

Comparison of Pressure Resistances of Different Esophagogastric Anastomosis Techniques: An Ex Vivo Ovine Model Study

Farklı Özofagogastrik Anastomoz Tekniklerinin Basınç Dirençlerinin Karşılaştırılması: Bir Ex Vivo Küçükbaş Hayvan Modeli Çalışması

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ABSTRACT

Background: Current anastomosis techniques including conventional esophageal (CEAT) and region expanding anastomosis techniques (REAT) in esophagus cancer surgeries have high mortality and morbidity rates, which underlines the lack of a golden standard method. Anastomosis techniques are one of responsible factors for stricture formation. In this regard, the study conducted on ex vivo ovine tissues was aimed to compare pressure resistances of different anastomosis techniques in term of stricture formation.

Material and Method: Thirty-five esophagus and gastric samples from 35 male lambs aged 12 months were used ex vivo for the study. Samples were divided into 5 groups according to anastomosis techniques including Hand-Made Sutured Technique (HM), Circular Stapler Sutured Technique (CS), Reinforced Circular Stapler Sutured Technique (rCS), Modified Plus "+" Incision Technique (mP+IT), and Modified Arrow-Bow Hand-Made Sutured Technique (mabHM). The intraluminal pressure resistance of the CEAT (e.g. the HM, CS and rCS) and REAT (e.g. the mP+IT and mabHM) were recorded.

Results: The pressures of different incision techniques from the highest to the lowest were found as follows: the rCS (114.71±3.77 cm H₂O) > the CS (95.43±3.45 cm H₂O) > the HM (84.14±3.67cm H₂O) > the mabHM (79.71±2.87 cm H₂O) > the mP+IT (77.14±6.23 cm H₂O) (p < 0.001). Except the comparison of the HM versus the mabHM (p=0.558), and the mP+IT versus the mabHM, the other techniques differ statistically significantly from each other.

Conclusion: In our study, the durability of anastomoses using CEAT was found to be higher and compatible with the literature. Although in vivo live animal studies are necessary, REAT can be safely used to prevent the development of stricture, which is the second most common complication of esophagogastric anastomoses. Our findings suggest that the CEAT especially the rCS can be safely administered to prevent leakage.

Keywords: *Esophagogastric Anastomosis, Stricture, Surgical Techniques, Esophagus, Stomach*

ÖZET

Giriş: Özofagus kanseri ameliyatlarında konvansiyonel özofagus (CEAT) ve bölge genişletici anastomoz teknikleri (REAT) gibi mevcut anastomoz tekniklerinin yüksek mortalite ve morbidite oranlarına sahip olması, altın standart bir yöntemin eksikliğinin altını çizmektedir. Anastomoz teknikleri, darlık oluşumundan sorumlu faktörlerden biridir. Bu bağlamda, ex vivo koyun dokuları üzerinde yapılan çalışmada, farklı anastomoz tekniklerinin basınç dirençlerinin darlık oluşumu açısından karşılaştırılması amaçlanmıştır.

Materyal ve Metod: Çalışma için 12 aylık 35 erkek kuzudan alınan otuz beş yemek borusu ve mide örneği ex vivo olarak kullanıldı. Örnekler anastomoz tekniklerine göre El Yapımı Dikiş Tekniği (HM), Circular Stapler Sütürlü Tekniği (CS), Reinforced Circular Stapler Sütürlü Tekniği (rCS), Modifiye Plus "+" İnsizyon Tekniği (mP+IT), ve Modifiye Ok-Yay El Yapımı Dikişli Tekniği (mabHM). CEAT (örn. HM, CS ve rCS) ve REAT'in (örn. mP+IT ve mabHM) intraluminal basınç direnci kaydedildi.

Bulgular: En yüksekten en düşüğe farklı kesi tekniklerinin basınçları şu şekilde bulundu: rCS (114.71±3.77 cm H₂O) > CS (95.43±3.45 cm H₂O) > HM (84.14±3.67cm H₂O) > mabHM (79.71±2.87 cm H₂O) > mP+IT (77.14±6.23 cm H₂O) (p < 0.001). HM ile mabHM'nin (p=0,558) ve mP+IT ile mabHM'nin karşılaştırılması dışında, diğer teknikler birbirinden istatistiksel olarak önemli ölçüde farklıdır.

Sonuç: Çalışmamızda CEAT kullanılan anastomozların dayanıklılığı daha yüksek ve literatürle uyumlu bulundu. İn vivo canlı hayvan çalışmaları gerekli olmakla birlikte, özofagogastrik anastomozların en sık görülen ikinci komplikasyonu olan darlık gelişimini önlemek için REAT güvenle kullanılabilir. Bulgularımız, sızıntıyı önlemek için CEAT'ın özellikle rCS'nin güvenli bir şekilde uygulanabileceğini göstermektedir.

Anahtar kelimeler: *Özofagogastrik Anastomoz, Darlık, Cerrahi Teknikler, Yemek Borusu, Mide*

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INTRODUCTION

Colonic, jejunal and gastric transposition methods are employed to conserve the continuity of gastrointestinal tract in surgeries to benign or malign esophagus pathologies (Bradshaw et al., 2018). Colon transposition is the most commonly used technique in pediatric patients; whereas in adult cancer patients, gastric pull-up technique is most commonly used, which involves use of stomach as a conduit (Bradshaw et al., 2018; Deng et al., 2020). Various anastomosis techniques are employed in gastric pull-up surgeries. Transpositions applied after esophagectomy surgeries have high morbidity and mortality. Most prominent early surgical complications are bleeding and leakage, while most prominent late surgical complication is stricture. Anastomotic leakage in cervical anastomosis of esophagectomy can be managed efficiently; however, strictures are developed on the anastomosis border such patients in comparison to other techniques and strictures more often and they are more challenging to manage in comparison to other techniques. On the other hand, although development anastomotic strictures are less frequent in intrathoracic anastomoses, sepsis following mediastinitis caused by anastomotic leakage has usually mortal (Shuangba et al., 2011; Deng et al., 2020).

Different approaches are suggested in the literature for the ideal anastomosis point and technique to minimize the surgical complications (Briel et al., 2004). In cervical region anastomoses, anastomotic leakages are easier to manage and thus mortality is lower than alternatives. Strictures are the most common long-term complications of cervical region anastomoses. Anastomotic stricture in the early postoperative period, cervical It is seen in 30-40% of anastomoses and 5-10% of intrathoracic anastomoses, and 3-4% of strictures become permanent (Ahmed et al., 2017). There are patient dependent risk factors for stricture formation (e.g. high collagen levels, diabetes mellitus etc.) but anastomosis technique is one of the modifiable risk factors. Reportedly, region expanding anastomosis techniques (REAT) reduces stricture formation. Major drawback of the REAT is the increased risk of leakage as the anastomosis area is larger (Melek and Cobanoglu, 2011). In this study; the REAT is compared with conventional esophageal anastomosis techniques (CEAT), used in gastric pull-up replacement in esophagectomy, by leakage tests in ex vivo animal models. Arrow-bow technique which is a modified combination of previously published techniques (Sharma and Wakhlu, 1980; Singh and Shun, 2001) is introduced as an alternative the REAT to be examined in future publications and included in the comparisons.

MATERIAL and METHOD

Esophagus and gastric specimens: Esophagus and gastric samples were collected from a slaughterhouse. Esophagus and gastric samples from 35 male lambs aged 12 months which were born on the same day in the same farm were collected by the attending

veterinary surgeon of the slaughterhouse. The samples were placed in a saline solution (0.85% NaCl) and were brought to General Surgery Department to eliminate the effects of the environmental factors.

Measurements and Standardized Procedures: All esophagus samples were prepared as 150 mm (Figure 1).

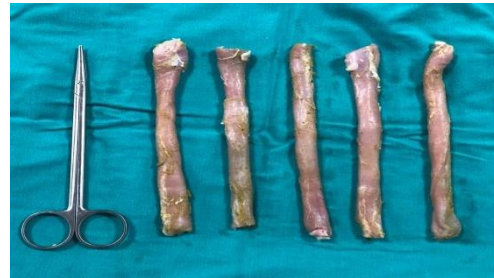


Figure 1. All esophagus samples were prepared as 150 mm

All gastric specimens were prepared to be 100 mm x 80 mm x 10 mm from the tripe of the lamb's gastric in equal volume and size for equal pressure control (Figure 2).

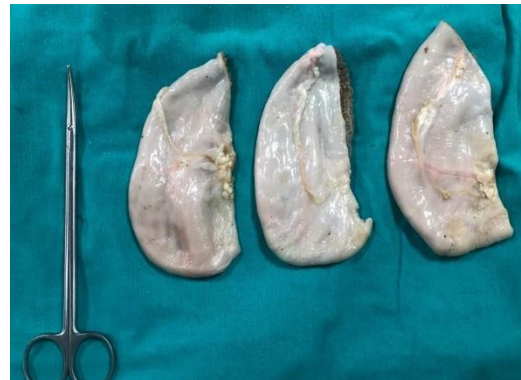


Figure 2. Gastric specimens were prepared as 100 mm x 80 mm x 10 mm from the tripe of the lamb's stomach in equal volume and size for equal pressure control.

Following the application of 5 different anastomosis techniques to a total of 35 samples, esophagus specimens were transected and tied with a 2-0 silk tie 5 cm above the anastomosis line, and the stomach specimens were transected near the cardia at 8 cm by a linear stapler (Ethicon Endo-Surgery Linear Cutter 75; Ethicon, Somerville, NJ), which was also used to close the gastric conduit to create a closed airtight system. Then the transected gastric lines were strengthened with continuous 2-0 silk sutures.

Techniques: Esophagus and gastric samples collected in an hour following slaughter were separated into 5 groups of 7. There were two main groups of surgical techniques: the CEAT and REAT.

Hand-Made Sutured Technique (HM): This technique is one of the CEAT. In this technique, the end-to-end single-layer anastomosis was performed with 2/0 prolene (nonabsorbable suture material- 2.0 polypropylene) interrupted sutures, between the distal esophagus and the part determined in the gastric fundus that was incised as equal as the esophagus diameter including the esophageal and gastric mucosa (Figure 3).



Figure 3. HM model

Circular Stapler Sutured Technique (CS): This technique is one of the CEAT. In this technique, the end-to-end anastomosis was performed with 21 mm circular stapler (21 mm single-use stapler, Covidien AG, Switzerland) between the distal esophagus and the part predetermined surgical site in the gastric fundus including the esophageal and gastric mucosa (Figure 4).



Figure 4. CS model

Reinforced Circular Stapler Sutured Technique (rCS): This technique is one of the CEAT. Anastomosis line was supported with 2/0 prolene Lambert sutures after anastomosis was performed as in the CS method (Figure 5).



Figure 5. rCS model

Modified Plus "+" Incision Technique (mP+IT): This technique is one of the REAT defined by Melek and Cobanoglu between esophageal ends in patients with esophageal atresia (Figure 6).

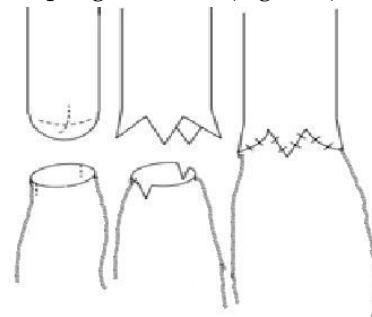


Figure 6. Illustration of mP+IT model.

In this study, we modified the plus "+" incision technique for better suitability in esophagogastric anastomoses. After forming "+" incision in the distal esophagus, same incision was also performed on the gastric wall. In order to increase anastomosis width and area as aimed, end-to-end anastomosis was performed with the protrusions in the recessed tissues with 2/0 prolene interrupted sutures including the esophageal and gastric mucosa (Figure 7).



Figure 7. mP+IT model

Modified Arrow-Bow Hand-Made Sutured Technique (mabHM): This technique is one of the REAT defined by Sharma and Wakhlu (1980) and Singh and Shun (2001). In their techniques the anastomosis is between the two esophageal ends in patients with esophageal atresia (Figures 8 and 9).

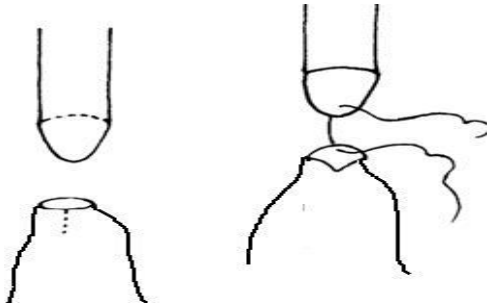


Figure 8. Sharma and Wakhlu's modification for esophago-gastric anastomosis

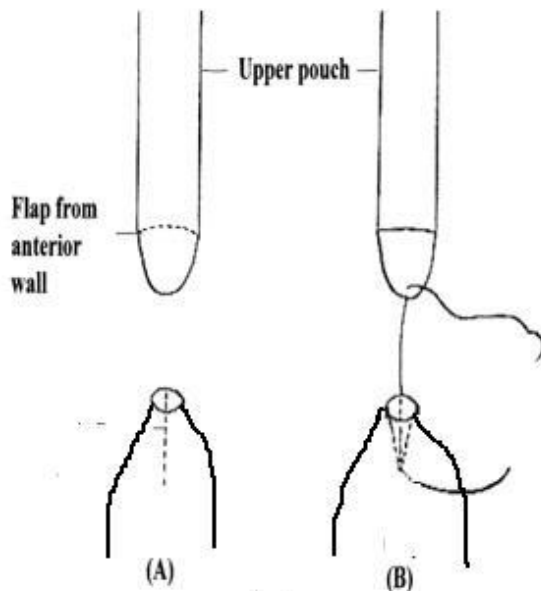


Figure 9. Singh and Shun's modification for esophago-gastric anastomosis

In this study, we combined these techniques with modifications for better suitability in esophagogastric anastomoses. There are two incisions: one on anterior hemi-circumference of upper pouch and another corresponding one vertical at the open posterior end of the lower pouch. Flap from the upper pouch is laid

into open V of lower pouch. In our modified technique, we incise the upper end of the esophagus to be anastomosed as a triangle, arrow or bow (Figure 10).



Figure 10. Modification model (Arrow-Bow) of Sharma and Singh

Then, we prepare the corresponding stomach incision, that is the lower end of the anastomosis, in the form of downward- V shaped. The triangle flap from esophagus is laid into the open downward- V shaped incised of part of the stomach. The anastomosis was performed with 2/0 prolene interrupted sutures including the esophageal and gastric mucosa.

Anastomotic Leakage Testing and Standardized

Procedures: Anastomotic leakage was tested as following; a blood pressure cuff catheter was placed in the end of the esophagus and inflated in each sample. The esophagus (5 cm above and 8 below the anastomosis) was tied with a 2-0 silk tie. BP (bursting pressure) or anastomosis leakage pressure was measured pneumatically using a sphygmomanometer by the method defined by El-Malt et al. (2001). The catheter was connected via a pressure transducer to the sphygmomanometer (Erka, D-83646 Bad Tolz, Perfect Aneroid, Germany). The esophagus was given a continuous air flow (1.5 mL/min) the pressure in the esophagus was monitored during pneuemoesophagus and BP (mm Hg) was recorded as the maximum pressure achieved during the pneuemoesophagus phase. The definition of bursting pressure is the air leakage in the anastomosis line. Concurrent with pressure monitoring, a syringe was used to progressively insulate the anastomosis until the discharge of air bubbles from the anastomosis when submerged in a water bath.

Statistical analysis: Normality was checked with Shapiro-Wilk test. Variance homogeneity was assessed with Levene test. All measurements were obtained by the same researcher under the same environmental conditions. The data were analyzed by One-Way ANOVA test and post-hoc Bonferroni test. A level of $p < 0.05$ was regarded as statistically significant.

RESULTS

Pressures at which anastomotic leakage is detected in 5 groups of a total of 35 samples. Since the data in each group were normally distributed, the numerical values were summarized as mean \pm standard deviation in Tables 1 and 2. The pressures corresponding to the incision techniques from the highest to the lowest were observed as follows: the

rCS (114.71±3.77 cm H₂O) > the CS (95.43±3.45 cm H₂O) > the HM (84.14±3.67cm H₂O) > the mabHM (79.71±2.87 cm H₂O) > the mP+IT (77.14±6.23 cm H₂O) (p < 0.001) (Table 1). Except the comparison of the HM versus the mabHM (p = 0.558), and the mP+IT versus the mabHM (p = 1.000), the other techniques differ statistically significantly from each other (Table 2). Figure 11 is a chart representing the perforation pressure.

Table 1. Morphometric data of the groups including the pressure of the esophageal samples

Groups	N	Mean (cm H ₂ O)	Std. Deviation	Minimum	Maximum
HM	7	84.14	3.67	79	90
CS	7	95.43	3.45	90	100
rCS	7	114.71	3.77	110	120
mP+IT	7	77.14	6.23	71	90
mabHM	7	79.71	2.87	76	84
p		<0.001			

Table 2. Comparison of different incision techniques

Parameter	Mean ± SD (cm H ₂ O)	Comparison	p
HM	84.14±3.67	CS	<0.001
		rCS	<0.001
		mP+IT	0.037
		mabHM	0.558
CS	95.43±3.45	rCS	<0.001
		mP+IT	<0.001
		mabHM	<0.001
rCS	114.71±3.77	mP+IT	<0.001
		mabHM	<0.001
mP+IT	77.14±6.23	mabHM	1.000
mabHM	79.71±2.87	-	-

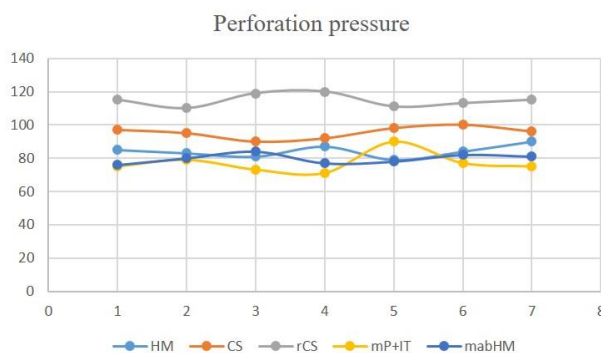


Figure 11. Perforation pressure according to techniques.

DISCUSSION

Despite the remarkable advances in medical sciences, mortality and morbidity of esophagus cancer surgeries are far beyond the desired levels. There are specialized centers achieving low mortality for certain cases; however, high morbidity still persists on the whole, since surgical site is not easily accessible and anatomically esophagus is in a critical position. Older age, comorbidities and admission at later stages are further potential morbidity increasing factors (Raman et al., 2017; Whooley et al., 2001; Verstegen et al.,

2019). Determination of right anastomosis site is crucial as determination of right reconstruction surgical technique following esophagectomy. Mediastinitis following an anastomotic leakage in intrathoracic anastomoses is usually mortal whereas cervical anastomotic leakages can get obliterated spontaneously with right medical management and thus have lower mortality. Along with this general advantage of cervical anastomoses, anastomotic strictures occur more frequently in cervical anastomoses, which can be listed as a disadvantage (Verstegen et al., 2019).

In this study we aimed to compare the reliabilities of the REAT and CEAT in an ex vivo animal model regarding esophageal strictures in cervical region, which can be regarded as the safer site. Wound healing in gastrointestinal anastomoses is a frequently studied subject in animal models (Koruda and Rolandelli, 1990; Hendriks and Mastboom, 1990). Administration of lower gastrointestinal anastomoses in laboratory animals, however, is rather challenging and so is to evaluate the healing quality of esophageal anastomoses in rodents (Levi et al., 1996; Urschel et al., 1997). There are limited number of studies involving ovines due to ethical and financial challenges. Thus, we believe ex vivo cadaveric studies would be helpful for esophagogastric anastomosis studies. Ovine model is chosen in this study for the morphological and dimensional similarity of the anastomosis sites to human esophagogastric anastomosis site.

Anastomotic leakage between esophagus and replaced tissue (i.e. stomach, colon or intestine tissue) is the most frequent complication following esophagectomy. Esophageal anastomotic leakage is the prominent cause of surgical sepsis and is held responsible for high mortality and morbidity. Esophageal anastomotic leakage rates, as high as 30%, are reported in the literature (Hsu et al., 1992). Etiology of the anastomotic leakage is multifactorial and related to patient dependent systemic factors and local wound site and associated factors. Lack of esophageal serosa, weak attachment of longitudinal muscles to sutures and limited accessibility of the surgical site are major adverse factors (Urschel et al., 1997).

The major long-term complication in esophageal replacement anastomoses is stricture formation along anastomosis line. Suture material, anastomosis tightness, ischemia, anastomotic leakage and presence of gastro-esophageal reflux are the major factors determining the severity of stricture (Singh and Shun, 2001; Spitz, 2007). Cui and Urschel (1999) have reported equal endurance to anastomotic pressure for interrupted simple suture and horizontal mattress suture in their animal study.

Various anastomosis techniques are developed and published in the literature in order to prevent short- and long-term complications. Factors such as ease of applicability, decrement in mortality and surgery duration determine the most suitable technique. In esophagus carcinoma surgery; both for cervical and

thoracic incisions, cervical esophagogastric anastomosis by newly introduced stapler took place of the traditional manual cervical anastomosis technique. It should be noted that the complications of the staple technique are laryngeal nerve injury, pneumothorax, perforation and especially anastomosis stricture (Chunwei et al., 2005).

Surgical site is more accessible with use of stapler and application is straight forward, thus it is expected to decrease the rate of anastomotic leakage (Peracchia et al., 1988). In comparison, when carried out by experienced surgeons, manual anastomosis can be as safe as use of stapler and has a financial advantage (Law et al., 1997). Although long-term cancer recurrence on the anastomosis line, early mortality and morbidity and survival rates are similar; the development of anastomosis stenosis is higher with use of stapler than other techniques. Shorter surgery duration is a clear advantage of use of stapler as reported in the literature (Urschel et al., 1997; Law et al., 1997). In the cervical anastomosis techniques explained by Law et al (1997), which are manual, single layered and continuous; anastomotic stenoses have more benign character. Although various methods have been proposed in esophageal anastomoses, end-to-end circular anastomosis is usually the preferred technique in practice (Ein and Ashcraft, 1981). Low rate of stricture formation is the most beneficial aspect of end-to-side anastomosis technique (Ein and Ashcraft, 1981). However, the general reliability of this technique is controversial since there is a risk of early and late recanalization of the ligated fistula in esophageal atresia surgery. A common undesirable feature of both end-to-end and end-to-side techniques is suture line being uniplanar. In the REAT described in our study, the suture line is in multiple planes and the risk of stenosis in the healing process is lower. The main purpose of these techniques is to achieve lower tension, wider area and suture line not being limited to a single plan (Sharma and Wakhlu, 1980; Gough, 1980). In the technique of Sharma and Wakhlu (1980), the aim is to have less tense posterior suture line. The first technique to eliminate the tension was defined by Sulamaa et al. (1951).

Singh and Shun (2001) reported that anastomosis stenosis would be minimized by having a large uniplanar anastomosis line. The anastomosis is made circumferentially larger; incidence of anastomotic stenosis is expected to reduce (perimeter of any circular anastomosis is reduced by a third during healing). The tension is mainly due to posterior sutures of the anastomosis; the anterior sutures can then be placed without stretching, since anterior regions are fully mobilized. The ascending anterior and posterior suture lines, due to their larger circumference, result in an obliquely created anastomosis, as in Figure 2, to reduce tension on each individual suture (Sharma and Wakhlu, 1980; Lindahl, 1987; De Carvalho et al., 1989).

Anastomosis stenosis is a common complication following esophageal surgery techniques. With this

method, we proposed an esophageal anastomosis technique within the REAT group with a large anastomosis area, which is resistant to pressure and can reduce the rate of stricture. The lower end of the esophagus was prepared as a triangle, arrow or bow ("arrow-bow"), and then the corresponding gastric incision which is the lower end of the anastomosis was prepared in the form of letter V. The triangular end of esophagus was inserted into an open V-shaped section of the stomach. This creates a large anastomosis and suture line, which is not limited to a single plane without disturbing tissue integrity. This simple and effective technique provides a long and multiplanar suture line. The REAT minimizes the risk of stenosis as side-by-side anastomosis (Sharma and Wakhlu, 1980; Melek and Cobanoglu, 2011).

If the suture line is confined to a smaller area, stenosis is more likely to occur during the healing process (Aumar et al., 2019). Minimization of stricture formation is aimed by a wide anastomosis area between esophagus and gastric tube, and a suture line not limited to a single plane. The described technique does not increase the distance between the pouch tips and does not cause anastomotic tension since it does not involve tissue loss on the blind pouch tips. Moreover, it minimizes stenosis occurrence as it provides a large multiplanar anastomosis line. One of the many factors that play a role in the pathogenesis of stricture formation is the type of anastomosis used. Transverse circular anastomosis seems to be the most commonly used technique (Aumar et al., 2019). Any type of circular anastomosis reduces healing duration in the wounded area. There is a greater risk of contraction in the healing area if suture line is uniplanar. Stenosis following transverse (uniplanar) circular anastomosis can be treated with oblique anastomosis, where the suture line is not confined to single plane. In addition, fibrosis following transverse circular anastomosis may cause stenosis in the anastomosis area. However, oblique anastomosis may form a wider anastomosis line due to non-circular fibrosis (Yurtçu et al., 2010; Melek and Cobanoglu, 2011).

In this study, we investigated the reliability of cervical esophagogastric anastomosis techniques for anastomotic leakage. Raman et al. (2017) reported that intraluminal pressure of 84 ± 38 cm H₂O is needed to disrupt an in vivo esophagogastric anastomosis. In our study, the durability of anastomoses using CEAT was found to be high and consistent with the literature. However, the use of REAT seems appropriate to prevent the development of stricture, which is the second most common complication of esophagogastric anastomoses. Considering the absence of wound healing process in ex vivo models, we propose that esophagogastric anastomosis techniques that reduce stricture formation incidence by increasing the anastomosis area can be reliable and easily applied.

Limitations: There are several important limitations of our study. Firstly, we used a sheep model that cannot be generalized to human patients. A sheep model may

not accurately reflect the pressure dynamics in humans. However, the similarity of esophageal histology and the use of the same materials minimized the variables. A similar study shows that in ex vivo and in vivo esophagectomy porcine models with anastomosis, there is no significant difference in the maximum tolerated pressure between ex vivo and in vivo esophagogastric anastomosis (Raman et al., 2017).

Conclusion

Our findings suggested that the durability of the CEAT was higher compared to the REAT. Therefore, the CEAT especially the rCS can be safely administered to prevent leakage. Considering that there is no difference between the two REAT as durability, we recommend the mabHM as the REAT method that keeps the anastomosis line wide. We think that the reliability of this method should be demonstrated in living tissues.

Conflict of interest

There are no conflict of interest.

Ethics Approval

The present study with the recordings of the participants has been approved by Experimental Animal Ethical Committee belonging to Van YYU (approval number: 2022/01-09).

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