherapy were not given in all patients. All the operations were performed at a single university esophageal surgical center.

The esophagogastric anastomosis was performed via open left thoracotomy. The operative procedures and operating time were recorded. Perioperative mortality and morbidity, such as anastomotic leakage and stricture

Table 1 Demographic data of the patients

Parameter	Layered anastomosis ($n = 1024$)	Stapled anastomosis ($n = 170$)	Whole-layer anastomosis ($n = 69$)	Statistics	p
Age (years), mean ± SD	65 ± 13	63 ± 11	61 ± 14	$F^a = 0.413$	0.663
Sex (M:F)	816:208	136:34	56:13	$\chi^2 = 0.091$	0.955
Chronic diseases					
Pulmonary disease	152 (14.8%)	21 (12.4%)	9 (13.0%)	$\chi^2 = 0.844$	0.656
Heart disease	83 (8.1%)	12 (7.1%)	4 (5.8%)	$\chi^2 = 0.642$	0.725
Diabetes	47 (4.6%)	6 (3.5%)	2 (2.9%)	$\chi^2 = 0.765$	0.682
Site of tumor				$\chi^2 = 11.328$	0.079
Upper thoracic	44 (4.3%)	5 (2.9%)	4 (5.8%)		
Middle thoracic	745 (72.8%)	128 (75.3%)	49 (71.0%)		
Lower thoracic	139 (13.6%)	12 (7.1%)	11 (15.9%)		
Gastric cardia	96 (9.4%)	25 (14.7%)	5 (7.2%)		
Stage of tumor				$\chi^2 = 2.038$	0.916
0/I	34 (3.3%)	6 (3.5%)	1 (1.4%)		
IIa	98 (9.6%)	20 (11.8%)	6 (8.7%)		
IIb	344 (33.6%)	52 (30.6%)	24 (34.8%)		
III	548 (53.5%)	92 (54.1%)	38 (55.1%)		
Position of anastomosis				$\chi^2 = 2.198$	0.699
Cervical region	109 (10.6%)	15 (8.8%)	7 (10.1%)		
Above the aortic arch	809 (79.0%)	132 (77.6%)	56 (81.6%)		
Under the aortic arch	106 (10.4%)	23 (13.5%)	6 (8.7%)		

Data are expressed as the observed number unless otherwise specified

[a] F: one-way analysis of variance (ANOVA)

formation, were the main observation parameters. The anastomosis was assessed by contrast barium esophagography performed at 5 to 10 postoperative days. Moreover, the duration of stay in the intensive care unit (ICU) and operative mortality (defined as death within 30 days following the operation) were also documented.

Discharged patients were followed up at the first month and then every 3 months until the present review period or the date of death if it occurred. Postoperative assessments include routine barium swallow and endoscopy if dysphagia developed. The grade of the stricture was classified according to the diameter of the anastomosis on barium swallow as: mild 0.6–0.9 cm, moderate 0.3–0.6 cm, severe > 0.3 cm.

Endoscopic water balloon dilation is used to treat esophageal stricture in our center.

Operative Procedure

After complete mobilization of the stomach, the esophagogastric junction was dissected. The gastric cardia was closed by suturing its mucosal and muscular layers separately with no. 4 silk suture. The esophagus with the tumor was mobilized from surrounding structures, and lymphadenectomy was performed. The whole stomach was used as the esophageal substitution in all patients.

For layered anastomosis, the esophagogastrostomy was completed with the assistance of a three-leaf clipper (Fig. 1a). The main surgical procedures included (1) placing two stitches of no. 4 silk suture in the gastric fundus as retention sutures to raise the gastric wall, clipping the stomach with one leaf of the three-leaf clipper (Fig. 1b), and incising the seromuscular layer of the stomach about 1.5 to 1.8 cm at the anastomosis position while keeping the submucosa and mucosa intact (Fig. 1c); (2) clipping the esophagus with another leaf of the three-leaf clipper and then cutting the muscular layer of the esophagus open at the anastomosis position the same way as in the stomach (Fig. 1d,e); (3) sewing the rear row muscular layer of the esophagus and the rear seromuscular layer of the stomach with six to eight stitches of interrupted 3/0 silk suture (Fig. 1f); (4) cutting the gastric mucosa layer open, leaving

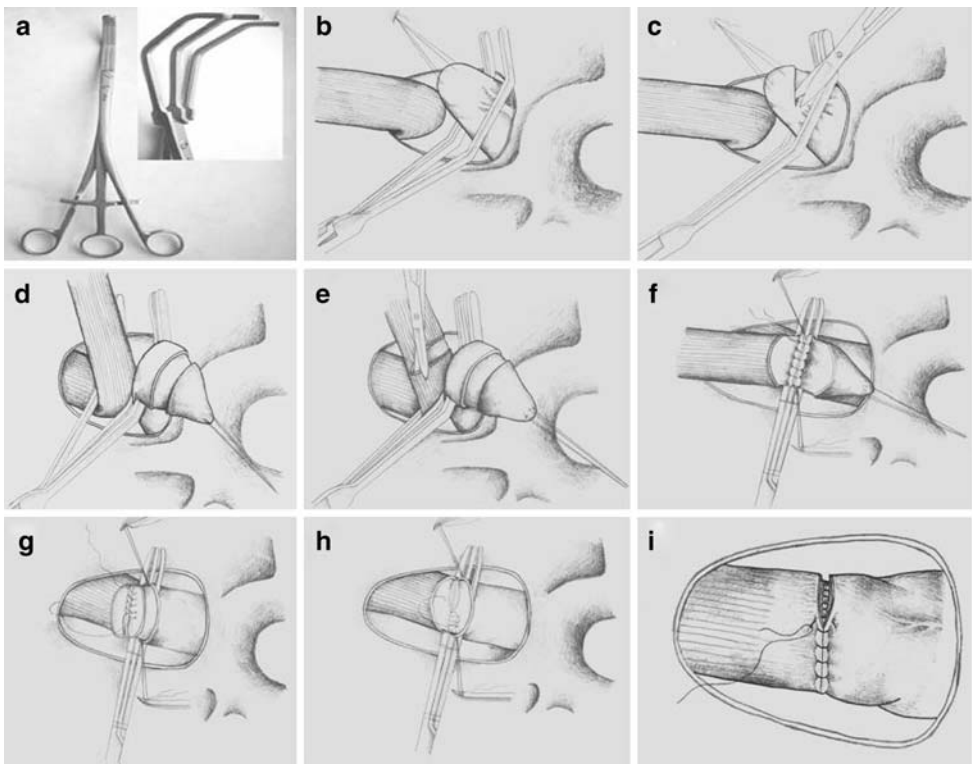

Fig. 1 Surgical procedure of layered anastomosis during esophagogastrostomy. **a** Three-leaf clipper. **b** Place two stitches in the gastric fundus as retention sutures to raise the gastric wall and then clip the stomach with one leaf of the three-leaf clipper. **c** Incise the seromuscular layer of the stomach while keeping the submucosa and mucosa intact. **d** Clip the esophagus with another leaf of the three-leaf clipper. **e** Cut open the muscular layer of the esophagus at the anastomosis position while keeping the submucosa and mucosa intact. **f** Sew the rear row of the muscular layer of the esophagus and the rear seromuscular layer of the stomach with interrupted 3/0 silk suture. **g** Cut open the esophageal and gastric mucosal layers and suture the rear mucosa continuously with 4/0 Vicryl plus antibacterial suture. **h** Suture the front mucosa continuously. **i** Sew the front muscular layer of the esophagus and front seromuscular layer of the stomach together with interrupted 3/0 silk suture

it about 0.8 cm longer than the muscular edge; (5) cutting the esophageal mucosa layer open, leaving it about 0.8 cm longer than the muscular edge, and then removing the specimen (the length of incision on the gastric wall should match the diameter of the esophageal lumen); (6) finishing the mucosa anastomosis by sewing the mucosal layers of esophagus and stomach continuously with 4/0 Vicryl plus antibacterial suture (polyglyconate), retaining the marginal distance of 0.2 cm from the mucosal cutting edge (Fig. 1 g,h); (7) removing the three-leaf clipper and then sewing the front muscular layers the same way as for the rear row with 3/0 silk suture (Fig. 1i); (8) fixing the anterior wall of the stomach to adjacent mediastinal pleura by no. 1 or 4 silk suture to reduce the tension at the anastomotic stoma.

For stapler anastomosis, the circular stapler of EEA 25 (Johnson & Johnson) was used. After finishing the anastomosis, reinforcement stitches were routinely added in the muscular layer for better securing the anastomosis. For whole-layer anastomosis, the conventional whole-layer, hand-sewn, embedded esophagogastrostomy with intermittent 3/0 silk suture was performed. The remaining operative procedures were identical to those in the layered group.

After finishing the anastomosis, a gastric tube was placed in the stomach and a feeding tube in the duodenum for early postoperative enteral nutrition support. The feeding could begin on the first postoperative day. Patients were able to take a liquid diet on postoperative day (POD) 5, semi-liquid diet on POD 9, and solid diet on POD 21.

Statistical Analysis

Continuous data were expressed as the mean ± SD and were analyzed using analysis of variance (ANOVA). Categorical variables were presented by frequency (%) and analyzed by the chi-squared test. Two-tailed $p < 0.05$ was considered statistically significant. The statistical analysis was performed by SPSS 11.0 for Windows (SPSS, Chicago, IL, USA).

Results

The layered group and the control groups did not differ in age, sex, preoperative health status, location of tumor, tumor stage, or position of the anastomosis (Table 1). The operative procedures, duration of operation, postoperative complications, intensive care unit (ICU) and hospital stays, and operative mortality are summarized in Table 2.

In the layered group, there was no anastomotic leakage after the operation. Seven patients died within 30 days after operation (0.7%). Five patients died of respiratory failure and two of myocardial infarction after discharge. Six patients suffered from mild anastomosis stricture (0.6%), and they recovered after one dilatation and then had no dysphagia after starting a solid diet.

In the stapler group, anastomotic leakage developed in six patients (3.5%): cervical anastomotic leakage in two patients and thoracic anastomotic leakage in four patients. Ten patients died within 30 days after operation (5.9%). Four died of anastomosis leakage, three of respiratory failure, one of liver failure, and two of a pulmonary embolism after discharge. Benign anastomosis strictures were noted in 16 patients (10.0%); 12 patients suffered from moderate or severe stricture, which need more than three dilatations.

In the hand-sewn whole-layer group, anastomotic leakage occurred in four patients (5.8%): cervical anastomotic leakage in one patient and thoracic anastomotic leakage in

Table 2 Operative and perioperative data

Parameter	Layered anastomosis ($n = 1024$)	Stapler anastomosis ($n = 170$)	Whole-layer anastomosis ($n = 69$)	Statistics	p
Operating time (min)	248 ± 32	230 ± 42	236 ± 39	$F = 1.899$	0.156
Anastomotic leakage	0	6 (3.5%)	4 (5.8%)*	$\chi^2 = 46.40$	0.000
Pulmonary complications[a]	140 (13.7%)	28 (16.5%)	10 (14.5%)	$\chi^2 = 0.953$	0.621
Cardiac complications[b]	98 (9.6%)	15 (8.8%)	7 (10.1%)	$\chi^2 = 0.130$	0.937
ICU stay (hours)	234	256	233	$F = 0.485$	0.615
Hospital stay (days)	9.6 ± 2.1	11.2 ± 3.6	12.5 ± 3.9	$F = 4.286$	0.016
Operative mortality	7 (0.7%)	10 (5.9%)	5 (7.2%)*	$\chi^2 = 35.94$	0.000
Anastomotic stricture[c]	6 (0.6%)	16 (10.0%)	5 (7.8%)*	$\chi^2 = 67.59$	0.000

Data are expressed as the observed number unless otherwise specified

[a] Pulmonary complications included aspiration pneumonia, bronchopneumonia, and respiratory failure

[b] Cardiac complications included arrhythmia, myocardial infarction, and cardiac failure

[c] Patients with operative mortality were excluded from anastomosis stricture

* $p < 0.001$, compared with layered anastomosis

three. The 30-day mortality rate was 7.2% (five patients): Three patients died of anastomosis leakage and two of respiratory failure. Five patients suffered from moderate stricture (7.8%).

Discussion

Compared with other operations, esophagogastrostomy anastomosis has a more problematic healing process, as evidenced by the high complication incidence and the poor healing quality [7]. Better healing quality needs better anastomosis skill and healing environment. Paying attention to the factors contributing to the development of leakage, particularly conduit ischemia and anastomotic technique, can reduce the incidence of anastomotic complications postoperatively [8, 9]. Several esophagogastric anastomosis methods have been proposed, with the whole-layer and stapler anastomoses being the most popular. However, no matter what methods were used, the main aim was to decrease as much as possible the incidence of anastomotic leakage and stricture [10].

The automatic esophagogastric suturing instrument has been advanced and improved. It has been extensively applied in the esophageal surgery field, aiming to shorten the operation time and tighten the anastomosis [11]. Several randomized studies found that stapled and hand-sewn esophagogastric anastomotic techniques had the same anastomotic leakage rates, but stricture was more common following stapler anastomosis [3, 4, 12, 13]. Some studies have concluded that the reasons may be that mucosal conjugation is not observed and the muscular layer is exposed during the anastomosis, producing a situation where an ulcer is formed at the anastomotic site. This could develop into stenosis and even leakage during the healing process [6, 14]. Another reason may be that stapler anastomosis distorts the blood flow in the anastomotic portion, which may cause anastomotic stricture and even leakage [15].

The development of leakage and stricture is complicated and is often related to various factors such as the anastomotic technique, infection, and the blood supply of the anastomosis. Some studies have shown that bacteria always exist in the esophagus even in the normal physiological situation [16, 17]. Those bacteria can easily cause anastomosis infection, especially when the suture is of poor quality. Esophagogastrostomy heals in a hyperacidic environment. Our previous study showed that the average acid reflux episode is 243.53 times/24 hours among patients who undergo esophagogastric anastomosis, and the total time for pH < 4 is 421.40 min/24 hr [18]. Gastric and esophageal mucosae have better anti-acid stress and anti-infection ability, but the anti-acid stress capability of the submucosa and muscle layer is poor. Moreover, the submucosa has excellent blood flow, so the union of the submucosa tends to occur much more easily than union of the muscular layer [19]; and the healing of a esophagogastrostomy relies mainly on union of the mucosa *and* submucosa [7, 20].

Based on the theories mentioned above, we designed the layered anastomosis with mucosa and submucosa sewed continuously with 4/0 Vicryl plus antibacterial suture during esophagogastrostomy and then the muscular/seromuscular layer of the esophagus/stomach interruptedly. This technique was firstly applied in animal experiments to observe and analyze the healing effect of the anastomosis [6]. Our experimental study demonstrated that the mucosa of a layered anastomosis was smoother with better elasticity than that in routine full-thickness anastomoses and complied with the nature of primary intention wound healing. The layered anastomosis during esophagogastrostomy in our study adopted mucosal and submucosal single-layer sutures. This ensured accurate apposition of the mucosal and muscular layers and avoided muscle exploration, as well as acid or alkali damage, and reduced the inflammation. At the same time, Vicryl plus antibacterial suture (an absorbable suture) was used for mucosa suturing, which might inhibit bacterial growth and consequently prevent postoperative infection [21]. Our animal experiment indicated that the inflammatory reaction and scar formation during the later period was slight, which might be the main reason for the low rate of anastomotic stricture formation. Moreover, with the assistance of the three-leaf clipper, exposure of the anastomosis stoma became easy, and contamination from esophageal or gastric contents was decreased. With this technique, there is no necessity to embed the anastomotic stoma. This would avoid overly tight embedment and angulation of the anastomotic stoma, thereby decreasing stricture formation factors due to the anastomotic technique itself.

Our clinical results showed that the layered anastomosis decreased anastomotic leakage effectively. There were no severe strictures, and only 0.6% (6/1024) of patients suffered from a mild benign stricture, which was cured after one dilatation. Cervical anastomoses consistently have higher leakage and stricture rates than intrathoracic anastomoses, regardless of whether they are stapled or manual anastomoses [5, 22]. Orringer et al. [23] had shown that their novel technique of side-to-side linear stapling greatly reduces the frequency of anastomotic leaks to 2.7%, although this technique still exposes the submucosal tissues of the esophagus to the lumen; hence, the risk of leakage or stricture still exists. In our series, 109 patients underwent cervical anastomosis without leakage or severe stricture formation.

Another advance is that the layered anastomosis is less expensive than the stapled anastomosis and so is more suitable for underdeveloped regions. Encouraged by the

excellent results with the layered manual anastomosis, we now use this technique for all patients undergoing esophagogastrostomy in our center.

Conclusions

Application of the three-leaf clipper-assisted manual layered anastomosis technique significantly reduces anastomotic leakage and stricture after esophagectomy. It has satisfactory consequences in clinical application and could be used as an alternative for esophagogastric anastomosis after resection of esophageal cancer.

References

1. Urschel JD (1995) Esophagogastrostomy anastomotic leaks complicating esophagectomy: a review. Am J Surg 169:634–640
2. Bardini R, Asolati M, Ruol A, et al. (1994) Anastomosis. World J Surg 18:373–378
3. Beitler AL, Urschel JD (1998) Comparison of stapled and hand-sewn esophagogastric anastomoses. Am J Surg 175:337–340
4. Law S, Fok M, Chu KM, et al. (1997) Comparison of hand-sewn and stapled esophagogastric anastomosis after esophageal resection for cancer: a prospective randomized controlled trial. Ann Surg 226:169–173
5. Hsu HH, Chen JS, Huang PM, et al. (2004) Comparison of manual and mechanical cervical esophagogastric anastomosis after esophageal resection for squamous cell carcinoma: a prospective randomized controlled trial. Eur J Cardiothorac Surg 25:1097–1101
6. Xie CH, Zhao YF, Kou YL, et al. (2004) The experimental study on the healing quality of the stoma in esophagogastrostomy by layering anastomosis. Chin J Thorac Cardiovasc Surg 20:261–263
7. Muller JM, Erasmi H, Stelzner M, et al. (1990) Surgical therapy of esophageal carcinoma. Br J Surg 77:845
8. Mitchell JD (2006) Anastomotic leak after esophagectomy. Thorac Surg Clin 16:1–9
9. Ercan S, Rice TW, Murthy SC, et al. (2005) Does esophagogastric anastomotic technique influence the outcome of patients with esophageal cancer? J Thorac Cardiovasc Surg 129:623–631
10. Bordini R, Bonavina L, Asolati M, et al. (1994) Single-layered cervical esophageal anastomosis: a prospective study of two suturing techniques. Ann Thorac Surg 58:1087–1090
11. Steichen FM, Ravitch MM (1980) Mechanical sutures in esophageal surgery. Ann Surg 191:373–381
12. Wong J, Cheng H, Liu R, et al. (1987) Esophagogastric anastomosis performed with a stapler: the occurrence of leakage and stricture. Surgery 101:408–415
13. Berrisford RG, Page RD, Donnelly RJ (1996) Stapler design and strictures at the esophagogastric anastomosis. J Thorac Cardiovasc Surg 111:142–146
14. Yoshiyuki F, Nobuyoshi H, Katsuya H, et al. (2005) Usefulness of automatic triangular anastomosis for esophageal cancer surgery using a linear stapler (TA-30). Ann Thorac Cardiovasc Surg 11:80–86
15. Aiko S, Ando N, Shinozawa Y, et al. (1993) Increased chemiluminescence and ulcer development in the low blood flowed state of the gastric tube for esophageal replacement. J Clin Gastroenterol 17:161–166
16. Xie CH, Yan Q, Zhao YF, et al. (2002) Esophageal bacteria research among sufferers of esophagus carcinoma in Sichuan Province China. Sichuan Med Magazine 23:369–370
17. Wang DB, chief translator (2000) Christopher Textbook of Surgery. 15th edition. People's Medical Publishing House, Beijing, pp 163–175
18. Zhao YF, Wan ZB, Wu C, et al. (1997) Gastric and esophageal episode after esophagus carcinoma resection. Chin J Clin Thorac Cardiovasc Surg 4:139–140
19. Pierie JP, De Graaf PW, Peon H, et al. (1994) Impaired healing of cervical esophagogastrostomies can be predicted by estimation of gastric serosal blood perfusion by Doppler flowmetry. Eur J Surg 160:599–603
20. Bardini R, Bonavinal L, Asolati M, et al. (1994) Single-layered cervical esophageal anastomosis: a prospective study of two suturing techniques. Ann Thorac Surg 58:1087–1090
21. Grau JM, Crespo M, Docobo F, et al. (2007) Prevention of surgical infection using reabsorbable antibacterial suture (Vicryl Plus) versus reabsorbable conventional suture in hernioplasty: an experimental study in animals. Cir Esp 81:324–332
22. Singh D, Maley RH, Santucci T, et al. (2001) Experience and technique of stapled mechanical cervical esophagogastric anastomosis. Ann Thorac Surg 71:419–424
23. Orringer MB, Becky M, Mark DI (2000) Eliminating the cervical esophagogastric anastomotic leak with a side-to-side stapled anastomosis [abstract]. J Thorac Cardiovasc Surg 119:277–288