Does preoperative ischaemic conditioning with gastric vessel ligation reduce anastomotic leaks in oesophagectomy?

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Abstract

A best evidence topic in thoracic surgery was written according to a structured protocol. The question addressed was ‘does preoperative ischaemic conditioning with gastric vessel ligation prior to oesophagectomy reduce anastomotic leaks?’ Altogether more than 70 papers were found using the reported search, of which 7 represented the best evidence to answer the clinical question. The authors, journal, date and country of publication, patient group studied, study type, relevant outcomes and results of these papers are tabulated. Five papers represent level III evidence while the remainder two are considered level IV. None of the seven papers reports statistically significant P-values, although one non-randomized controlled cohort study approaches statistical significance at $P = 0.07$. Three of the level III papers suggest that preoperative ischaemic conditioning prior to oesophagectomy may be associated with a lower anastomotic leak severity; being managed endoscopically rather than with a surgical intervention, however, again, none reached statistical significance. Preoperative ischaemic conditioning prior to oesophagectomy may not be associated with an increase in blood loss or length of time at definitive operation, reported by one of the seven studies. One paper reports that the timing of preoperative ischaemic conditioning may be associated with a better anastomotic leak profile if carried out 2 weeks previously as opposed to 5 days ahead of definitive surgery, although not statistically significant. The most consistent method in the literature reported ligation or division of the left gastric artery reported in six of the seven papers. We, therefore, cannot conclude that preoperative ischaemic conditioning with gastric vessel ligation prior to oesophagectomy is associated with reduced anastomotic leaks.

Keywords: Review • Oesophagectomy • Ischaemic conditioning • Anastomosis leak • Complication

INTRODUCTION

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

THREE-PART QUESTION

In [patients undergoing oesophagectomy for cancer] is [preoperative ischaemic conditioning] beneficial in reducing [anastomotic leaks]?

CLINICAL SCENARIO

You are a registrar doing a diagnostic staging laparoscopy on a gentleman who is booked to come next week for an oesophagectomy for cancer. Your consultant is in theatre, supervising and observing. You ask whether he prefers you to ligate or divide the left gastric artery ahead of next week’s planned oesophagectomy for preoperative ischaemic conditioning in order to improve the blood supply to the potential anastomotic site? He responds ‘neither: there is no proven benefit for ischaemic conditioning on anastomotic leak rates and by mobilizing the artery it may cause unwanted adhesions’. You resolve to check the literature yourself.

SEARCH STRATEGY


SEARCH OUTCOME

Seventy papers were found as a result of the reported search. From these, seven papers were identified as relevant to the clinical question; specifically those papers written in English and addressing anastomotic leak incidence or rates in humans only were considered. Papers that addressed animal models or those related to mucosal saturations or increases in perfusion to the gastric conduit as their only outcome measure were excluded for the purposes of this paper. We identify seven papers that provided the
Table 1:  Best evidence papers

<table>
<thead>
<tr>
<th>Author, date, journal and country</th>
<th>Patient group</th>
<th>Outcomes</th>
<th>Key results</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ney and Kumar (2010), Ann Thorac.</td>
<td>Total 77 consecutive patients (thoracoscopic esophageal mobilization, laparoscopic gastric tube formation and cervical anastomosis)</td>
<td>Anastomotic leak managed conservatively</td>
<td>1/22: ischaemic conditioning 4/55: control</td>
<td>Overall, there was less gastric conduit morbidity in the ischemic conditioning group with left gastric artery ligation, but difference did not reach statistical significance 2/22 vs 11/55 (P = 0.211)</td>
</tr>
<tr>
<td>Yong et al. (2013), J Cardiothorac Surg, USA</td>
<td>55 patients did not undergo ischemic conditioning (control group)</td>
<td>Tip necrosis requiring resection and re-anastomosis</td>
<td>0/22: ischemic conditioning 5/55: control</td>
<td>No significant difference in operative time in the ligation group 407 min; control 425 min</td>
</tr>
<tr>
<td>Yetasook et al. (2013), Dis Esophagus, USA</td>
<td>22 patients ischemic conditioning 2 weeks previously with ligation of the left gastric artery</td>
<td>Conduit necrosis needing resection and esophagectomy</td>
<td>1/22: ischemic conditioning 2/55: control</td>
<td>No significant difference in operative blood loss in ligation or control group of 500 ml</td>
</tr>
<tr>
<td>Hölscher et al. (2007), Ann Surg, Germany</td>
<td>Retrospective review of 24 consecutive patients with esophageal cancer undergoing laparoscopic ischemic conditioning (ligation of left and short gastric arteries), 4–10 days prior to formal resection</td>
<td>Conversion to open Reoperations (e.g. control of haemorrhage from staple line, chylothorax)</td>
<td>3/23: anastomotic leak 6/23: delayed gastric emptying 2/23: anastomotic stricture</td>
<td>Laparoscopic ischemic conditioning was shown to be technically feasible and safe with a 13% anastomotic leak rate</td>
</tr>
<tr>
<td>Berrisford et al. (2009), Eur J Cardiothorac Surg, UK</td>
<td>83 patients (44 adenocarcinoma, 39 squamous cell carcinoma). All patients underwent laparoscopic division of left gastric artery with Ligasure. A delay of 4.3 (mean value) days later a right thoraco-abdominal oesophagectomy with gastric conduit and high intrathoracic oesophagogastrostomy anastomosis was performed</td>
<td></td>
<td>5/83 patients developed small anastomotic leakages with minor clinical symptoms. All gastric conduits were found to be well vascularized. All anastomotic leaks healed with endoscopic self-expanding metal stent (Boston Scientific) insertion</td>
<td>Ischemic conditioning followed by reconstruction depend upon the onset of the effects of devascularization and the development of intra-abdominal adhesions of the gastric conduit. With increasing time from conditioning, it was noted that gastric conduit pull-up was more technically difficult</td>
</tr>
<tr>
<td>Veeramooto et al. (2010), Surg Endosc, UK</td>
<td>23/24: formal Ivor-Lewis oesophagectomy</td>
<td></td>
<td>26/83 patients had minor complications (tachyarrhythmia, pneumonia, pleural effusion, transient recurrent laryngeal nerve palsy, delayed gastric emptying, infection)</td>
<td>Ischemic conditioning may improve anastomotic healing</td>
</tr>
<tr>
<td>Ney and Kumar (2010), Ann Thorac.</td>
<td>97 patients underwent MIO</td>
<td>ICF graded I, II and III</td>
<td>No ischemic conditioning: ICF 11/55 Grade I = 4, II = 5, III = 2</td>
<td>The 5-day ischemic conditioning cohort was terminated early because of concern with significant ICF</td>
</tr>
<tr>
<td>Yong et al. (2013), J Cardiothorac Surg, USA</td>
<td>35/97 patients had laparoscopic ischemic conditioning at 2 weeks prior to MIO</td>
<td>I—simple anastomotic leak II—conduit tip necrosis (requiring refashion of anastomosis)</td>
<td>Two-week ischemic conditioning: ICF 2/35 Grade I = 1, II = 0, III = 1</td>
<td>Anastomotic leak rates were lower if ischemic conditioning was carried out 2 weeks prior to oesophagectomy, approaching statistical significance P = 0.07</td>
</tr>
<tr>
<td>Yetasook et al. (2013), Dis Esophagus, USA</td>
<td>7/97 patients had laparoscopic ischemic conditioning 5 days prior to MIO</td>
<td>III—global necrosis needing delayed reconstruction</td>
<td>7/7 (4 recognized in MIO). Therefore, of 3 remaining Grade I = 2, II = 1 and III = 0</td>
<td></td>
</tr>
<tr>
<td>Hölscher et al. (2007), Ann Surg, Germany</td>
<td>22 patients is ischemic conditioning</td>
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Continued
best evidence to answer the question. These are presented in Table 1.

### RESULTS

Berrisford et al. [2] included 77 consecutive patients who underwent minimally invasive, thoracoscopic oesophagectomy with gastric conduit formation and cervical anastomosis. Of these, 22 underwent preoperative ischaemic conditioning (left gastric artery ligation) of the conduit 15.5 days (median) earlier by staging laparoscopy. There was no difference in terms of total blood loss or operative time at minimally invasive oesophagectomy. However, overall, there was a lower anastomotic leak rate in the pre-emptive ischaemic conditioning group, but this did not reach statistical significance: 2 of 22 in the ischaemic conditioning group and 11 of 55 in the non-conditioning group ($P = 0.211$).

Yetasook et al. [3] conducted a retrospective observational study of 24 consecutive patients who underwent ischaemic conditioning with ligation of left and short gastric arteries, 4–10 days prior to formal oesophagectomy. They reported a 13% overall leak rate and deemed laparoscopic ischaemic conditioning technically feasible and safe.

Holscher et al. [4] reported a prospective cohort of 83 consecutive patients undergoing left gastric artery division with Ligasure 4.3 days (mean) who all then went on to an oesophagectomy for cancer with right thoraco-abdominal, gastric conduit formation and intrathoracic oesophagogastronomy anastomosis. Five of 83 developed small anastomotic leakages with minor clinical symptoms. All gastric conduits were found to be well vascularized at endoscopy and all anastomotic leaks healed with endoscopic self-expanding metal stent (Boston Scientific) insertion.

Veeramooto et al. [5] included 97 consecutive patients undergoing minimally invasive oesophagectomy as part of a retrospective study. Of these 97 patients, 35 and 7 underwent laparoscopic...
ischaemic conditioning 2 weeks and 5 days prior to oesophagectomy, respectively, either with clip ligation or with division of left gastric artery. Fifty-five of 97 did not undergo ischaemic conditioning. Ischaemic conditioning 2 weeks prior to definitive operation was associated with lower overall leak rates (5.7%) than in the cohort with no ischaemic conditioning (20%); this tended towards statistical significance, P = 0.07. They also showed that leak rates were less likely if the ischaemic conditioning occurred at 2 weeks (5.7%) prior to surgery compared with 5 days (100%) prior to surgery, P < 0.0001.

Schröder et al. [6] retrospectively analysed over a 12-year period 419 patients undergoing Ivor–Lewis operations with or without preoperative ischaemic conditioning by laparoscopic mobilization of the stomach 4–5 days previously. Lower rates of anastomotic leak were observed in the ischaemic conditioning group: 7.6% against 9.4%, P = 0.503. Furthermore, the majority of leaks in the ischaemic conditioning group were late leaks (occurring >10 days post-operation) and the majority of anastomotic leaks in the non-conditioning group were early (<10 days postoperative), P = 0.229.

Nguyen et al. [7] reported outcomes in 152 patients. Eighty-one of 152 patients were subjected to ischaemic conditioning for anywhere between 2 and 75 days (mean 6.0 ± 5.4) before oesophagectomy and with division of left gastric artery ± short gastric arteries. Anastomotic leaks were higher in the ischaemic conditioning group, 11.1% when compared with 8.5% in the non-ischaemic conditioning group, but not statistically significant. However, anastomotic leaks that did occur in the ischaemic conditioning group did trend towards a more non-surgical management modality (i.e. endoscopy); 88.9% compared with 66.7% in the non-ischaemic conditioning group.

Akiyama et al. [8] utilized preoperative embolization therapy to both right and left gastric arteries and the splenic artery in 54 patients, comparing outcomes with those of 25 patients who had no such intervention. They reported a 2% leak rate in the embolization group compared with 8% in the non-ischaemic conditioning group, but no statistical significance. They also reported an intervention profile of fever, abdominal pain and vomiting to be associated with embolization therapy and made no comment on the temporal association between ischaemic conditioning and oesophagectomy.

**CLINICAL BOTTOM LINE**

Preoperative ischaemic conditioning with gastric vessel ligation/division prior to oesophagectomy is not associated with reduced anastomotic leak rates. Preoperative ischaemic conditioning with gastric vessel ligation/division prior to oesophagectomy is not associated with a lower anastomotic leak severity. The most consistent reported technique to carry out preoperative ischaemic conditioning was ligation or division of the left gastric artery.

**Conflict of interest:** none declared.

**REFERENCES**


