# Proximal Resection Margin in Ivor-Lewis Oesophagectomy for Cancer

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## Abstract

**Objective:** The aim of this study was to investigate whether a long proximal oesophageal resection margin is associated with improved survival after oesophagectomy for cancer and to identify the optimal margin to aim for in patients undergoing oesophagectomy for malignant disease.

**Methods:** A prospectively maintained database identified 174 patients who underwent Ivor-Lewis oesophagectomy for cancer. Demographic, clinical and pathological data were collected. The proximal Resection Margin (PRM) was obtained from pathology reports. Electronic patient records were interrogated to calculate Disease Free Survival (DFS) and Overall Survival (OS). X-tile software was used to identify the optimal resection point. Two models were analysed: single point resection requiring comparison of two groups ('short' and 'long') and two resection points requiring 3 groups ('short', 'medium' and 'long') to provide a range. Survival analysis was performed using Kaplan-Meier curves and Cox Proportional Hazards (PH) model.

**Results:** The median PRM was 4.0cm (inter-quartile range: 2.5cm to 6.0cm). The length of PRM was adjusted for significant confounders noted on univariable analysis (adjuvant treatment, grade of disease, age at diagnosis and recurrence) in the multivariable Cox PH model. In the two group analysis ('short' and 'long'), the optimal resection margin was 1.7cm and in the three group analysis the optimum PRM was between 1.7 and 3cm ('medium' group).

In the two group analysis, the 'long' margin had no effect on DFS (p=0.37), but carried a significantly improved OS (HR=0.46, 95%CI: 0.25-0.87, p=0.02). In the three group analysis, DFS was the same in all 3 groups, but the 'medium' and' 'long' groups had improved OS compared to the 'short' group (on average 54%, HR≥0.45, p≤0.04). Further analysis demonstrated that the optimal PRM is between 1.7 and 3cm irrespective of confounding variables. The 5-year DFS and OS rates were highest in the 'medium' PRM group (48% and 57% respectively).

**Conclusion:** Optimal survival following oesophagectomy for cancer is achieved with a PRM of greater than 1.7cm, but a PRM of >3cm does not yield a further survival advantage. Thus, the optimal PRM is likely to be between 1.7 and 3cm.

## Introduction

Oesophageal cancer remains a devastating disease, with an increasing incidence worldwide, particularly in Western countries.[1,2] Although multi-modality treatment has improved outcomes over the last decade, early diagnosis and surgical resection remain the mainstay of curative treatment.[3] However, an oesophagectomy has significant risks, with mortality reported between 1-23%.[4] Local recurrence after surgery can cause distressing symptoms, with death ensuing soon after. A key prognostic factor affecting local recurrence and long-term survival is tumour involvement at the resection margins.[5-7]

The importance of a negative circumferential resection margin has been well-established for many cancers, including oesophageal cancer.[8,9] However, there have been few studies on the importance of the proximal resection margin (PRM).[10-15] The first study specifically assessing this was by Miller in 1962, which recommended a 12cm proximal resection margin to achieve adequate clearance. This was based on the observation of microscopic skip lesions of tumour along the oesophagus, thought to be running in intra-mural lymphatics.[10] Further work by Skinner elaborated on this recommendation, and advocated a 10cm margin.[11] In contemporary practise, a margin of 4-6cm is commonly employed. The critical step in an oesophagectomy is fashioning a gastro-oesophageal anastomosis. The most debilitating complication of the operation, which can cause death, is an anastomotic leak. A more proximal anastomosis may be associated with a higher leak rate, with its associated morbidity and mortality.[16-18] This is thought to relate to the blood supply and tension at the anastomosis.

The aim of this study was to examine the implications of the length of the proximal resection margin in patients undergoing oesophagectomy, in terms of disease free and overall survival and to investigate the optimum proximal resection margin for oesophageal cancer.

## Methods

A prospectively maintained database was searched and patient details on all oesophagectomies performed between November 2000 and January 2011 were retrieved. Further clinical information was obtained from patients' records.

A total of 213 consecutive cases were identified. Patients who had oesophagectomy for benign disease or transhiatal surgery were excluded. Patients who had a histologically confirmed diagnosis of malignancy of the oesophagus or gastro-oesophageal junction (Siewert type 1)[19] who required an oesophagctomy, were included. All cases were discussed at a multi-disciplinary meeting, where neo-adjuvant, surgical and adjuvant treatment proposals were agreed. All surgery was performed by specialist oncological gastro-oesophageal surgeons, and histopathology reported by specialist

gastro-intestinal pathologists. Ivor-Lewis oesophagectomy involves a two-compartment approach with either a laparotomy or laparoscopy and a right thoracotomy to mobilise the stomach, resect the oesophagus and fashion the gastro-oesophageal anastomosis. The oesophageal resection was associated with a two-field nodal resection. The operating surgeon would aim for a macroscopic 5cm resection margin from the tumour. A cuff of crura was resected in continuity with the tumour, and meso-oesophageal tissue was excised to the aorta and azygos vein, including all peri-oesophageal nodes and the thoracic duct *en bloc*.

Following exclusion, a total of 174 cases were included in the study. Clinicopathological features of each case were analysed. Staging was assigned according to the Tumour Node Metastases (TNM) classification system.[20,21] Follow-up data were collected from patient's records. Recurrence was defined as either pathological or radiological evidence of disease after surgery. Patients were followed up at 3 monthly intervals for the first year, 6 monthly for the second year and annually thereafter. Computerised tomography (CT) and endoscopy was performed for patients with symptoms suggestive of recurrence, but routine surveillance investigations were not performed. All references to PRM are microscopic descriptions based on measurements of the formalin fixed specimen.

**Statistical Analysis**

Distribution of the Proximal Resection Margins (PRM) was assessed with Notched Box-and-whisker plots. Overall survival (OS) was measured from date of surgery to death or last follow-up, and disease-free survival (DFS) was from date of surgery to confirmed diagnosis of local or distant recurrence. Kaplan–Meier plots were used to analyse DFS and OS, with corresponding log rank tests.[22] Univariable analysis was performed for all factors using the Cox Proportional Hazards (PH) model, with multivariable analysis performed for PRM including and adjusting for the significant patient and tumour factors found in univariable analysis for each outcome measure.

Categorical data analysis involved the assessment of the optimal PRM for factors without validated normal ranges. This was performed using the X-Tile statistical package (X-Tile version 3.6.1 Yale University 2003-05, New Haven, CT).[23] This enables specific resection margins to be evaluated in order to ascertain whether the resected length had any effect on survival. The X-Tile software divides the cohort (n=174) into two independent data sets—a test set and a validation set—in a 1:2 ratio. It then determines the optimal resection margin length as a factor for the test set, and applies this to the validation set.

The proportional hazards assumption for each predictor in the final models was assessed using scaled Schoenfeld residuals. This assumption was not rejected in any of the models. Statistical analyses were performed using statistical software package Intercooled STATA 12.0 (Stata Corp, College Station, TX). A $p$ value $<0.05$ was considered statistically significant.

## Results

### *Patient and Tumour Factors*

The median age at diagnosis was 64 years (Inter-Quartile Range: 58-70), see, Table 1. Of the 174 patients included in this study, 137 (78.7%) were male. The vast majority of the tumours were adenocarcinoma (90.8%), with 8.6% squamous cell carcinoma and one small cell carcinoma. Most of the tumours were oesophageal in origin (89%), with the remainder arising from the gastro-oesophageal junction (Siewert 1). The majority of patients received neo-adjuvant chemotherapy (78.7%) as advised by the multidisciplinary team. Sixty-two percent had a laparoscopic gastric mobilisation and 38% underwent an open approach.

On histopathological analysis of the resected specimen, 63.2% were Grade 3, 29.9% grade 2 and 6.9% Grade 1. The pathological TNM stage distribution was T3 in 58.6%, T2 in 21.2%, -T1 in 19% and one patient was Stage T4 (1.2%). The nodal status was negative in 40.2%, N1 in 43.2% with the remainder N2. Lymphovascular invasion was present in 44.8% of cases and perineural invasion in 34.4%.

Thirty six (20.6%) patients received post-operative chemotherapy, and 26 (15%) received adjuvant radiotherapy. Univariable analysis, using Cox's PH model, demonstrated that DFS was significantly dependent on adjuvant treatment and the grade of the disease while OS was significantly dependent on adjuvant treatment, grade of disease, age at diagnosis and recurrence. Table 1 demonstrates the key patient and tumour characteristics.

Median follow-up was 19.6 months (Range 1-124 months-). Sixteen patients were lost to complete follow-up, but their data has been included on an intention to treat basis.

### *Complications and Surgical Outcomes*

Six patients died within thirty days of surgery (one from anastomotic leak, four from respiratory complications and one from cardiovascular disease). The anastomotic leak rates were similar in the 'short', 'medium' and 'long' groups (8.7%, 7.9% and 8.8% respectively). The rate of post-operative pulmonary complications was highest in the 'long' PRM group (24.8%) compared to the 'short' and 'medium' group (17.4 and 18.4% respectively).

### *Resection Margin*

Four patients had an involved PRM, constituting 2.3% of all patients. Six patients (3.4%) had an involved distal margin and nine patients (5.2%) had a positive circumferential margin. Three patients had two or more involved margins, all of which were T3 tumours.

The median microscopic PRM was 4cm, with a range of 0 to 12cm (Figure 1). The greatest number of these lay between 2.5 and 6cm (n=98; 56%). As a continuous co-variate, the PRM was not significantly predictive of either disease free (p=0.84) or overall survival (p=0.63) on univariable analysis.

We documented anastomotic recurrence in 4 patients (2.3%) of whom three patients had an involved or <1mm margin (1 PRM, and 2 circumferential margins). Two of these patients were concurrently found to have disseminated metastatic disease and two had extensive nodal recurrence.

| **Risk Factors** | ***Number of patients (%)*** |
|---|---|
| **Age (years)** | Median 64, IQR: 58-70 |
| **Sex** | |
| **Male** | 137 (78.7) |
| **Female** | 37 (21.3) |
| **Tumour** | |
| **SCC*** | 15 (8.6) |
| **Adenocarcinoma** | 158 (90.8) |
| **Small Cell** | 1 (0.6) |
| **Site** | |
| **Oesophageal** | 155 (89) |
| **Gastro-Oesophageal Junction** | 19 (11) |
| **Grade** | |
| **I** | 12 (6.9) |
| **II** | 52 (29.9) |
| **III** | 110 (63.2) |
| **Tumour Size†** | |
| **T1** | 33 (19) |
| **T2** | 37 (21.2) |
| **T3** | 102 (58.6) |
| **T4** | 2 (1.2) |
| **Nodal Status†** | |
| **N0** | 70 (40.2) |
| **N1** | 75 (43.2) |
| **N2** | 18 (10.3) |
| **N3** | 11 (6.3) |
| **Metastases†** | |
| **M0** | 172 (98.8) |
| **M1** | 2 (1.2) |
| **Lymphovascular Invasion** | 78 (44.8) |
| **Perineural Invasion** | 60 (34.4) |
| **Surgery** | |
| **Laparoscopic Ivor-Lewis** | 108 (62) |
| **Open Ivor-Lewis** | 66 (38) |
| **Neo-Adjuvant** | |
| **Chemotherapy** | 137 (78.7) |
| **Radiotherapy** | 3 (1.7) |
| **Adjuvant** | |
| **Chemotherapy** | 36 (20.6) |

| | |
|---|---|
| **Radiotherapy** | 26 (15) |

**Table 1. Patient and Tumour Characteristics** *SCC- Squamous Cell Carcinoma; †Based TNM Classification[20,21]

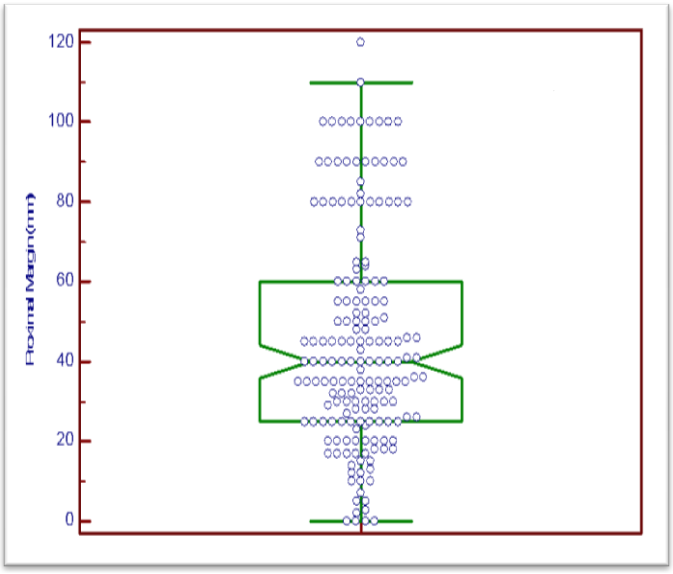



**Figure 1. Notched Box-and-whisker plot distribution of proximal resection margins**

***The Optimal Proximal Resection Margin (PRM)***

The optimal PRM was determined to be between 1.7cm and 3cm, based on analysis of outcome measures for the 174 patients, adjusted for the significant confounding variables (adjuvant treatment, grade of disease, age at diagnosis and recurrence).

The statistical software utilised to determine the optimum resection margin involved a division of the study population into a test and validated cohort in a 1:2 ratio, thereby allowing both an analysis and application to the continuous data. The purpose of this analysis was to establish an optimal PRM. At this optimal resection margin, any further proximal resection would not improve survival, but a shorter resection margin would confer a disadvantage. The X-Tile software used for this analysis was performed twice for each of the two outcomes (DFS and OS): once with a single resection point (and thus 2 groups) and secondly with two resection points (and thus 3 groups), the latter to give a range rather than a single optimal PRM.

In the two group analysis, the optimal resection margin was identified as 1.7cm (-'short' n=21 versus 'long' n=153) for both DFS and OS. In, the three groups analysis, the margin was determined as a 'short' resection margin of less than 1.7cm (n=21), a 'medium' resection margin of between 1.7cm

and 3cm (n=38) and a 'long' margin of greater than 3cm (n=115) for both outcome measures (Table 2).

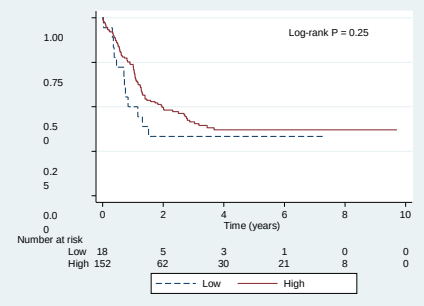
| 2 Group analysis | *n* | 3 Group analysis | *n* |
|---|---|---|---|
| **Short** (<1.7cm) | 21 | **Short** (<1.7cm) | 21 |
| | | **Medium** (1.7cm - ≤3 cm) | 38 |
| **Long** (≥1.7cm) | 153 | **Long** (≥3cm) | 115 |

**Table 2. The number of patients in each group according to their proximal resection margin in both the 2 group and 3 group analysis.**

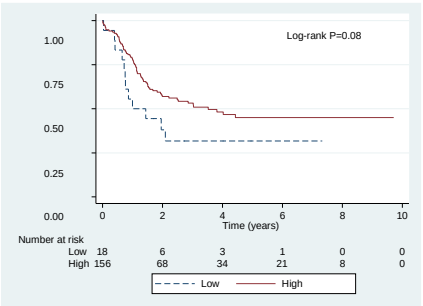
**Commented [SS1]:** All the results in Table 2 are now included in the text and also in Table 4. Therefore, Table 2 is redundant and should be deleted. However, if you still want to present Table 2, then remove sample sizes (n=21, n=153 etc) from the text (above the table) to avoid repetition.

The Kaplan-Meier survival curves, with associated log-rank test for the two group analysis (Figure 2(i) and (ii)) did not demonstrate a significant difference in disease free or overall survival between the two groups. In the three group analysis (Figure 2(iii) and (iv)),the curves illustrate that for both DFS and OS, the 'medium' PRM group had improved survival compared to both the 'short' and 'long' group. This indicates that a longer PRM of more than 3cm may not confer a greater survival advantage as compared to the 'medium' group.

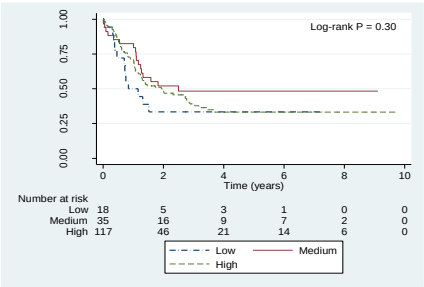
(i) Disease-free Survival




(ii) Overall Survival




(iii) Disease-free Survival




(iv) Overall Survival

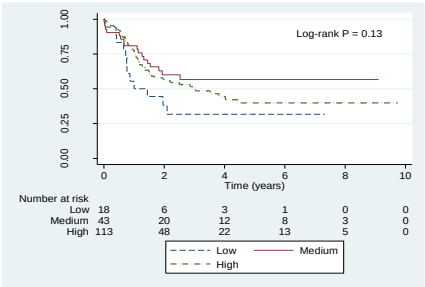



**Figure 2. Kaplan-Meier curves for (i) Disease-free survival based on optimal resection point of Short<1.7cm and Long≥1.7cm; (ii) Overall survival based on optimal resection point of Short<1.7cm and Long≥1.7cm; (iii) Disease-free survival based on optimal resection points of Short<1.7cm, Medium 1.7cm to ≤3.0cm and Long>3.0cm; and (iv) Overall survival based on optimal resection points of Short<1.7cm, Medium 1.7cm to ≤3.0cm and Long>3.0cm.**

In the multivariable Cox PH model (Table 3), the optimal PRM was adjusted for the confounding effects of the statistically significant factors noted in the univariable analysis. In the two group analysis, the 'long' margin had no significant effect on disease free survival (p=0.37), but a significant effect on overall survival (HR=0.46, 95%CI: 0.25-0.87, p=0.02). In the three group analysis, disease free survival did not vary significantly in terms of PRM, but the 'medium' and 'long' groups had a statistically significant higher chance of overall survival, on average 54% (HR≥0.45, p≤0.04) compared to the 'short' group. Re-running of the multivariable Cox PH model for OS with the 'medium' group of PRM as the reference category showed that 'long' PRM group had on average 3% higher hazards of death compared to the 'medium' PRM patients (p≥0.60), suggesting that the

optimal PRM lay between 1.7 and 3cm irrespective of adjuvant treatment, disease grade, age at diagnosis and recurrence.

In the multivariable analysis, in addition to the PRM, grade was a significant predictor for both DFS and OS. Age was a significant predictor for OS only. Adjuvant treatment was associated with reduced disease free survival.

| Variable | Disease-Free Survival[1] | | Overall survival[2] | |
|---|---|---|---|---|
| | **HR (95% CI)** | ***P*** | **HR (95% CI)** | ***P*** |
| **Model (i) PRM with resection point at 1.7cm** | | | | |
| Proximal margin (cm) | | | | |
| Short (<1.7cm) | 1.00 | | 1.00 | |
| Long (≥1.7cm) | 0.76 (0.41 – 1.39) | 0.37 | 0.46 (0.25 – 0.87) | 0.02 |
| Grade* | | 0.03 | | <0.001 |
| I | 1.00 | | 1.00 | |
| II | 2.24 (0.68 – 7.45) | 0.19 | 4.25 (0.56 – 32.28) | 0.16 |
| III | 3.20 (0.99 – 10.27) | 0.05 | 8.90 (1.20 – 66.12) | 0.03 |
| Adjuvant treatment | | | | |
| No | 1.00 | | 1.00 | |
| Yes | 1.78 (1.15 – 2.76) | 0.01 | 1.27 (0.77 – 2.12) | 0.35 |
| Age at diagnosis | | | 1.05 (1.02 – 1.08) | 0.003 |
| Recurrence* | | | | <0.001 |
| No recurrence | | | 1.00 | |
| Local recurrence | | | 6.22 (3.17 – 12.19) | <0.001 |
| Distant recurrence | | | 9.30 (4.99 – 17.33) | <0.001 |
| **Model (ii) PRM with two resection points at 1.7cm and 3.0cm** | | | | |
| Proximal margin (cm)* | | 0.60 | | 0.09 |
| Short (PRM<1.7cm) | 1.00 | | 1.00 | |
| Medium (1.7cm≤PRM≤3 cm) | 0.68 (0.32 – 1.43) | 0.30 | 0.45 (0.21 – 0.96) | 0.04 |
| Long (PRM>3 cm) | 0.78 (0.42 – 1.44) | 0.43 | 0.46 (0.25 – 0.89) | 0.02 |
| Grade* | | 0.04 | | <0.001 |
| I | 1.00 | | 1.00 | |
| II | 2.22 (0.67 – 7.37) | 0.19 | 4.23 (0.56 – 32.19) | 0.16 |
| III | 3.15 (0.98 – 10.13) | 0.06 | 8.87 (1.19 – 65.92) | 0.03 |
| Adjuvant treatment | | | | |
| No | 1.00 | | 1.00 | |
| Yes | 1.76 (1.13 – 2.73) | 0.01 | 1.27 (0.76 – 2.12) | 0.36 |
| Age at diagnosis | | | 1.05 (1.02 – 1.08) | 0.003 |
| Recurrence* | | | | <0.001 |
| No recurrence | | | 1.00 | |
| Local recurrence | | | 6.19 (3.15 – 12.19) | <0.001 |
| Distant recurrence | | | 9.28 (4.97 – 17.31) | <0.001 |

**Table 3. Multivariable survival analyses for all patients based on (i) PRM with one resection point at 1.7cm and (ii) PRM with two resection points at 1.7cm and 3.0cm** *Likelihood ratio test P-value to test for overall significance of the variable in the model; 1. Disease-free survival models adjusted for adjuvant treatment and grade of disease; 2. Overall survival models adjusted for adjuvant treatment, grade, age at diagnosis and recurrence

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***Long Term Survival***

The 5-year OS for all patients was 44% and DFS was 37% (Table 4). When the 5-year survival was analysed for the different resection point groups, the 5-year DFS and OS were highest for the patients with a 'medium' PRM (between 1.7cm and 3.0cm) at 48% and 57% respectively. The 5-year OS rate for the 'long' group was slightly higher than that of the 'short' group in both the 2 group and 3 group analysis.

| | 5-year DFS Survival rate (95% CI) | 5-year OS Survival rate (95% CI) |
|---|---|---|
| **All patients** | 37% (0.29 - 0.45) | 44% (0.35 - 0.52) |
| **i)** | | |
| Short (PRM<1.7cm), n=21 | 33 (0.14 - 0.55) | 32% (0.12 - 0.54) |
| Long (PRM≥1.7cm), n=153 | 37% (0.29 - 0.46) | 45% (0.35 - 0.54) |
| **ii)** | | |
| Short (PRM<1.7cm), n=21 | 33% (0.14 - 0.55) | 32% (0.12 - 0.54) |
| Medium (PRM >1.7cm - ≤3.0cm), n=38 | 48% (0.30 - 0.64) | 57% (0.40 - 0.71) |
| Long (PRM>3.0cm), n=115 | 33% (0.24 - 0.43) | 40% (0.28 - 0.51) |

**Table 4. Five-year survival rate with 95% CI for all patients based on (i) PRM with on optimal resection point at 1.7cm and (ii) PRM with two optimal resection points at 1.7cm and 3.0cm**

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**Discussion**

We present a large series assessing the significance of PRM in Ivor-Lewis oesophagectomy for cancer. The importance of the circumferential and distal margins is well established. [5-9] Traditionally, long proximal resection margins have been advocated; we investigated whether those recommended in the literature were still relevant in contemporary practice.

We have found through objective assessment that the optimum resection margin, in terms of disease free and overall survival, required for patients undergoing oesophagectomy lies between 1.7 and 3 cm. A longer resection margin did not confer any advantage, but in fact was associated with reduced OS.

Patient and tumour factors in our series were consistent with epidemiological data available in the literature. Multivariable analysis demonstrated the age at diagnosis, administration of adjuvant treatment and increasing grade of the tumour were statistically significant factors for overall survival, which is consistent with other studies.[1,2, 24]

The single optimal PRM was determined to be 1.7cm, and the optimal range was between 1.7 and 3cm. In the analysis with either one or two resection points, a PRM less than 1.7cm adversely affected survival. An involved margin carried a 46% higher risk of death as compared to a clear proximal resection margin. There was a more profound effect of a PRM <1.7cm on OS as compared to the DFS. We considered that his may be related to the fact that these patients are more likely to

receive adjuvant chemo- or radiotherapy to treat residual disease following surgery. However, multivariable analysis demonstrated that adjuvant treatment adversely affected survival. This is likely to be a reflection of its use in involved margins and more aggressive disease.

A PRM of greater than 1.7cm was found to be significant in improving OS, but there was a greater chance of survival with the 'medium' resection group as compared to the 'long' group. Long-term (5-year) survival rates for the 'medium' group were highest. Additional analysis of the 'medium' PRM group as a reference (rather than the test cohort), illustrated a 3% increased hazards of death with a PRM >3cm. This indicates that a >3cm resection margin does not confer any further survival benefit, but may be associated with a slightly higher risk of mortality. There are several reasons for this which have been alluded to in other studies, in particular relating to post-operative and long term complications.[16-18]

In this study, the anastomotic leak rates were the same across the 'short', 'medium' and 'long' groups. Given this finding, a further analysis was performed to assess why the long PRM group had a poorer outcome when compared to the medium group. There was a higher proportion of Grade 3 tumours in the 'long' group (65% versus 53% in the 'medium' group) and a greater proportion of T3 and T4 tumours (60% versus 53%). The nodal burden was also greater in the 'long' PRM group (19% N2 or N3, compared to 11% in the 'medium' PRM group) and the incidence of lymphovascular and perineural invasion was higher (51% and 40% versus 24% and 16% respectively). These findings may aid the explanation of why the long PRM group had poorer outcomes than the medium group. The rate of post-operative pulmonary complications was highest in the long PRM group (24.8%) compared to the short and medium group (17.4 and 18.4%). This concurs with the literature which supports the finding of post-operative respiratory complications being more common with proximal anastomosis.[25,26] The poorer survival for patients with longer resection margins is also likely to be because the longer resection margin is easily achieved for tumours of the gastroesophageal junction. These are known to have a poorer prognosis than tumours confined to the oesophagus.[27]

During oesophagectomy, it may not be possible to attain the resection margins recommended in the literature.[11,28] There may not be 4-5cm of oesophagus available in more proximal tumours.[29] The mortality rate associated with an anastomotic leak is reportedly as high as 40%, highlighting the importance of a tension-free, vascularised and secure anastomosis.[30] With trans-thoracic surgery, it is technically difficult to access the apex of the thorax and to construct a satisfactory anastomosis, necessitating a cervical anastomosis. The cervical approach is associated with increased morbidity, including potential damage to the laryngeal nerves.[25] The incidence of anastomotic leakage and subsequent stenosis is higher in cervical anastomoses. This is probably due to the poorer blood supply to the proximal stomach which would be used for the anastomosis in the neck, but would be discarded in a thoracic anastomosis. There is also increased incidence of long term aspiration and respiratory complications.[25,26] Also, the increasing practise of minimally invasive techniques, utilising a mini-thoracotomy in association with laparoscopic gastric mobilisation preclude anastomosis high in the thorax without extension of the thoracotomy incision.[31,32]

Historically, a 10-12cm margin was recommended to ensure excision of intra-mural skip lesions,[10,11] but these may be of reduced importance in modern practise. In the last decade, improved endoscopic techniques and higher resolution three-dimensional imaging have enabled improved accuracy and mapping of mucosal abnormalities. Neo-adjuvant chemotherapy may have a role in

controlling submucosal lymphatic spread. Patient selection has changed; patients with a greater tumour burden may not be offered resection due to metastases identified by highly sensitive staging investigations. Other studies have also found that a long PRM may not be warranted. Barbour suggested a clearance of 3.8cm based on 352 oesopahagectomy specimens[7] and Mariette recommended 7cm, although this study assessed only gastro-oesophageal junction tumours.[33] Another study assessing junctional tumours demonstrated that a PRM of 2cm was sufficient, with no further survival advantage achieved from more proximal resections [34]. In addition, Takubo described skip lesions at a distance of over 16cm from the primary tumour which would not be encompassed by a long PRM.[35] These tumours with distant intramural or lymphatic spread demonstrate a poorer prognosis even if completely excised.[36]

Of the 174 cases, 16 patients (9.2%) had microscopic positive resection margins, which is lower than the reported literature.[12,13,33,34] This may relate to careful patient selection, the regular use of neo-adjuvant treatment and to our standard practise of resecting a generous cuff of crura and meso-oesophageal tissue in continuity with the tumour reducing circumferential margin involvement.

Another possible explanation for our low longitudinal resection margin involvement is the small number of squamous cell carcinomas (SCC) in our series (n=15; 8.6%). It is our usual practice to treat SCC with radical chemoradiotherapy, restricting resectional surgery for T1b tumours. SCC are considered to demonstrate a higher incidence of submucosal extension and skip lesions which led to the original recommendations of long resection margins. Submucosal extension and skip lesions are associated with widespread lymphatic infiltration and likely lymphatic metastases. Current routine use of positron emission tomography will identify distant metastases which would not have been identified with historical imaging techniques. These patients would be excluded from resection.[37,38] In the presence of accurate and detailed staging information, it has been suggested that localised tumours can be adequately treated with shorter resection margins.[39]

In our series, only four (2.3%) patients developed an anastomotic recurrence despite a total of sixteen patients with involved margins. This is lower than many other series and may be explained by the use of adjuvant chemoradiotherapy in cases with involved or close resection margins with low nodal burden. Also, as in other series it is likely that patients with microscopic involved margins had more biologically aggressive tumours and died of metastatic disease before clinical evidence of local recurrence became apparent .[40,41]

***Limitations***

There were a small number of cases in the short groups and those with involved resection margins, which may be responsible for some of the non significant results. Also, we included both squamous and adenocarcinoma of the oesophagus which may behave differently. The high proportion of tumours with poor prognostic indicators in the long resection group may explain the poorer outcome in this group.

## Conclusion

A proximal resection margin of greater than 1.7cm improved overall survival, but a PRM of >3cm did not yield a further survival advantage. Thus, the optimal PRM for Ivor-Lewis oesophagectomy for

cancer is likely to be between 1.7 and 3cm, regardless of confounding variables; adjuvant treatment, disease grade, age at diagnosis and recurrence.

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**Contributions**

YAQ and RCW collected clinical data. YAQ and S-J S wrote the manuscript. S-J S performed all the statistical analyses. FSH designed the study and edited the manuscript.

**Conflicts of interest**

None declared.

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