

## Intrathoracic anastomotic stenosis after resection in esophageal cancer

### Özofagus kanserinde rezeksiyon sonrası intratorasik anastomoz darlığı

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**Background:** In this study, we assessed the postoperative anastomotic stenosis in patients undergoing intrathoracic esophagogastric anastomosis with the stapler.

**Methods:** Between January 2000 and December 2007, 132 patients who were operated due to esophageal cancer in Thoracic Surgery Clinic were retrospectively analyzed. The reconstruction was performed by the resection of 7-8 cm tumor free tissue proximally and distally. For all patients, the transthoracic esophagogastric anastomosis with end-to-end anastomosis (EEA) stapler was performed.

**Results:** The in-hospital mortality rate was 5.3% (n=7), while 15 patients (12.0%) developed anastomotic stenosis. The incidences of the anastomotic stenosis in female and male patients were 11.7% (9/77) and 12.5% (6/48), respectively. The anastomotic stenosis was developed in nine (13.4%) and six (10.3%) patients in which the anastomosis were performed by using 25 mm and 28 mm stapler, respectively. The rate of the anastomotic stenosis were 25% (13/52) and 2.9% (2/69) in patients with the tumor located in 1/3 middle or 1/3 distal and cardia, respectively. The mean duration of the stenosis development was 3.9 months (range, 2-8 months). The mean dilatation cure was 1.7 sessions (range, 2-6 sessions). Symptoms of all patients were relieved by means of balloon dilatation and no complication related to the procedure was seen.

**Conclusion:** Although the stapler contributes to the improvement of morbidity and mortality after the resection in esophageal cancer, it usually does not decrease the incidence of the anastomotic stenosis. We believe that surgical techniques should be improved and appropriate stapler devices should be developed to reduce the complications which may affect the patient comfort and psychology adversely.

**Key words:** Anastomotic stenosis; esophageal cancer; stapled anastomosis.

**Amaç:** Bu çalışmada stapler ile intratorasik özofagogastrik anastomoz uygulanan hastalarda ameliyat sonrası gelişen anastomoz darlığı değerlendirildi.

**Çalışma planı:** Ocak 2000 - Aralık 2007 tarihleri arasında Göğüs Cerrahisi Kliniği'nde özofagus kanseri nedeni ile ameliyat edilen 132 hasta retrospektif olarak değerlendirildi. Tümörün proksimal ve distalinden 7-8 cm'lik tümörsüz alan çıkarılarak rekonstrüksiyon gerçekleştirildi. Tüm hastalarda uç-uç anastomoz (EEA) stapler ile transtorasik özofagogastrik anastomoz uygulandı.

**Bulgular:** Hastane içi mortalite oranı %5.3 (n=7) iken, 15 hastada (%12.0) anastomoz darlığı gelişti. Kadınlarda darlık insidansı %11.7 (9/77), erkeklerde ise %12.5 (6/48) idi. Yirmi beş milimetre stapler ile anastomoz uygulanan hastaların dokuzunda (13.4%), 28 mm stapler ile anastomoz uygulanan hastaların altısında (10.3%) anastomoz darlığı gelişti. Anastomoz darlığı 1/3 orta özofagusta yerleşmiş tümörlerde %25 (13/52), 1/3 distal ve kardiyak yerleşimli tümörlerde ise %2.9 (2/69) oranında görüldü. Darlık gelişme süresi ortalama 3.9 ay (dağılım, 2-8 ay) idi. Ortalama dilatasyon kürü 1.7 seans (dağılım, 2-6 seans) idi. Balon dilatasyonu ile hastaların hepsinde semptomlarda düzelme sağlandı ve dilatasyon işlemine bağlı herhangi bir komplikasyon gözlenmedi.

**Sonuç:** Stapler özofageal rezeksiyon sonrası morbidite ve mortaliteye olumlu katkılar sağlamasına rağmen, genellikle anastomoz darlığı insidansını azaltmamaktadır. Hasta konforu ve psikolojisini olumsuz yönde etkileyen bu komplikasyonun azaltılması için, cerrahi teknikte ilerleme ve daha uygun aletlerin geliştirilmesinin gerekliliğine inanıyoruz.

**Anahtar sözcükler:** Anastomoz darlığı; özofagus kanseri; staplerle anastomoz.



Currently, surgery is the most effective treatment for cancer of the esophagus. However, considerable morbidity and mortality occur postoperatively, with postoperative complication and hospital mortality rates having been reported as approximately 50% and 5-10%, respectively.<sup>[1]</sup> Anastomotic leakage and pulmonary issues are the most common early complications associated with the high mortality rate in this type of cancer.<sup>[1,2]</sup>

Although it is not life-threatening, anastomotic stenosis is a common complication that occurs after a few months postoperatively. The incidence of anastomotic stenosis has been reported between 10% and 56% in various studies.<sup>[3]</sup> In the present study, postoperative anastomotic stenosis was evaluated retrospectively in patients who underwent intrathoracic esophagogastric anastomosis with a stapler, and the results were compared with the literature.

## PATIENTS AND METHODS

A total of 132 consecutive patients (48 male, 84 female; mean age 56.7±12.5 years; range 16 to 80 years) who were operated on for esophageal cancer via esophageal resection and transthoracic esophagogastric anastomosis in the Atatürk University, Medical Faculty, Thoracic Surgery Clinic between January 2000 and December 2007 were evaluated retrospectively. Patients who had been treated with palliative resection or neoadjuvant chemotherapy, those who had undergone additional surgical procedures other than an Ivor-Lewis esophagectomy, and those with other reconstructive organs were excluded from the study.

Out of the 125 patients included in the study, four had a tumor located in the upper one-third of the esophagus, 52 had a tumor in the middle third, and 69 had a tumor in the distal third of the esophagus/cardia. Forty-four patients (35.2%) had concomitant diseases. Hypertension was identified in 21 patients (16.8%), eight had diabetes mellitus (DM) (6.4%), nine had been diagnosed with chronic obstructive lung disease (COLD) (7.2%), eight suffered from hyperthyroidism (6.4%), seven had previous heart failure (5.6%), six had peptic ulcers (4.8%), two had been diagnosed with deep venous thrombosis (DVT) (1.6%) and one had lymphoma (0.8%).

After a median laparotomy, in order to keep the omentum majus supplied with blood, the skeletonization method was performed. The abdomen was closed by esophageal hiatus enlargement, and the esophagus was liberated after a right thoracotomy by the fifth intercostal interval. Reconstruction was performed by an end-to-end anastomosis (EEA) stapler device which was used

to cut the 7-8 cm tumor proximally and distally. In 67 women (53.6%), the anastomosis was performed with a 25 mm EEA stapler, and in 58 (46.4%) patients (48 male, 10 female), a 28 mm EEA stapler was used. A two-sided lymph node dissection was performed on all patients, and the surrounding tissue and gastric suture line were covered by the omentum when the esophagogastric anastomosis was completed.

All patients were diagnosed with stenosis via barium X-ray (Figure 1). Data was collected based on the medical, surgical, endoscopic, pathological, and outpatient records, and the results were then compared with the literature.

## RESULTS

Resection margins were cancer-free in all patients. In five patients (3.8%), anastomotic leakage was recorded. The hospital mortality rate was 5.3% (7/125), and the most common cause was anastomotic leakage, which occurred in three women (42.8%). In addition, two patients died from respiratory failure, one from multiple organ deficiency, and another from renal failure.

In 15 of the 125 patients (12.0%) anastomotic stenosis was observed, with an incidence rate of 11.7% (9/77) and 12.5% (6/48) in the female and male patients, respectively. Two patients with stenosis also developed hypertension. In the patients for whom anastomosis was performed by either the 25 mm (9/15) or 28 mm stapler (6/15), the rate of the anastomotic stenosis was 13.4% and 10.3%, respectively.

Additionally, the rate of anastomotic stenosis was 25% (13/52) and 2.9% (2/69) in patients with the tumor located in the middle third of the esophagus or distal third of the esophagus/cardia, respectively.

The mean duration of the stenosis development was 3.9 (range; 2-8) months, and the mean dilatation cure was 1.7, and it occurred one, two, three, and six times for 10 (66.7%), two (13.3%), two (13.3%) and one (6.7%) patient, respectively. Improvement was observed in all patients who underwent balloon dilatation without any complications. One patient who had anastomotic stenosis at three months postoperatively developed a recurrence of the tumor after two years, and an esophageal stent was then applied.

## DISCUSSION

Postoperative anastomotic stenosis is a common complication caused by alkaline/acid reflux, technical error, or local recurrence. Furthermore, hypotension and hypoxemia may lead to a reduction in perfusion



**Figure 1.** Barium X-ray shows a stenosis in a 59-year-old female patient.

and oxygenation of the anastomosis, and stenosis may significantly contribute to a reduced perfusion of the gastric conduit.<sup>[2,4]</sup> A consensus definition of stenosis is hard to find, but it usually means having the need for a type of intervention, for example dilatation. Various anastomotic stenosis rates have been reported in the literature, depending on the differences in surgical techniques and the anastomotic site.

In one large-scale meta-analysis, the incidence of symptomatic stenosis was reported as 28% and 16% in cervical anastomosis and Ivor-Lewis resection, respectively.<sup>[5]</sup> The high rate of leakage after cervical anastomosis may have contributed to these rate differences, and anastomotic leakage is an important risk factor for stenosis development. However, stenosis development caused by anastomotic leakage has been observed in only a few patients because mortality due

to the leakage is high, particularly in the thorax. In our study, three out of five patients who developed anastomotic leakage did not survive, but no patient developed a stenosis caused by this leakage.

In studies that have evaluated the risk factors of stenosis development, anastomotic leakage, intraoperative blood loss, and gastric tube vascularization failure have been determined to be the main causes. In another retrospective study, the use of a stapler device, anastomotic leakage, and cardiac disease were detected as associated factors in patients who underwent a transhiatal esophagectomy.<sup>[6]</sup> Moreover, Briel et al.<sup>[7]</sup> detected that preoperative weight loss increased the incidence of stenosis. It has also been reported that stenosis incidence and severity were higher in gastric reconstruction than in colonic reconstruction.<sup>[7]</sup> In this study, infection, ischemia, and mechanical condition

of the stapler were identified as the three factors that affect postoperative stenosis development. For optimal blood supply to the anastomosis, the gastric fundus and esophageal vascularization are essential. In this way, ischemic necrosis may be prevented. In addition, it has been observed that cardiovascular pathologies, such as arterial hypotension, cardiac ischemic diseases, and chronic vascular diseases, considerably facilitate anastomotic stenosis development.<sup>[8]</sup>

In several studies, it has been demonstrated that the incidence of leakage was higher in one-layer anastomosis while the stenosis incidence was higher in two-layer anastomosis.<sup>[9]</sup>

Many surgeons prefer to use a circular stapler in esophago-gastric anastomosis. This type of stapler has some advantages not only regarding anastomotic safety, but also the operation time. After the circular stapler was put into use, the incidence of anastomotic leakage dropped considerably. However, an increased incidence in stenosis has been observed, but this generally involves manual suture techniques. Beitler and Urschel<sup>[10]</sup> found that the stenosis rate was higher for anastomosis done with a stapler than for hand-sewn anastomosis in four randomized and seven nonrandomized comparison studies. McManus et al.<sup>[11]</sup> reported the benign stenosis rate as 13% and 1.6% in stapler and manual groups, respectively. However, in several studies, no difference was found between manual suturing and suturing with a circular stapler in anastomotic stenosis. Even if this is true, the stapler offers the advantage of reducing the dependence on the surgeon and lowering the fistula and stenosis rates.<sup>[12]</sup>

Mechanical factors may contribute to the development of stenosis, especially in the EEA staplers used for anastomosis. In a randomized study that evaluated the use of the EEA stapler in Ivor-Lewis anastomoses, the stenosis incidence was 43% with the 25 mm EEA stapler. However, the incidence of anastomotic stenosis with the 29 mm stapler was lower at 12.5%, and no anastomotic stenosis was observed with the 33 mm stapler.<sup>[13]</sup> Similarly, Griffin et al.<sup>[14]</sup> reported that the stenosis incidence was significantly higher with the 25 mm EEA stapler compared with the 28 mm stapler. The linear stapler-to-back wall and manual suture-to-front wall techniques have been utilized successfully in cervical anastomosis, and this has reduced the rate of stenosis. In our study, the rates of anastomotic stenosis development were 13.4% and 10.3% with the 25 mm EEA stapler and 28 mm EEA stapler, respectively, and the rates of anastomotic stenosis development in females and males was 11.7% and

12.5%, respectively. Considering that the 25 mm stapler was only used with the female patients and that the anastomotic stenosis risk was higher with the 25 mm stapler, it seems that male gender may be a risk factor for anastomotic stenosis development.

Kaplan et al.<sup>[15]</sup> reported that no association was found between the stenosis incidence and size of the stapler device. In that study, no difference was found between tumors in the upper one-third of the esophagus and those in the middle third with regard to stenosis incidence. However, in our study, the anastomotic stenosis incidence was significantly lower with regard to tumors in the upper one-third of the esophagus versus those found in the middle third.

Polglase et al.<sup>[16]</sup> showed that early development of the epithelial bridge and primary healing cause mucosal apposes in colonic and rectal anastomosis with careful suture techniques. In colorectal anastomosis with an EEA stapler, they observed a 2-4 mm mucosal gap; however, granulation tissue healed the gap.

Wong et al.<sup>[17]</sup> suggested that an improved stapler design might decrease the incidence of stenosis development. The use of absorbable/steel, circumferential/radial, and symmetric circular/eccentric staplers along with mucosal apposition and tissue necrosis in the bowel lumen are issues that should be investigated further to verify this hypothesis.

Anastomotic stenosis is a complication that occurs in the early postoperative period. The rate of the tumor recurrence at side anastomosis is between 2% and 32%.<sup>[18]</sup> Since late stenosis may be caused by disease recurrence, these patients should be evaluated by endoscopy and computed tomography (CT). Anastomotic recurrent tumors are seen as nodular stenosis in a barium esophagography, with the postoperative stenoses being short, concentric images. Indeed, tomography is an important device for showing anastomotic recurrence. In CT, anastomotic recurrence is revealed via the image of a soft tissue mass or nodular wall thickness in the esophagus or stomach.<sup>[19]</sup>

Anastomotic stenosis is the most common complication in esophageal cancer surgery. However, the use of proton pump inhibitors and safe dilatation techniques have proven to be key factors in the treatment of this complication. Furthermore, mucosal bleeding and lacerations should be avoided at the level of stenosis.<sup>[8]</sup> Honkoop et al.<sup>[20]</sup> observed two perforations out of 519 dilatation performances. They didn't observe any mortality. Law et al.<sup>[13]</sup> reported dilatation rates of 53% (once), 20% (twice), 12% (three times), and 8% (four times). In both studies, none of the patients

underwent surgery again. In our study, no complication was observed in 26 dilatation procedures.

Balloon dilatation has been successful when used to treat postoperative intrathoracic stenoses. However, stent placement may be needed with persistent stenoses, and sometimes resection is required with benign recurrent stenoses. Resection can also be applied when technical difficulties occur with malignant stenosis. Radiotherapy, stent therapy, and photodynamic therapy can be used with patients that are unsuitable for surgery with distant metastases.<sup>[21-23]</sup>

In conclusion, although anastomotic stenosis development is not a life-threatening condition, and dilation is possible, difficulty in swallowing can cause patient discomfort. In addition, anxiety caused by previous symptoms experienced in the early cancer and endoscopic disturbance can also cause discomfort. We believe that the stapler device provides positive contributions regarding morbidity and mortality after esophageal resection. Moreover, there is a need to improve the surgical techniques and appropriate stapler devices so as to decrease the complications in patients suffering from esophageal cancer.

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