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Should oesophagectomy be performed with cervical or intrathoracic anastomosis?

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Abstract

A best evidence topic was written according to a structured protocol. The question addressed was: In [patients undergoing oesophagectomy for oesophageal cancer] is a [cervical anastomosis or intrathoracic anastomosis] superior in terms of [post-operative outcomes]. In total, 47 papers were found suitable using the reported search, and nine of these represented the best evidence to answer the clinical question. The authors, date, journal, study type, population, main outcome measures and results are tabulated. We conclude that there is no convincing evidence that cervical anastomosis is superior to intrathoracic anastomosis with respect to post-operative outcomes. Only one prospective study showed significantly increased risk of anastomotic leak with cervical anastomosis, but this study was significantly limited due to patient selection and variations in surgical approach and technique. Cervical anastomosis was also shown to increase pharyngeal reflux on pH monitoring compared with intrathoracic anastomosis, but this did not influence symptoms or development of subsequent anastomotic complications. One randomized study showed intrathoracic anastomosis significantly increased risk of respiratory complications, but in this study patient treatment was variable and study design was limited. Intrathoracic anastomosis was also shown to correlate with anastomotic stricture formation and this was attributed to increased anastomotic stapling in this patient group compared with cervical anastomosis. Post-operative pain as measured by grouped symptom scales significantly increased with intrathoracic anastomosis compared with cervical anastomosis. This did not correlate with development of other cardiorespiratory complications and the difference between the two groups resolved within 24 months. Overall, there is currently insufficient evidence to show a significant difference between cervical and intrathoracic anastomosis with respect to post-operative complications and hospital mortality. The wide variety in methodology and outcomes reinforce the need for further randomized trials to more accurately establish significant differences in outcomes.

Keywords: Oesophagectomy • Anastomosis • Oesophagus • Cancer • Obesity • Complications

INTRODUCTION

A best evidence topic was constructed according to a structured protocol. The protocol is fully described in *ICVTS* [1].

THREE-PART QUESTION

In [patients undergoing oesophagectomy for oesophageal cancer] is a [cervical anastomosis or intrathoracic anastomosis] superior in terms of [post-operative outcomes].

CLINICAL SCENARIO

A patient is referred to your clinic with a T3N0M0 tumour of the distal oesophagus, which requires you to perform an oesophagectomy. A visiting professor from China cites the propensity of cervical anastomoses to leak and asks whether or not you would consider performing an intrathoracic anastomosis. You decide to search the literature to determine whether there are any significant differences in post-operative outcomes between cervical and intrathoracic anastomosis.

SEARCH STRATEGY

A Medline search from January 1950 to December 2011 was performed using OVIDSP interface (expesophagectomy/OR oesophagectomy.mp OR esophagectomy.mp) AND (expintrathoracicanastomosis/OR intrathoracic.mp). References were also retrieved from key articles and reviewed.

SEARCH OUTCOME

Literature search identified 47 articles. These were reviewed and nine articles were identified that provided the best answer to the question. These articles are presented in Table 1.

Chasseray *et al.* [2] conducted a prospective randomized trial comparing cervical anastomoses created using the three-stage ($n = 35$) or transhiatal ($n = 8$) approach, and intrathoracic

Table 1: Best evidence papers

Author, date, journal and country Study type (level of evidence)	Patient group	Outcomes	Key results	Comments
Chasseray *et al.* (1989), Surg Gynaecol Obstet, France [2] Prospective randomized trial (level 2)	Prospective randomized study (n = 123) comparing cervical (n = 43) and intrathoracic (n = 49) anastomoses following oesophagectomy for squamous cell carcinoma In total 31 patients excluded because of noncompliance with randomization Cervical anastomosis group treated with three-stage approach (n = 35) or transhiatal approach (n = 8). Intrathoracic anastomosis performed with two-stage approach (n = 49) The groups were comparable with respect to smoking, alcohol abuse, pre-existing pulmonary disease, serum albumin concentration and weight loss		Cervical vs intrathoracic	Cervical anastomosis associated with significantly increased risk of anastomotic leak Authors attribute increased incidence of anastomotic leak in cervical anastomosis to excessive mobilization of oesophagus and increased tension on conduit promoting ischaemia at anastomotic site No significant difference between groups with respect to cardiorespiratory complications, post-operative mortality or length of hospital stay Limitations: Methodology not standardized with respect to approach for cervical anastomosis, positioning of gastric tubes and pyloroplasty procedure. Operative technique may have promoted selection bias
		Length of operation (h) [median (range)]	7 (4.5–10.0) vs 7 (3.5–10)	
		Transfusion requirements (ml) [median (range)]	1250 (0–8500) vs 1250 (0–5000)	
		Length of macroscopically normal oesophagus above tumour (cm) [median (range)]	4 (0.2–9.0) vs 1.5 (0.2–9.5), $P < 0.05$	
		Length of hospital stay (days) [median (range)]	19.5 (3–71) vs 18 (2–122)	
		Median survival (months) [median (range)]	23 (1–52) vs 20 (1–48)	
		30-day mortality rate (%)	4 (9.3%) vs 7 (14.2), P = NS	
		Fistula formation (%)	11 (26%) vs 2 (4%), $P < 0.02$	
		Stricture formation (%)	23 (53%) vs 14 (29%), P = NS	
		Respiratory complications (%)	7 (16%) vs 15 (29%), P = NS	
		Chylothorax	2 (5%) vs 4 (8%), P = NS	
		Other (cardiac failure, myocardial infarction, septicaemia, acute cholecystitis, pulmonary embolus)	6 (14%) vs 6 (12%), P = NS	
Okuyama *et al.* (2007), Surg Today, Japan [3] Prospective randomized trial (level 2)	Prospective randomized study comparing hand-sewn cervical anastomosis (n = 18) and stapled intrathoracic (n = 14) anastomosis following oesophagectomy for middle or lower thoracic oesophageal cancer Cervical anastomosis performed through three-stage approach and intrathoracic anastomosis performed with two-stage approach All patients underwent routine post-operative bronchoscopy and water-soluble contrast medium. Patients with metastases excluded from study		Cervical vs intrathoracic	No significant difference between the two groups with respect to the rate of anastomotic leak, stricture formation, recurrent laryngeal nerve injury (RLN) or symptoms 6 months after surgery Increased incidence of RLN injury and greater proximal resection margins with cervical anastomosis did not impact on post-operative symptoms and survival Limitations: small sample size, variations in anastomotic approach and technique
		Operating time (min) (mean ± SD)	547 ± 95 vs 593 ± 57, P = NS	
		Blood loss (ml) (mean ± SD)	537 ± 281 vs 702 ± 252, P = NS	
		Number of dissected lymph nodes (mean ± SD)	53 ± 21 vs 48 ± 17, P = NS	
		Anastomotic leaks	3 (16.7%) vs 1 (7.1%), P = NS	
		Recurrent laryngeal nerve palsy	8 (38.8%) vs 1 (7.1%), $P < 0.05$	
		Pneumonia	2 (11.1%) vs 5 (35.7%), P = NS	
		Hospital mortality	0 vs 0, P = NS	
		Diameter of anastomosis (mm) (mean ± SD)	14 ± 6 vs 15 ± 5, P = NS	
		Anastomotic stricture	0 vs 2 (14.2%), P = NS	
Ribet *et al.* (1992), J Thoracic Cardiovasc Surg, France [4]	Prospective randomized trial comparing clinical and pathological outcomes in oesophagectomy with cervical (n = 30) and intrathoracic		Cervical vs intrathoracic	Respiratory complications significantly more common in cervical than intrathoracic anastomosis. Authors comment that this may be secondary to
		Mean operation time (min)	405 vs 375	
		Mean hospital stay (days)	24.2 vs 16.6	

Continued

Table 1: Continued

Author, date, journal and country Study type (level of evidence)	Patient group	Outcomes	Key results	Comments
Prospective randomized trial (level 2)	anastomosis ($n = 28$) Tumours staged pre-operatively (UICC 1987): Stage I, $n = 2$; Stage II, $n = 19$; Stage III, $n = 9$; Stage IV, $n = 30$; and were almost equally distributed amongst the two groups Intrathoracic anastomosis performed with the two-stage approach and cervical anastomosis with the three-stage approach. Hand-sutured two-layer anastomosis in all cases Radiotherapy started 5–6 weeks post-operatively (cervical, $n = 23$; intrathoracic $n = 27$)	Brochopulmonary infection Vocal cord palsy—Temp Vocal cord palsy—Perm Median survival Mean supratumor margin (cm) (shrunken tissue) Mean tumour length (cm)	21 (70%) vs 11 (29.3%), $P = 0.01$ 3 (10%) vs 0 (0%), P = NS 3 (10%) vs 1 (3.6%), P = NS 9 months vs 12 months, P = NS 5.01 vs 2.83 5.08 vs 5.3	more extensive dissection and vocal cord damage in the cervical group No significant difference between groups with respect to risk of anastomotic leak or mortality Cervical anastomosis improved resection of undetected supratumour lesions and lymph node harvesting. This did not correlate with any difference in long-term survival between groups Limitations: patients not matched for neoadjuvant therapy, limited data on other post-operative complications and large variation in extra-oesophageal resections at time of surgery
Walther *et al.* (2003), Ann Surg, Sweden [5] Prospective randomized study (level 2)	Prospective randomized trial comparing hand-sewn cervical ($n = 41$) with stapled intrathoracic anastomoses ($n = 42$) To evaluate selection bias, non-randomized patients undergoing oesophagectomy over same time period ($n = 29$) were followed and results were compared with those randomized ($n = 83$) Measurements of anastomotic level and diameter were assessed with an endoscope and balloon catheter 3, 6, and 12 months after surgery	Operating time [median (range)] Blood loss (ml) [median (range)] Anastomotic stricture formation (%) Chest drainage (days) [median (range)] Anastomotic leak (%) Airway complication (%) Cardiac complication (%) Vocal cord palsy (%) Reoperation (%) Hospital stay (days) [median (range)] Uncomplicated (%) Hospital mortality (%)	Cervical vs intrathoracic vs non-randomised 555 (382–850) vs 553 (290–750) vs 615 (459–886), $P = 0.0018$ 950 (250–3000) vs 950 (200–4000) vs 1300 (400–3000), P = NS 8/41 (19.5) vs 12/42 (28.6%), $P = 0/443$ 7 (5–65) vs 7 (0–55) vs 7 (4–71), P = NS 1 (2.4) vs 0 (0) vs 1 (3.4), P = NS 2 (4.9) vs 4 (9.5) vs 2 (6.9), P = NS 4 (9.8) vs 4 (9.5)vs 0 (0), P = NS 1 (2.4) vs 0 (0) vs 2 (6.9), P = NS 3 (7.3) vs 2 (4.8) vs 3 (10.3), P = NS 14 (8–68) vs 14 (0–83) vs 15 (10–75), P = NS 28 (68) vs 29 (69) vs 19 (66), P = NS 1 (2.4) vs 1 (2.4) vs 0 (0), P = NS	No significant difference between the groups with respect to cardiorespiratory complications, anastomotic leak or mortality High incidence of stricture formation in intrathoracic anastomosis attributed to increased stapling of anastomosis in this group. No difference in anastomotic diameter between groups at 3, 6 and 12 months following surgery Only significant factor affecting the survival was disease stage Limitations: variation in the use of stapled and sutured anastomosis at each site. Low incidence of anastomotic leak making correlation to site and severity difficult
Lam *et al.* (1992), J Thoracic Cardiovasc Surg, Hong Kong [6]	Prospective non-randomised study comparing cervical ($n = 294$) and intrathoracic ($n = 117$) anastomosis	Anastomotic leak: hand-sewn	Cervical vs intrathoracic 4/75 (5.3%) vs 5/106 (4.7%)	No significant difference between the groups with respect to anastomotic leak rate or mortality

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Table 1: Continued

Author, date, journal and country Study type (level of evidence)	Patient group	Outcomes	Key results	Comments
Prospective non-randomized study (level 3)	post-oesophagectomy Patients grouped according to the location of tumour in relation to aortic arch and preoperative respiratory function. Groups comparable except palliative resections more frequent in cervical group Anastomosis formed between residual proximal area of oesophagus and stomach, jejunum or colon	Anastomotic leak: stapled Anastomotic leak: whole stomach substitution Anastomotic leak: distal stomach substitution Anastomotic leak: jejunum substitution Anastomotic leak: colon substitution Anastomotic stricture: hand-sewn Anastomotic stricture: stapled	7/219 (3.2%) vs 0/11 (0.0%) 8/240 (3.3%) vs 4/91 (4.4%) 2/49 (4.1%) vs 0/8 (0.0%) 0/3 (0.0%) vs 0/0 Half (50%) vs 1/18 (5.5%) 6/62 (9.7%) vs 6/78 (7.7%) 36/158 (22.8%) vs 2/11 (18.2%)	Increased incidence of benign stricture formation with intrathoracic anastomosis attributed to increased use of stapling device in this group Limitations: study not randomized, variations in approaches for cervical anastomosis and use of substitutes and limited data on other post-operative complications
Johansson *et al.* (1999), J Thoracic Cardiovasc Surg, Sweden [7] Prospective non-randomized study (level 3)	Prospective study comparing pharyngeal reflux after gastric pull-up oesophagectomy between cervical ($n = 20$) and intrathoracic anastomoses ($n = 27$) Intrathoracic anastomoses formed using the two-stage approach and intrathoracic anastomoses created using the three-stage approach Placement of pH probes proximal and distal to oesophageal remnant for 24 h. Acid exposure in the gastric pull expressed as total percentage of time pH <4 during a 24-h period. This was also measured at 3, 6 and 12 months post-operatively	pH levels: 3 vs 6 vs 12 months [mean (95%CI)] Anastomotic height from incisors (cm) [mean (95% CI)] Dilated for anastomotic stricture at 3 months Oesophagitis after 3 months	In general: 46% (29–63%: $n = 14$) vs 32% (14–50%: $n = 13$) vs 31% (9–53%: $n = 11$) 21.2 (19.4–21.3) vs 24.8 (23.8–25.3) 3 (15%) vs 5 (18.5%) 2 (10%) vs 7 (25.9%)	Acid exposure to the pharynx and oesophageal remnant increased during the first year with cervical anastomosis but not with intrathoracic anastomosis. This did not increase oesophagitis or subsequent stricture formation Authors attributed increased reflux with cervical anastomosis to extensive neck dissection impairing swallowing Limitations: very limited data on other post-operative complications. Comorbidities affecting reflux not accounted for and significant variation in the formation of gastric tubes
Nguyen *et al.* (2008), Ann Surg, USA [8] Prospective non-randomized study (level 3)	Prospective study evaluating the outcomes of 104 minimally invasive oesophagectomy (MIE) procedures for the treatment of benign and malignant disease Indications for surgery included oesophageal cancer ($n = 80$), Barrett oesophagus ($n = 8$), gastrointestinal stromal tumour ($n = 3$) and gastric cardia cancer ($n = 7$) Conversion rate to laparotomy 3/104 (2.9%) Overall mortality 2/104 (1.9%)	Operative time (min) Estimated blood loss (ml) Length of hospital stay (days) Length of ICU stay (days) Major complications (%) Anastomotic stricture (%) Anastmotic leaks (%)	MIE with cervical vs MIE with intrathoracic anastomosis 333 ± 75 vs 249 ± 72 263 ± 179 vs 146 ± 117 12.1 ± 12.2 vs 9.7 ± 8.1 4.8 ± 9.1 vs 2.9 ± 4.4 12.8 vs 11.8 23.4 vs 27.5 6.4 × 9.8	No significant difference between MIE with cervical and intrathoracic anastomosis with respect to post-operative outcomes or mortality Overall, the authors report MIE associated with low conversion rate, acceptable morbidity and low mortality Limitations: varying approaches for anastomotic formation, data includes surgery for non-malignant disease and patients not matched for neo-adjuvant therapy
Blewett *et al.* (2001), Ann Thoracic Cardiovasc Surg, Canada [9]	Retrospective cohort study comparing histological and clinical outcomes between cervical ($n = 19$) and intrathoracic anastomoses ($n = 55$)	Anastomotic leaks Mortality due to leak	Cervical vs intrathoracic anastomosis 1/19 (5%) vs 9/55 (16%), $P = 0.21$ 0/19 (0%) vs 1/55 (2%),	Anastomotic site not related to risk of anastomotic leak or post-operative mortality Comment in conclusion suggests that anastomotic wound healing

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Table 1: Continued

Author, date, journal and country Study type (level of evidence)	Patient group	Outcomes	Key results	Comments
Retrospective cohort study (level 3)	Cervical anastomoses formed through three-stage ($n = 16$) or transhiatal approach ($n = 3$). All intrathoracic anastomoses formed using two-stage approach No significant difference between the two groups with respect to age, gender, histology, stage, adjuvant therapy and overall survival		$P = 0.90$	is multifactorial. Surgical experience, technique and adequacy of gastric conduit vascularity highlighted as critical determinants of anastomotic wound healing Limitations: retrospective study with low incidence of anastomotic leaks, lack of data on other post-operative complications and varying approaches for cervical anastomosis
		Operative mortality (all cases)	0/19 (0%) vs 3/55 (5%), $P = 0.40$	
		Medial survival (months)	13.9 vs 13.5, $P = 0.55$	
		Positive resection margins	2/19 (11%) vs 9/55 (16%), $P = 0.42$	
Egberts *et al.* (2008), Ann Surg Oncol, Germany [10] Prospective longitudinal study type (level 3)	Prospective longitudinal study ($n = 105$) comparing QOL following cervical ($n = 33$) and intrathoracic anastomosis ($n = 72$) post-oesophagectomy QOL assessed using cancer-specific questionnaire (EORTC QLQ-C30) with an oesophagus-specific module that assessed functional, symptomatic and global health of patients QOL assessed preoperatively, at discharge, 3, 6, 12 and 24 months following surgery		Cervical vs intrathoracic	No significant difference between cervical and intrathoracic anastomosis with respect to cardiorespiratory or wound complications, anastomotic leak, or hospital mortality Post-operative pain significantly greater following intrathoracic anastomosis than cervical anastomosis. This was attributed to additional thoracotomy procedure in intrathoracic group. Difference between groups resolved within 24 months Limitations: missing patient data due to death, disease progression and poor compliance. Limited data on the site of pain and analgesia used. Poor standardization of approach for cervical anastomosis. Patients not matched for neo-adjuvant therapy
		Cumulative morbidity	23 (69.7%) vs 39 (54.2%), $P = 0.133$	
		Anastomotic leakage	11 (33.3%) vs 13 (18.1%), $P = 0.083$	
		Peritonitis	0 (0%) vs 1 (1.4%), $P = 0.496$	
		Oesophagotracheal fistula	0 (0%) vs 3 (4.2%), $P = 0.234$	
		Haemorrhage	2 (6.1%) vs 2 (2.8%), $P = 0.415$	
		Damage of the recurrent laryngeal nerve	1 (3.0%) vs 1 (1.4%), $P = 0.568$	
		Wound complication	2 (6.1%) vs 3 (4.2%), $P = 0.672$	
		Cardiac complications	4 (12.1%) vs 14 (19.4%), $P = 0.355$	
		Pneumonia	11 (33.3%) vs 20 (27.8%), $P = 0.562$	
		Renal failure	1 (3.0%) vs 3 (4.2%), $P = 0.778$	
		30-day mortality	1 (3.0%) vs 2 (2.8%), $P = 0.943$	
		Hospital mortality	2 (6.1%) vs 5 (6.9%), $P = 0.866$	

anastomoses performed through the two-stage approach ($n = 49$). Cervical anastomosis significantly increased risk of anastomotic leak, but there were no significant differences in terms of cardiorespiratory complications, length of hospital stay or 30-day mortality between the two groups. In this study, the surgical approach for the cervical anastomosis, gastric tube formation and pyloroplasty were not standardized.

Okuyama *et al.* [3] conducted a prospective randomized study, which showed no significant difference between cervical hand-sewn anastomosis ($n = 18$) and stapled intrathoracic anastomosis ($n = 14$) with respect to the rates of anastomotic leak, stricture formation, recurrent laryngeal nerve palsy or post-operative symptoms. Patients with previous gastric surgery or preoperative chemoradiotherpy were excluded from the study. In this study, the patient population was small with operative approach and anastomotic technique varying between the two groups.

Ribet *et al.* [4] conducted a prospective randomized study comparing three-stage cervical anastomoses ($n = 30$) with two-stage intrathoracic anastomoses ($n = 28$). Cervical anastomosis significantly increased the risk of respiratory complications, but this did not correlate with incidence of anastomotic leak or post-operative mortality. In this study, patients were not matched for neoadjuvant therapy and operative technique varied considerably with some patients having hepatic and pulmonary wedge resections at the time of oesophagectomy.

Walther *et al.* [5] conducted a prospective randomized study showing no significant difference between manually sutured

cervical anastomosis ($n = 41$) and mechanically stapled intrathoracic anastomosis ($n = 42$) with respect to risk of anastomotic leak, cardiorespiratory complications, reoperation rates or hospital mortality. Increased stricture formation in the intrathoracic group was attributed to wound retraction associated with the stapling device. In this study, cervical and intrathoracic anastomoses were created using different techniques and low incidence of anastomotic leak made correlation to site and severity difficult.

Lam *et al.* [6] conducted a prospective non-randomized trial, which grouped patients according to anatomical location of the tumour and preoperative respiratory function. This study showed no significant difference between cervical ($n = 117$) and intrathoracic anastomosis ($n = 294$) with respect to anastomotic leak rates or post-operative mortality. Increased incidence of stricture formation in the intrathoracic group was attributed to a greater use of the stapling device in this group compared with the cervical group. In this study, cervical anastomoses were constructed using different surgical approaches and use of colonic and jejunal substitutes was not standardized.

Johansson *et al.* [7] conducted a prospective study comparing pharyngeal reflux between manually sutured cervical anastomosis ($n = 20$) and stapled intrathoracic anastomosis ($n = 27$) post-oesophagectomy. There was increased acid reflux during the first year of life with cervical anastomosis, but this did not correlate with any difference in symptoms or stricture formation between the two groups. This study did not account for related comorbidities that influence acid reflux and presented very limited data on other post-operative complications.

Nguyen *et al.* [8] conducted a prospective study into minimally invasive oesophagectomy and showed no significant difference between cervical and intrathoracic anastomosis with respect to anastomotic leak rate, structure formation, length of hospital stay or mortality. Surgical approaches included thoracoscopic/laparoscopic oesophagectomy with a cervical anastomosis ($n = 47$), minimally invasive Ivor–Lewis oesophagectomy ($n = 51$), laparoscopic hand-assisted blunt transhiatal oesophagectomy ($n = 5$) and laparoscopic proximal gastrectomy ($n = 1$). Results included data for non-malignant surgery and variations in approach for anastomoses.

Blewett *et al.* [9] conducted a retrospective cohort study comparing three-stage ($n = 16$) and transhiatal ($n = 3$) cervical anastomoses with two-stage intrathoracic anastomoses ($n = 55$). The two groups were similar with respect to age, gender, histology, stage and adjuvant therapy. There were no significant differences between the two groups with respect to anastomotic leak rate or post-operative mortality. This was a retrospective study with a significant preponderance for intrathoracic anastomoses and very limited data on post-operative morbidity.

Egberts *et al.* [10] conducted a prospective study ($n = 105$) investigating the impact of anastomotic site on quality of life (QOL) following oesophagectomy. Intrathoracic anastomosis ($n = 72$) was associated with significantly increased pain at discharge compared with cervical anastomosis ($n = 33$), but this difference resolved by 24 months. There was no significant difference between the two groups in any of the other QOL categories or overall post-operative mortality. In this study, significant data was missing due to patient deaths and disease progression, which may have bias the results and overestimated the positive effects of any treatment.

CLINICAL BOTTOM LINE

Studies comparing cervical and intrathoracic anastomosis following oesophageal resection are small in size, poorly standardized with respect to surgical approach and anastomotic technique, and include patients who are poorly matched for neo-adjuvant therapy. Overall, there is currently insufficient evidence to show a significant difference between cervical and intrathoracic anastomosis with respect to post-operative complications and hospital mortality. Post-operative complications are unlikely to be independently related to the site of anastomosis and other factors such as surgical experience, technique and comorbidities affecting gastric conduit vascularity may be critical determinants of outcomes. The wide variety in methodology and outcomes reinforce the need for further randomized trials to more accurately establish any possible differences in outcomes.

Conflict of interest: none declared.

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eComment. Oesophagectomy: Could the anastomotic location be an independent prognostic factor?

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