Minimally invasive techniques for transthoracic oesophagectomy for oesophageal cancer: systematic review and network meta-analysis

K. Siaw-Acheampong1, S. K. Kamarajah2,3, R. Gujjuri1, J. R. Bundred1, P. Singh4 and E. A. Griffiths5,6

1College of Medical and Dental Sciences, and 2Department of Hepatobiliary, Pancreatic and Transplant Surgery, Freeman Hospital, Newcastle University NHS Foundation Trust Hospitals, and 3Institute of Cellular Medicine, University of Newcastle, Newcastle upon Tyne, 4Regional Oesophago-Gastric Unit, Royal Surrey County Hospital NHS Foundation Trust, Guildford, and 5Institute of Cancer and Genomic Sciences, College of Medical and Dental Sciences, University of Birmingham, and 6Department of Upper Gastrointestinal Surgery, University Hospitals Birmingham NHS Foundation Trust, Birmingham, UK

Correspondence to: Mr E. A. Griffiths, Department of Upper Gastrointestinal Surgery, Area 6, 7th Floor, Queen Elizabeth Hospital Birmingham, Mindelsohn Way, Edgbaston, Birmingham B15 2WB, UK (e-mail: ewenagriffiths@gmail.com)

Background: Oesophagectomy is a demanding operation that can be performed by different approaches including open surgery or a combination of minimal access techniques. This systematic review and network meta-analysis aimed to evaluate the clinical outcomes of open, minimally invasive and robotic oesophagectomy techniques for oesophageal cancer.

Methods: A systematic literature search was conducted for studies reporting open oesophagectomy, laparoscopically assisted oesophagectomy (LAO), thoracoscopically assisted oesophagectomy (TAO), totally minimally invasive oesophagectomy (MIO) or robotic MIO (RAMIO) for oesophagectomy. A network meta-analysis of intraoperative (operating time, blood loss), postoperative (overall complications, anastomotic leaks, chyle leak, duration of hospital stay) and oncological (R0 resection, lymphadenectomy) outcomes, and survival was performed.

Results: Ninety-eight studies involving 32 315 patients were included in the network meta-analysis (open 17 824, 55.2 per cent; LAO 1576, 4.9 per cent; TAO 2421 7.5 per cent; MIO 9558, 29.6 per cent; RAMIO 917, 2.8 per cent). Compared with open oesophagectomy, both MIO and RAMIO were associated with less blood loss, significantly lower rates of pulmonary complications, shorter duration of stay and higher lymph node yield. There were no significant differences between surgical techniques in surgical-site infections, chyle leak, and 30- and 90-day mortality. MIO and RAMIO had better 1- and 5-year survival rates respectively compared with open surgery.

Conclusion: Minimally invasive and robotic techniques for oesophagectomy are associated with reduced perioperative morbidity and duration of hospital stay, with no compromise of oncological outcomes but no improvement in perioperative mortality.

Funding information
No funding

Paper accepted 24 June 2020
Published online 7 September 2020 in Wiley Online Library (www.bjsopen.com). DOI: 10.1002/bjs5.50330

Introduction

Oesophageal cancer remains a challenging disease worldwide, with over 570,000 new cases in 20181. In managing this disease, oesophagectomy remains the mainstay of radical treatment with curative intent, with the transthoracic approach the most commonly employed. However, variation exists in surgical access techniques, with approximately 40 per cent of oesophagectomies in the UK now employing minimally invasive approaches2. The most common procedure is hybrid oesophagectomy where a laparoscopic gastric mobilization is performed with an open thoracotomy; a thoracoscopic–open abdominal hybrid procedure is uncommon. Less commonly both thoracoscopic and laparoscopic techniques are used in totally minimally invasive oesophagectomy (MIO).
The use of robotic surgery for oesophagectomy is also increasing. Since the development of minimally invasive approaches to oesophagectomy in the 1990s, an evidence base has been growing to suggest similar, if not better, results in terms of morbidity and survival without compromising oncological benefit. This includes various pairwise meta-analyses of mainly non-randomized evidence. Many of these studies grouped MIO together with hybrid procedures when comparing outcomes with those of open oesophagectomy.

Given the limited evidence and understanding of the potential benefits of different minimally invasive techniques for oesophagectomy, this systematic review and network meta-analysis aimed to compare oncological safety and perioperative outcomes between these different surgical approaches and transthoracic oesophagectomy for cancer, along with impact on long-term survival.

Methods

Search strategy

This study was conducted according to PRISMA guidelines. A systematic and comprehensive search was undertaken of the MEDLINE, Embase and Cochrane Library databases, for studies published up to 25 February 2019. Search terms included the following, individually or in combination: ‘oesophagectomy’ or ‘oesophagectomy’ and ‘minimally invasive surgical procedures’ or ‘laparoscopy’ and ‘anastomotic leak’ or ‘postoperative complications’ or ‘lymph nodes examined’ or ‘survival’ and ‘oesophageal cancer’ or ‘esophageal cancer’. The full search strategy with all included search terms is shown in Table S1 (supporting information). Manual scoping of reference lists in recent reviews was also undertaken. The protocol for this study was registered with the prospective PROSPERO database (CRD42019125848).

Inclusion and exclusion criteria

Inclusion criteria were: comparative studies comparing any approach to two- or three-stage transthoracic oesophagectomy in human subjects with cancer of the oesophagus or gastro-oesophageal junction, and studies published in the English language. Exclusion criteria were: review articles; conference abstracts; studies with non-comparative analyses of surgical approach including case reports; studies reporting transhiatal or left thoracoabdominal approaches; studies using a non-gastric replacement conduit; and studies reporting pharyngolaryngoesophagectomy. After performing the literature search and removing all duplicates, two researchers screened the remaining titles and abstracts independently. Where a study was considered for inclusion, the full text was obtained. Discrepancies between the judgement of the two primary researchers were resolved through consensus with the other authors. Additionally, during full-text review, authors of papers with mixed groups of both hybrid and totally minimally invasive techniques were contacted for separate data regarding each technique. Where multiple studies analysed the same data set or population, the most recent article was selected unless different outcomes were reported.

Study outcomes

Outcome measures were: oncological – lymph node yield, R0 resection margins; intraoperative – blood loss and duration of operation; postoperative – duration of hospital stay, 30- and 90-day mortality, overall, pulmonary, gastrointestinal and cardiac complications, anastomotic leak and chyle leak, and 1-, 3- and 5-year overall survival. The Esophageal Complications Consensus Group definitions of complications were used. R0 status was defined using both College of American Pathologists and Royal College of Pathology definitions: absence of residual tumour at or within 1 mm of the resection margin respectively.

Data extraction

Two researchers extracted data on study characteristics (author, year of publication, country, study interval, number of participants), patient characteristics (age, sex, BMI, overall TNM stage, location of anastomosis (cervical, thoracic), anastomotic technique (stapled versus handsewn), details of surgical approach and reported clinical outcomes.

Definitions

Open oesophagectomy was defined as oesophagectomy carried out with laparotomy and open thoracotomy. MIO was defined as total MIO where laparoscopy was used for the abdominal phase and thoracoscopy for the thoracic phase. Laparoscopically assisted hybrid oesophagectomy (LAO) was defined as a laparoscopic abdominal phase combined with open thoracotomy. Thoracoscopically assisted hybrid oesophagectomy (TAO) was defined by an open abdominal phase combined with a thorascopic chest phase. Robotic MIO (RAMIO) was defined as oesophagectomy where either the abdominal or thoracic phase was performed using a robotic platform, including hybrid approaches. Regardless of access approach, two- and three-stage oesophagectomies, with intrathoracic and cervical anastomoses respectively, were included, and
MIO, minimally invasive oesophagectomy.

a subgroup analysis was planned based on location of the anastomosis.

Assessment of study quality

Methodological quality and standard of outcome reporting was assessed in each study by two independent researchers. Disagreements were settled through discussion between these researchers or consensus with all authors. For cohort studies, the Newcastle–Ottawa Scale27,28 was used to formally assess quality, whereas the Cochrane risk-of-bias tool29 was used for RCTs.

Statistical analysis

This systematic review and meta-analysis was conducted in accordance with the recommendations of the Cochrane Library and PRISMA guidelines, as reported previously30. Dichotomous outcomes were compared using risk ratios (RRs), produced by meta-analysis using random-effects DerSimonian–Laird models. Heterogeneity between studies was assessed using the $\chi^2$ value, with values of less than 25, 25–75 and over 75 per cent considered to represent low, moderate and high degrees of heterogeneity respectively. Both randomized and non-randomized studies were pooled into a network meta-analysis comparing the above surgical approaches with transthoracic oesophagectomy. For each outcome, graphical representations of treatments (nodes) and comparisons (lines) were mapped. Network maps were then analysed for closed loops to be entered into network analyses.

Networks were examined for the presence of inconsistency, allowing for comparisons between direct and indirect treatment effects. Initially, this was assessed by checking for overall inconsistency throughout the entire
| Reference | Study design | Country | Comparison | No. of patients | Tumour location (U/M/L) | Anastomosis level | Anastomosis type | Risk of bias/NOS score* |
|-----------|-------------|---------|------------|----------------|------------------------|-----------------|----------------|-----------------------|
| 34        | RCT         | Austria | LAO versus open | 26             | n.r./n.r./n.r.         | 0               | 26             | n.r.                  |
| 7         | RCT         | France  | LAO versus open | 207            | 3/63/141              | 0               | 207            | n.r.                  |
| 35        | RCT         | China   | MIO versus open | 144            | 11/80/43              | n.r.            | n.r.           | n.r.                  |
| 36        | RCT         | Netherlands, Spain, Italy | MIO versus open | 115            | 4/48/n.r.             | 75              | 32             | n.r.                  |
| 6         | RCT         | Netherlands, Spain, Italy | MIO versus open | 115            | 4/48/63              | 75              | 32             | n.r.                  |
| 37        | RCT         | China   | MIO versus open | 114            | 0/0/0                | 114             | 0              | 0                     |
| 38        | RCT         | China   | MIO versus TAO | 68             | 7/39/22              | 68              | 0              | 36                    |
| 39        | RCT         | Netherlands | RAMIO versus open | 109            | 1/13/55              | 106             | 0              | 106                  |
| 40        | PCS         | Serbia  | LAO versus open | 88             | 0/34/54              | 0               | 88             | n.r.                  |
| 41        | PCS         | UK      | LAO versus open | 70             | n.r.                | 0               | 70             | n.r.                  |
| 42        | PCS         | UK      | MIO versus LAO versus open | 75            | n.r.                | 0               | 75             | 26                    |
| 43        | PCS         | UK      | MIO versus LAO versus open | 86            | n.r.                | n.r.            | n.r.           | n.r.                  |
| 44        | PCS         | Sweden  | MIO versus open | 366            | n.r.                | 261             | 105            | n.r.                  |
| 45        | PCS         | Taiwan  | MIO versus open | 190            | 15/91/83             | 190             | 0              | 99                    |
| 46        | PCS         | UK      | MIO versus open | 106            | 0/4/46               | 0               | 106            | 1                     |
| 47        | PCS         | Korea   | MIO versus TAO | 98             | 0/24/74              | 0               | 98             | 0                     |
| 48        | PCS         | Japan   | MIO versus TAO versus LAO versus open | 210         | 26/133/51            | 198             | 0              | 105                  |
| 49        | PCS         | Australia | TAO versus open | 487            | 0/43/355             | n.r.            | 110            | n.r.                  |
| 50        | PCS         | Japan   | TAO versus open | 84             | n.r.                | n.r.            | n.r.           | n.r.                  |
| 51        | RCS         | Japan   | MIO versus TAO | 315            | n.r.                | 315             | 0              | 315                  |
| 52        | RCS         | Japan   | MIO versus TAO | 64             | 6/14/44              | 64              | 0              | n.r.                  |
| 53        | PCS         | Germany | LAO versus MIO | 60             | n.r.                | 0               | 60             | 0                     |
| 54        | RCS         | Sweden  | LAO versus MIO | 173            | 4/28/6               | n.r.            | n.r.           | n.r.                  |
| 55        | RCS         | Japan   | LAO versus MIO | 105            | 18/67/17             | n.r.            | n.r.           | 39                    |
| 56        | RCS         | Japan   | LAO versus open | 216            | 41/108/67            | 216             | 0              | 0                     |
| 57        | RCS         | South Korea | LAO versus open | 115            | n.r./36/79           | 0               | 115            | 3                     |
| 58        | RCS         | China   | LAO versus open | 685            | n.r.                | 0               | 685            | n.r.                  |
| 59        | RCS         | Germany | LAO versus open | 120            | 0/16/104             | 0               | 120            | n.r.                  |
| 60        | RCS         | France  | LAO versus open | 140            | 0/123/17             | 0               | 140            | n.r.                  |
| 61        | RCS         | France  | LAO versus open | 280            | 0/110/170            | 0               | 280            | n.r.                  |
| 62        | RCS         | Italy   | LAO versus open | 68             | n.r.                | 13              | 55             | n.r.                  |
| 63        | RCS         | UK      | MIO versus LAO versus open | 334         | 0/22/122             | n.r.            | 67             | n.r.                  |
| 64        | RCS         | China   | MIO versus LAO/TAO versus open | 548         | 154/331/63           | 548             | 0              | n.r.                  |
| 65        | RCS         | Pakistan | MIO versus LAO/TAO versus open | 216         | n.r.                | n.r.            | n.r.           | n.r.                  |
| 66        | RCS         | Japan   | MIO versus open | 98             | 8/60/30              | 9               | 89             | 12                    |
| 67        | RCS         | Japan   | MIO versus open | 171            | 3/44/45              | 171             | 0              | 0                     |
| 68        | RCS         | Japan   | MIO versus open | 130            | n.r.                | 65              | 65             | n.r.                  |
| 69        | RCS         | China   | MIO versus open | 63             | n.r.                | 0               | 63             | n.r.                  |
| 70        | RCS         | China   | MIO versus open | 228            | 3/130/95             | n.r.            | n.r.           | n.r.                  |
| Reference | Study design | Country | Comparison | No. of patients | Tumour location (U/M/L) | Anastomosis level | Anastomosis type | Risk of bias/NOS score* |
|-----------|-------------|---------|------------|-----------------|------------------------|-------------------|----------------|----------------------|
| 71 RCS    | China       | MIO versus open | 269 | 0/191/78 | 0 | 269 | n.r. | n.r. | n.r. | 7 |
| 72 RCS    | China       | MIO versus open | 221 | 20/154/47 | n.r. | n.r. | n.r. | n.r. | n.r. | 7 |
| 73 RCS    | USA         | MIO versus open | 39  | n.r. | 39 | 0 | n.r. | n.r. | n.r. | 6 |
| 74 RCS    | China       | MIO versus open | 257 | 54/169/34 | 257 | 0 | 62 | 0 | 195 | 8 |
| 75 RCS    | Netherlands | MIO versus open | 866 | 16/189/517 | 563 | 303 | n.r. | n.r. | n.r. | 8 |
| 76 RCS    | China       | MIO versus open | 183 | 24/118/41 | 183 | 0 | n.r. | n.r. | n.r. | 7 |
| 77 RCS    | China       | MIO versus open | 80  | 7/56/17 | 80 | 0 | 80 | 0 | 6 |
| 78 RCS    | Finland     | MIO versus open | 153 | n.r. | 0 | 153 | 79 | 0 | 73 | 7 |
| 79 RCS    | USA         | MIO versus open | 168 | n.r. | n.r. | n.r. | n.r. | n.r. | n.r. | 6 |
| 80 RCS    | USA         | MIO versus open | 130 | 0/5/72 | n.r. | n.r. | n.r. | n.r. | n.r. | 7 |
| 81 RCS    | USA         | MIO versus open | 114 | n.r. | 0 | 114 | 0 | 0 | 114 | 8 |
| 82 RCS    | Japan       | MIO versus open | 62  | 9/34/9 | 62 | 0 | n.r. | n.r. | n.r. | 7 |
| 83 RCS    | China       | MIO versus open | 113 | 0/113/0 | 113 | 0 | 0 | 0 | 113 | 6 |
| 84 RCS    | China       | MIO versus open | 230 | 94/115/21 | 230 | 0 | n.r. | n.r. | n.r. | 7 |
| 85 RCS    | Finland, Sweden | MIO versus open | 1614 | n.r. | n.r. | n.r. | n.r. | n.r. | n.r. | 6 |
| 86 RCS    | USA         | MIO versus open | 146 | 0/3/0 | 138 | 8 | n.r. | n.r. | n.r. | 8 |
| 87 RCS    | UK          | MIO versus open | 80  | n.r./n.r./10 | 49 | 31 | n.r. | n.r. | n.r. | 6 |
| 88 RCS    | China       | MIO versus open | 379 | n.r. | 0 | 379 | 0 | 0 | 379 | 7 |
| 89 RCS    | China       | MIO versus open | 118 | 7/74/37 | 118 | 0 | n.r. | n.r. | n.r. | 8 |
| 90 RCS    | China       | MIO versus open | 447 | n.r. | 348 | 99 | n.r. | n.r. | n.r. | 7 |
| 91 RCS    | Netherlands, Spain, Italy | MIO versus open | 575 | n.r. | n.r. | n.r. | n.r. | n.r. | n.r. | 7 |
| 92 RCS    | USA         | MIO versus open | 4047 | n.r. | n.r. | n.r. | n.r. | n.r. | n.r. | 8 |
| 93 RCS    | China       | MIO versus open | 118 | 0/49/69 | n.r. | n.r. | n.r. | n.r. | n.r. | 7 |
| 94 RCS    | China       | MIO versus open | 194 | 35/87/72 | n.r. | n.r. | n.r. | n.r. | n.r. | 8 |
| 95 RCS    | UK          | MIO versus open | 7502 | n.r. | n.r. | n.r. | n.r. | n.r. | n.r. | 8 |
| 96 RCS    | Belgium     | MIO versus open | 166 | n.r. | 166 | 0 | n.r. | n.r. | n.r. | 7 |
| 97 RCS    | Japan       | MIO versus open | 92  | 6/60/26 | 92 | 0 | n.r. | n.r. | n.r. | 8 |
| 98 RCS    | China       | MIO versus open | 174 | 15/127/32 | 174 | 0 | n.r. | n.r. | n.r. | 7 |
| 99 RCS    | China       | MIO versus open | 162 | n.r. | n.r. | n.r. | n.r. | n.r. | n.r. | 7 |
| 100 RCS   | China       | MIO versus open | 407 | 25/290/92 | n.r. | n.r. | n.r. | n.r. | n.r. | 7 |
| 101 RCS   | China       | MIO versus TAO | 172 | 54/73/45 | 172 | 0 | n.r. | n.r. | n.r. | 8 |
| 102 RCS   | Japan       | MIO versus TAO | 64  | 7/23/34 | 64 | 0 | 64 | 0 | 6 |
| 103 RCS   | Italy       | MIO versus TAO | 160 | 6/29/125 | 80 | 80 | 0 | 160 | 0 | 8 |
| 104 RCS   | China       | MIO versus TAO versus LAO | 109 | 16/59/34 | n.r. | n.r. | n.r. | n.r. | n.r. | 7 |
| 105 RCS   | Japan       | MIO versus TAO versus LAO | 242 | 36/137/69 | 242 | 0 | n.r. | n.r. | n.r. | 8 |
| 106 RCS   | Japan       | MIO versus TAO versus LAO | 185 | 33/85/67 | 170 | 15 | 97 | 0 | 88 | 7 |
| 107 RCS   | China       | MIO versus TAO versus LAO | 138 | 23/n.r./n.r. | 138 | 0 | n.r. | n.r. | n.r. | 6 |
| 108 RCS   | Thailand    | MIO versus TAO versus LAO | 83  | 17/41/25 | 83 | 0 | n.r. | n.r. | n.r. | 7 |
| 109 RCS   | Australia   | MIO versus TAO versus LAO | 446 | 10/84/262 | n.r. | n.r. | n.r. | n.r. | n.r. | 6 |
| 110 RCS   | Australia   | MIO versus TAO versus LAO | 858 | 15/78/524 | 858 | 0 | n.r. | n.r. | n.r. | 7 |
| 111 RCS   | Taiwan      | RAMIO versus MIO | 68  | 20/34/14 | 68 | 0 | n.r. | n.r. | n.r. | 8 |
| 112 RCS   | South Korea | RAMIO versus MIO | 105 | 15/24/66 | 56 | 35 | n.r. | n.r. | n.r. | 6 |
| 113 RCS   | China       | RAMIO versus MIO | 54  | 4/33/n.r. | 54 | 0 | 0 | 0 | 54 | 8 |
network. A further check was then performed by fitting node side-splitting models to identify loop inconsistency, within all three-way treatment comparison loops, as described by Dias and colleagues. If $P$ exceeded 0.050, representing acceptance of the null hypothesis, consistency was assumed and networks were entered into consistency modelling. Consistency models used a restricted maximum likelihood model, generating network forest plots. Heterogeneity was examined by calculation of $\tau^2$. These were supplemented with interval plots of pooled effect estimates. Surgical approaches were then ranked using $P$-scores, whereby a $P$-score greater than 0-900 was considered to indicate the best technique with high probability. Subgroup analyses were conducted according to location of anastomoses, either cervical or thoracic, and for a more recent time cohort (2010 onwards). Statistical analyses for network meta-analysis were undertaken using R version 3.2.1 (R Foundation for Statistical Computing, Vienna, Austria), with the netmeta packages, as described previously.

### Results

#### Study characteristics

The review identified 98 studies comparing surgical approaches for oesophagectomy, involving 32315 patients. Of these, 55.2 per cent (17 824), 4.9 per cent (1576), 7.5 per cent (2421), 29.6 per cent (9558) and 2.8 per cent (917) were open oesophagectomy, LAO, TAO, MIO and RAMIO respectively. Study characteristics are presented in Table 1. The majority of studies were non-randomized (90). Eight studies were RCTs. Most studies compared two different oesophagectomy techniques; 14 compared at least three different techniques.

### Intraoperative outcomes

Table 2 shows the results of pairwise comparisons between intraoperative outcomes, and network maps are presented in Fig. S1 (supporting information). Duration of operation was reported in 77 studies. Open surgery resulted in significantly shorter operating times than MIO (mean...
Minimally invasive transthoracic oesophagectomy

Table 2 Summary of intraoperative outcomes of overall network meta-analysis

| Duration of surgery (min) | Blood loss (ml) |
|---------------------------|-----------------|
| **No. of studies** | **Mean difference** | **P** | **No. of studies** | **Mean difference** | **P** |
| Open versus TAO | 15 | −21 (−37, −5) | 0.011 | 16 | 91 (49, 133) | <0.001 |
| Open versus LAO | 13 | 0 (−19, 19) | 0.997 | 4 | 84 (16, 153) | 0.016 |
| Open versus MIO | 37 | −37 (−48, −26) | <0.001 | 36 | 173 (146, 200) | <0.001 |
| Open versus RAMIO | 3 | −75 (−104, −46) | <0.001 | 3 | 163 (99, 226) | <0.001 |
| MIO versus TAO | 12 | 16 (−1, 33) | 0.063 | 12 | −82 (−125, −39) | <0.001 |
| MIO versus LAO | 5 | 37 (16, 58) | <0.001 | 4 | −88 (−158, −20) | 0.012 |
| MIO versus RAMIO | 4 | −38 (−67, −9) | 0.011 | 5 | −10 (−73, 52) | 0.750 |
| LAO versus TAO | 1 | −21 (−45, 3) | 0.090 | 1 | 7 (−71, 85) | 0.867 |
| RAMIO versus TAO | 0 | 54 (21, 86) | 0.001 | 0 | −72 (−145, 2) | 0.056 |
| RAMIO versus LAO | 0 | 75 (40, 109) | <0.001 | 0 | −78 (−170, 13) | 0.093 |

Values in parentheses are 95 per cent confidence intervals. TAO, thoracoscopically assisted oesophagectomy; LAO, laparoscopically assisted oesophagectomy; MIO, minimally invasive oesophagectomy; RAMIO, robotic minimally invasive oesophagectomy.

Table 3 Ranking of surgical techniques for intraoperative, oncological and postoperative outcomes according to P-scores

| Rank | Duration of operation | Blood loss |
|------|-----------------------|------------|
| 1    | Open (P = 0.874)      | LAO (P = 0.863) | TAO (P = 0.505) | MIO (P = 0.257) | RAMIO (P = 0.002) |
| 2    | MIO (P = 0.905)       | RAMIO (P = 0.825) | TAO (P = 0.399) | LAO (P = 0.369) | Open (P = 0.002) |
| 3    | RAMIO (P = 0.872)     | LAO (P = 0.672) | MIO (P = 0.657) | TAO (P = 0.199) | Open (P = 0.101) |
| 4    | MIO (P = 0.872)       | TAO (P = 0.632) | RAMIO (P = 0.550) | LAO (P = 0.414) | Open (P = 0.031) |
| 5    | TAO (P = 0.887)       | LAO (P = 0.688) | MIO (P = 0.548) | Open (P = 0.443) | RAMIO (P = 0.367) |

LAO, laparoscopically assisted oesophagectomy; TAO, thoracoscopically assisted oesophagectomy; MIO, minimally invasive oesophagectomy; RAMIO, robotic minimally invasive oesophagectomy.

difference (MD) 37 min; P < 0.001), RAMIO (MD 75 min; P < 0.001) and TAO (MD 21 min; P = 0.011) (Table 2). Open surgery had the shortest operating time, with a high probability, followed by hybrid operations then MIO and RAMIO (Table 3). Open oesophagectomy was ranked first for cervical anastomosis, whereas LAO was ranked first for thoracic anastomosis (Tables S2 and S3, supporting information).

Blood loss was reported in 65 studies. Open oesophagectomy had significantly higher blood loss than TAO (MD 91 ml; P < 0.001), LAO (MD 84 ml; P = 0.016), RAMIO (MD 163 ml; P < 0.001) and MIO (MD 173 ml; P = 0.001). MIO was ranked first for lowest blood loss, with a high probability, followed by RAMIO (Table 3). MIO was ranked first for both cervical and thoracic anastomosis, followed by RAMIO (Tables S2 and S3, supporting information).

Postoperative outcomes

The results of all pairwise comparisons of each surgical approach for postoperative complications are shown in Tables 4 and 5, and network maps in Fig. S2 (supporting
Overall complications

Overall complications were reported in 39 studies. LAO (RR 0.63; \( P = 0.010 \)) and MIO (RR 0.65; \( P < 0.001 \)) had significantly lower rates of overall complications than open surgery (Table 4). RAMIO was ranked best for overall complications (Table 3). MIO was ranked first for cervical anastomosis, whereas RAMIO was ranked first for thoracic anastomosis (Tables S3 and S4, supporting information).

Pulmonary complications

Pulmonary complications were reported in 79 studies. MIO (RR 0.52; \( P < 0.001 \)) and TAO (RR 0.60; \( P = 0.004 \)) were associated with significantly lower rates of pulmonary complications than open surgery. MIO was ranked the best technique in terms of pulmonary complications overall (Table 3), and in subgroups of cervical and thoracic anastomoses (Tables S3 and S4, supporting information).

Cardiac complications

Cardiac complications were reported in 46 studies. RAMIO (RR 0.35; \( P = 0.003 \)) and MIO (RR 0.84;
Anastomotic leak was reported in 74 studies. LAO was significantly associated with a higher rate of anastomotic leak than TAO (RR 1.69; \(P = 0.048\)) and MIO (RR 1.63; \(P = 0.030\)) (Table 4). TAO was ranked first for anastomotic leak (Table 3). In terms of anastomotic leakage, TAO was ranked first for thoracic anastomosis, whereas RAMIO was ranked first for cervical anastomosis (Tables S3 and S4, supporting information).

**Duration of hospital stay**

Length of hospital stay was reported in 72 studies. MIO (MD 3.00 days; \(P < 0.001\)), RAMIO (MD 3.85 days; \(P < 0.001\)) and TAO (MD 2.77 days; \(P < 0.001\)) were associated with significantly shorter duration of stay compared with open oesophagectomy. RAMIO (MD 2.98 days; \(P = 0.011\)) and TAO (MD 1.90 days; \(P = 0.036\)) were also associated with significantly shorter hospital stay than LAO. RAMIO was ranked first, with a high probability, followed by MIO (Table 3).

### Overall survival

One-year overall survival was reported in 53 studies. The open approach was associated with significantly lower 1-year survival than TAO (RR 1.62; \(P = 0.043\)) and MIO (RR 1.35; \(P = 0.035\)) (Table 5). Overall, TAO was ranked first for 1-year survival (Table 3). However, MIO and LAO were ranked first for cervical and thoracic anastomosis respectively (Tables S3 and S4, supporting information). Three-year overall survival was reported in 46 studies. There were no significant differences in outcomes between any techniques. Five-year overall survival was reported in 34 studies. Open oesophagectomy was associated with significantly lower 5-year survival than RAMIO (RR 4.00; \(P = 0.042\)) (Table 5). Overall, RAMIO was ranked the best technique, with high probability (Table 3). A sensitivity analysis for 1- and 5-year survival including studies from 2010 onwards yielded similar results.
### Oncological outcomes

**Lymph nodes examined**

The results of all pairwise comparisons of oncological outcomes for each surgical approach technique are shown in Table 6, and network maps in Fig. S3 (supporting information). Lymph node assessment was reported in 77 studies. LAO (mean difference 3.53; \( P = 0.031 \)) and open surgery (mean difference 3.11; \( P = 0.024 \)) were associated with significantly lower numbers of lymph nodes examined than RAMIO. RAMIO was ranked as the best technique, with high probability, followed by MIO (Table 3).

**R0 resection**

R0 resections were reported in 40 studies. MIO was associated with higher rates of R0 resection (RR 1.37; \( P = 0.002 \)) than open surgery. RAMIO was ranked first, followed by MIO (Table 3).

### Discussion

This network meta-analysis compared all combinations of open, minimally invasive and robotic approaches to transthoracic oesophagectomy. The analysis demonstrated that minimally invasive surgery for oesophagectomy was associated with increased operating time, but decreased operative blood loss, fewer pulmonary complications and shorter length of hospital stay, compared with open approaches. In addition, the review identified significantly decreased overall postoperative complications with minimally invasive surgery compared with the open approach. Importantly, no significant differences in perioperative mortality (either 30 or 90 day) were observed between any surgical approach. In addition, MIO and RAMIO were associated with significantly higher 1- and 5-year survival rates respectively than open oesophagectomy. These findings were not altered in a sensitivity analysis including studies from 2010 onwards. Based on the present evidence, no one approach demonstrates clear overall superiority over all others, but there is increasing evidence of the specific benefits related to minimally invasive techniques.

Network meta-analysis allows assessment of different surgical techniques by combining direct evidence within studies and indirect evidence across studies. Hence, it enables indirect comparisons of surgical techniques that have not been studied directly in a head-to-head fashion\(^{130}\). By including evidence from both direct and indirect comparisons, a network meta-analysis may increase the precision in estimates of the relative effects of treatments and improve power compared with standard pairwise meta-analyses that include only direct evidence\(^ {131}\). Network meta-analysis may yield more reliable and definitive results, and allows visualization and interpretation of a wider picture of the available evidence, and to calculate treatment rankings with probabilities, compared with a standard pairwise meta-analysis\(^ {130}\).

This study has some limitations. The majority of the studies included in this network meta-analysis subject it to heterogeneity owing to patient selection criteria and demographics, such as age, sex, BMI and different disease stages. The amount of evidence a treatment carries and the number of comparisons available between treatments determines the diversity and strength of a network meta-analysis. Imbalance in terms of the amount of evidence available may affect the power and reliability of the network meta-analysis as inferences may be driven largely from the evidence from few treatments and...
comparisons. Some of the studies assessed new techniques or technologies and may have incorporated a learning curve in the novel arm.

Previous standard pairwise meta-analyses comparing open versus minimally invasive resection for oesophagectomy demonstrated that, although laparoscopic surgery increased operative time, it resulted in significantly reduced blood loss and wound infection, increased R0 resection rate and shorter hospital stay. In addition, the present review identified significantly decreased overall postoperative complications with minimal access compared with open surgery, and this may be related to the lower wound infection rate and pulmonary complications of the minimally invasive approach.

This network meta-analysis identified that minimally invasive surgery was associated with significantly more examined lymph nodes compared with open surgery, specifically with RAMIO and MIO techniques. Evidence from RCTs is limited as none have demonstrated the superiority of either laparoscopic or open techniques. This network meta-analysis also showed that rates of R0 resection were better with MIO compared with open surgery. This is an important point as one of the barriers to adoption of the minimally invasive approach in routine clinical practice over conventional open oesophagectomy was concern over oncological clearance as R0 resections are recognized to be an important prognostic marker of long-term survival following surgery. It is also important to note that differences in R0 resection rates may also be attributed to differences in the R0 classification systems used.

Both RAMIO and MIO techniques were associated with significantly lower rates of pulmonary complications and shorter length of hospital stay compared with conventional open oesophagectomy. However, there were no significant differences in outcomes between robotic and conventional MIO techniques. No significant differences between MIO and open techniques in rates of wound or diaphragm complications, gastrointestinal complications and chyle leak were identified. Operative blood loss is difficult to measure accurately, and the clinical relevance of the small differences in operative blood loss between the surgical techniques is debatable. However, previous studies have suggested that volume of blood loss is an independent risk factor for postoperative adverse events, cancer recurrence and poorer overall survival. Furthermore, the potential advantages of the MIO approach, and especially the robotic approach, in decreasing operative trauma and blood loss, and improving postoperative recovery, may allow greater preservation of immune function, reduce the risk of tumour progression and allow earlier access to adjuvant treatment.

A recent meta-analysis reported that minimally invasive approaches for oesophagectomy significantly improved long-term survival of patients compared with conventional open surgery. However, that review did not address the impact of the different techniques on long-term outcomes given the heterogeneity of each approach as identified by the present review. In this network meta-analysis, TAO and MIO were only associated with a significant survival benefit compared with open surgery at 1 year, and not 3- or 5-year survival. This may reflect higher rates of negative resection margins and number of lymph nodes examined with MIO and RAMIO, as identified by this review.

Based on current evidence, no single approach demonstrates clear overall superiority over all others, but there is increasing evidence of the clinical benefits of minimally invasive over open surgery.

**Acknowledgements**

K.S.-A., S.K.K and R.G. contributed equally to this work.

**Disclosure**: The authors declare no conflict of interest.

**References**

1. Ferlay J, Colombet M, Soerjomataram I, Siegel R, Torre L, Jamal A. Global and Regional Estimates of the Incidence and Mortality for 38 Cancers: GLOBOCAN 2018. International Agency for Research on Cancer: Lyon, 2018.
2. Varagunam M, Park MH, Sinha S, Cromwell D, Maynard N, Crosby T et al. National Oesophago-Gastric Cancer Audit 2018; 2019. https://www.nogca.org.uk/reports/2018-anual-reports/ [accessed 10 July 2020].
3. Luketich JD, Nguyen NT, Weigel T, Ferson P, Keenan R, Schauer P. Minimally invasive approach to esophagectomy. JSL 1999; 2: 243–247.
4. Watson DI, Davies N, Jamieson GG. Totally endoscopic Ivor Lewis esophagectomy. Surg Endosc 1999; 13: 293–297.
5. Cuschieri A. Endoscopic subtotal oesophagectomy for cancer using the right thoracoscopic approach. Surg Oncol 1993; 2: 3–11.
6. Bierre SSAY, van Berge Henegouwen MI, Maas KW, Bonavina L, Rosman C, Garcia JR et al. Minimally invasive versus open oesophagectomy for patients with oesophageal cancer: a multicentre, open-label, randomised controlled trial. Lancet 2012; 379: 1887–1892.
7. Mariette C, Markar SR, Babakuyo-Yonli TS, Meunier B, Pezet D, Collet D et al. Hybrid minimally invasive esophagectomy for esophageal cancer. N Engl J Med 2019; 380: 152–162.
8. Bierre SSAY, Cuesta MA, van der Peet DL. Minimally invasive versus open esophagectomy for cancer: a systematic review and meta-analysis. Minerva Chir 2009; 64: 121–133.
9 Sgourakis G, Gockel I, Radtke A, Musholt TJ, Timm S, Rink A et al. Minimally invasive versus open esophagectomy: meta-analysis of outcomes. *Dig Dis Sci* 2010; **55**: 3031–3040.

10 Nagpal K, Ahmed K, Vats A, Yakoub D, James D, Ashrafian H et al. Is minimally invasive surgery beneficial in the management of esophageal cancer? A meta-analysis. *Surg Endosc* 2010; **24**: 1621–1629.

11 Dantoc M, Cox MR, Eslick GD. Evidence to support the use of minimally invasive esophagectomy for esophageal cancer: a meta-analysis. *Arch Surg* 2012; **147**: 768–776.

12 Zhou C, Ma G, Li X, Li J, Yan Y, Liu P et al. Is minimally invasive esophagectomy effective for preventing anastomotic leakages after esophagectomy for cancer? A systematic review and meta-analysis. *World J Surg Oncol* 2015; **13**: 269.

13 Yibulayin W, Abulizi S, Lv H, Sun W. Minimally invasive oesophagectomy versus open esophagectomy for resectable esophageal cancer: a meta-analysis. *World J Surg Oncol* 2016; **14**: 304.

14 Lv L, Hu W, Ren Y, Wei X. Minimally invasive esophagectomy versus open esophagectomy for esophageal cancer: a meta-analysis. *Onco Targets Ther* 2016; **9**: 6751–6762.

15 Guo W, Ma X, Yang S, Zhu X, Qin W, Xiang J et al. Combined thorascoscopic-laparoscopic esophagectomy versus open esophagectomy: a meta-analysis of outcomes. *Surg Endosc* 2016; **30**: 3873–3881.

16 Xiong W-L, Li R, Lei H-K, Jiang Z-Y. Comparison of outcomes between minimally invasive oesophagectomy and open oesophagectomy for oesophageal cancer. *ANZ J Surg* 2017; **87**: 165–170.

17 Jin D, Yao L, Yu J, Liu R, Guo T, Yang K et al. Robotic-assisted minimally invasive esophagectomy versus the conventional minimally invasive one: a meta-analysis and systematic review. *Int J Med Robot* 2019; **15**: e1988.

18 Gottlieb-Vedi E, Kauppila JH, Malietzis G, Nilsson M, Markar SR, Lagergren J. Long-term survival in esophageal cancer after minimally invasive compared to open esophagectomy: a systematic review and meta-analysis. *Ann Surg* 2019; **I**: 1005–1017.

19 Moher D, Liberati A, Tetzlaff J, Altman DG; PRISMA Group. Preferred reporting items for systematic reviews and meta-analyses: the PRISMA statement. *PLoS Med* 2009; **6**: e1000097.

20 Low DE, Alderson D, Cecconello I, Chang AC, Darling GE, D’Journo XB et al. International consensus on standardization of data collection for complications associated with esophagectomy: Esophagectomy Complications Consensus Group (ECCG). *Ann Surg* 2015; **262**: 286–294.

21 Washington K, Berlin J, Branton P, Burgart LJ, Carter DK, Fitzgibbons P et al. Protocol for the Examination of Specimens from Patients with Carcinoma of the Esophagus; 2012. https://webapps.cap.org/apps/docs/committees/cancer/cancerprotocols/2012/Esophagus_12protocol_3111.pdf [accessed 10 July 2020].

22 Grabsch HI, Mapstone NP, Novelli M. Dataset for Histopathological Reporting of Oesophageal and Gastric Carcinoma (2nd edn); 2019. https://www.rcpath.org/uploads/assets/f811ea3d-5529-4f85-984e8d4d8535e0b7/068e9093-0aea-4316-bd49f771564784df9/g006-dataset-for-histopathological-reporting-of-oesophageal-and-gastric-carcinoma.pdf [accessed 10 July 2020].

23 Lewis I. The surgical treatment of carcinoma of the oesophagus, with special reference to a new operation for growths of the middle third. *Br J Surg* 1946; **34**: 18–31.

24 McKeown KC. Total three-stage esophagectomy for cancer of the oesophagus. *Br J Surg* 1976; **63**: 259–262.

25 van Hillegersberg R, Boone J, Draaisma WA, Broeders IAMJ, Giezeman MJMM, Rinkes IHMB. First experience with robot-assisted thoracoscopic esophagogastric lymphadenectomy for esophageal cancer. *Surg Endosc* 2006; **20**: 1435–1439.

26 Kernstine KH. The first series of completely robotic esophagectomies with three-field lymphadenectomy: initial experience. *Surg Endosc* 2008; **22**: 2102–2102.

27 Lo CK-L, Mertz D, Loeb M. Newcastle–Ottawa Scale: comparing reviewers’ to authors’ assessments. *BMC Med Res Methodol* 2014; **14**: 45.

28 Stang A. Critical evaluation of the Newcastle–Ottawa scale for the assessment of the quality of nonrandomized studies in meta-analyses. *Eur J Epidemiol* 2010; **25**: 603–605.

29 Higgins JP, Altman DG, Gotzsche PC, Juni P, Moher D, Oxman AD et al.; Cochrane Bias Methods Group; Cochrane Statistical Methods Group. The Cochrane Collaboration’s tool for assessing risk of bias in randomised trials. *BMJ* 2011; **343**: d5928.

30 Stroup DF, Berlin JA, Morton SC, Olkin I, Williamson GD, Rennie D et al. Meta-analysis of observational studies in epidemiology: a proposal for reporting. *Meta-analysis Of Observational Studies in Epidemiology (MOOSE) group.* *JAMA* 2000; **283**: 2008–2012.

31 Dias S, Welton NJ, Caldwell DM, Ades AE. Checking consistency in mixed treatment comparison meta-analysis. *Stat Med* 2010; **29**: 932–944.

32 Kamarajah SK, Bundrej J, Tan BHL. Body composition assessment and sarcopenia in patients with gastric cancer: a systematic review and meta-analysis. *Gastric Cancer* 2019; **22**: 10–22.

33 Kamarajah SK, Sonnenday CJ, Cho CS, Frankel TL, Bednar F, Lawrence TS et al. Association of adjuvant radiotherapy with survival after margin-negative resection of pancreatic ductal adenocarcinoma: a propensity-matched national cancer database (NCDB) analysis. *Ann Surg* 2019; https://doi.org/10.1097/SLA.0000000000003242 [Epub ahead of print].

34 Paireder M, Asari R, Kristo I, Rieder E, Zacherl J, Kabon B et al. Morbidty in open versus minimally invasive hybrid esophagectomy (MIOMIE): long-term results of a
randomized controlled clinical study. *Eur Surg* 2018; 50: 249–255.

35 Ma G, Cao H, Wei R, Qu X, Wang L, Zhu L et al. Comparison of the short-term clinical outcome between open and minimally invasive esophagectomy by comprehensive complication index. *J Cancer Res Ther* 2018; 14: 789–794.

36 Straatman J, van der Wielen N, Cuesta MA, Daams F, Roig Garcia J, Bonavina L et al. Minimally invasive versus open esophageal resection: three-year follow-up of the previously reported randomized controlled trial: the TIME trial. *Ann Surg* 2017; 266: 232–236.

37 Hong L, Zhang Y, Zhang H, Yang J, Zhao Q. The short-term outcome of three-field minimally invasive esophagectomy for Siewert type I esophagogastric junctional adenocarcinoma. *Ann Thorac Surg* 2013; 96: 1826–1831.

38 Yuan Y, Xia Z, Yin N, Yin B, Hu J. Modified thoracoscopic versus minimally invasive esophagectomy in curative resection of oesophageal cancer. *J Int Med Res* 2011; 39: 904–911.

39 van der Sluis PC, van der Horst S, May AM, Schippers C, Brosens LAA, Joore HCA et al. Robot-assisted minimally invasive thoracolaparoscopic esophagectomy versus open transthoracic esophagectomy for resectable esophageal cancer: a randomized controlled trial. *Ann Surg* 2019; 269: 621–630.

40 Bjelovic M, Babic T, Spica B, Gunjic D, Veselinovic M, Trajkovic G. Could hybrid minimally invasive esophagectomy improve the treatment results of esophageal cancer? *Eur J Surg Oncol* 2016; 42: 1196–1201.

41 Bailey L, Khan O, Willows E, Somers S, Mercer S, Toh S. Open and laparoscopically assisted oesophagectomy: a prospective comparative study. *Eur J Cardiothorac Surg* 2013; 43: 268–273.

42 Hamouda AH, Forshaw MJ, Tsigritis K, Jones GE, Noorani AS, Rohatgi A et al. Perioperative outcomes after transition from conventional to minimally invasive Ivor-Lewis esophagectomy in a specialized center. *Surg Endosc* 2010; 24: 865–869.

43 Parameswaran R, Titcomb DR, Blencowe NS, Berrisford RG, Wajed SA, Streets CG et al. Assessment and comparison of recovery after open and minimally invasive esophagectomy for cancer: an exploratory study in two centers. *Ann Surg Oncol* 2013; 20: 1970–1977.

44 Kleveland F, Scandavini CM, Kamiya S, Nilsson M, Lundell L, Rouvelas I. Single center consecutive series cohort study of minimally invasive versus open resection for cancer in the esophagus or gastroesophageal junction. *Dis Esophagus* 2018; 31: 1–6.

45 Liu CY, Lin CS, Shih CS, Huang YA, Liu CC, Cheng CT. Cost-effectiveness of minimally invasive versus open esophagectomy for esophageal squamous cell carcinoma. *World J Surg* 2018; 42: 2522–2529.

46 Noble F, Kelly JJ, Bailey IS, Byrne JP, Underwood TJ, South Coast Cancer Collaboration – Oesophago-Gastric (SC3-OG). A prospective comparison of totally minimally invasive versus open Ivor Lewis esophagectomy. *Dis Esophagus* 2013; 26: 263–271.

47 Lee JW, Sung SW, Park JK, Park CH, Song KY. Laparoscopic gastric tube formation with pyloromyotomy for reconstruction in patients with esophageal cancer. *Ann Surg Treat Res* 2015; 89: 117–123.

48 Nozaki I, Mizusawa J, Kato K, Igaki H, Ito Y, Daiko H et al. Impact of laparoscopy on the prevention of pulmonary complications after thoracoscopic esophagectomy using data from JCOG0502: a prospective multicenter study. *Surg Endosc* 2018; 32: 651–659.

49 Barbour AP, Cormack OMM, Baker PJ, Hirst J, Krause L, Brosda S et al. Long-term health-related quality of life following esophagectomy: a nonrandomized comparison of thoracoscopically assisted and open surgery. *Ann Surg* 2017; 265: 1158–1165.

50 Ikeguchi M, Fukumoto Y. Prognostic benefits of thoracoscopic esophagectomy for thoracic esophageal squamous cell carcinomas. *Chirurgia* 2016; 111: 313–317.

51 Ichikawa H, Miyata G, Miyazaki S, Onodera K, Kamei T, Hoshida T et al. Esophagectomy using a thoracoscopic approach with an open laparotomic or hand-assisted laparoscopic abdominal stage for esophageal cancer: analysis of survival and prognostic factors in 315 patients. *Ann Surg* 2013; 257: 873–885.

52 Oshikiri T, Yasuda T, Kawasaki K, Harada H, Oyama M, Hasegawa H et al. Hand-assisted laparoscopic surgery (HALS) is associated with less-restrictive ventilatory impairment and less risk for pulmonary complication than open laparotomy in thoracoscopic esophagectomy. *Surgery* 2016; 159: 459–466.

53 Berth F, Plum PS, Chon SH, Gutschow CA, Bolschweiler E, Holscher AH. Total minimally invasive esophagectomy for esophageal adenocarcinoma reduces postoperative pain and pneumonia compared to hybrid esophagectomy. *Surg Endosc* 2018; 32: 4957–4965.

54 Nilsson M, Kamiya S, Lindblad M, Rouvelas I. Implementation of minimally invasive esophagectomy in a tertiary referral center for esophageal cancer. *J Thorac Dis* 2017; 9: S817–S825.

55 Kitagawa H, Namikawa T, Munekage M, Fujisawa K, Munekage E, Kobayashi M et al. Outcomes of thoracoscopic esophagectomy in prone position with laparoscopic gastric mobilization for esophageal cancer. *Langenbecks Arch Surg* 2016; 401: 699–705.

56 Yamasaki M, Miyata H, Fujiiwa Y, Takiguchi S, Nakajima K, Kurokawa Y et al. Minimally invasive esophagectomy for esophageal cancer: comparative analysis of open and hand-assisted laparoscopic abdominal lymphadenectomy with gastric conduit reconstruction. *J Surg Oncol* 2011; 104: 623–628.

57 Yun JS, Na KJ, Song SY, Kim S, Jeong IS, Oh SG. Comparison of perioperative outcomes following hybrid minimally invasive versus open Ivor Lewis esophagectomy for esophageal cancer. *J Thorac Dis* 2017; 9: 3097–3104.
58 Fang WM, Ruan WZ, Lin SF, Chen YM, Zhu KS. Comparative outcomes of laparoscopy-assisted and open Ivor Lewis esophagectomy for esophageal squamous cell carcinoma: experience at a single, high-volume center. *Int J Clin Exp Med* 2018; 11: 2350–2360.

59 Glatz T, Marjanovic G, Kulemann B, Sick O, Hopt UT, Hoeppner J. Hybrid minimally invasive esophagectomy vs. open esophagectomy: a matched case analysis in 120 patients. *Langenbecks Arch Surg* 2017; 402: 323–331.

60 Rinieri P, Ouattara M, Brioude G, Loundou A, de Briez N, Piessen G, Torres F, Lebuffe G, Triboulet JP, Burdall OC, Boddy AP, Fullick J, Blazeby J, Krysztopik R, Mu JW, Gao SG, Xue Q, Mao YS, Wang D, Zhao J, Khan M, Ashraf MI, Syed AA, Khattak S, Urooj N, Kanekiyo S, Takeda S, Tsutsui M, Nishiyama M. Long-term outcome of open versus hybrid minimally invasive Ivor Lewis esophagectomy: a propensity score matched study. *Eur J Cardiothorac Surg* 2017; 51: 223–229.

61 Briez N, Piessen G, Torres F, Lebuffe G, Triboulet JP, Mariette C. Effects of hybrid minimally invasive esophagectomy on major postoperative pulmonary complications. *Br J Surg* 2012; 99: 1547–1553.

62 Scarpa M, Cavallin F, Saadeh LM, Pinto E, Alfieri R, Cagol M et al. Hybrid minimally invasive esophagectomy for cancer: impact on postoperative inflammatory and nutritional status. *Dis Esophagus* 2016; 29: 1064–1070.

63 Burdall OC, Boddy AP, Fullick J, Blazey J, Krysztopik R, Streets C et al. A comparative study of survival after minimally invasive and open esophagectomy. *Surg Endosc* 2014; 29: 431–437.

64 Mu JW, Gao SG, Xue Q, Mao YS, Wang D, Zhao J et al. Updated experiences with minimally invasive McKeown esophagectomy for esophageal cancer. *World J Gastroenterol* 2015; 21: 12873–12881.

65 Khan M, Ashraf MI, Syed AA, Khattak S, Urooj N, Muzaffar A. Morbidity analysis in minimally invasive McKeown esophagectomy for oesophageal cancer versus conventional over the last 10 years, a single institution experience. *J Minim Invasive Surg* 2017; 13: 192–199.

66 Miyasaka D, Okushiba S, Sasaki T, Ebihara Y, Kawada M, Kitashiro S et al. Clinical evaluation of the feasibility of minimally invasive surgery in esophageal cancer. *Asian J Endosc Surg* 2013; 6: 26–32.

67 Kunisaki C, Kosaka T, Ono HA, Oshima T, Fujii S, Takagawa R et al. Significance of thoracoscopic-assisted surgery with a minithoracotomy and hand-assisted laparoscopic surgery for esophageal cancer: the experience of a single surgeon. *J Gastrointest Surg* 2011; 15: 1939–1951.

68 Kanekiyo S, Takeda S, Tsutsui M, Nishiyama M, Kitahara M, Shindo Y et al. Low invasiveness of thoracoscopic esophagectomy in the prone position for esophageal cancer: a propensity score-matched comparison of operative approaches between thoracoscopic and open esophagectomy. *Surg Endosc* 2018; 32: 1945–1953.

69 Zhao Y, Jiao W, Zhao J, Wang X, Luo Y, Wang Y. Anastomosis in minimally invasive Ivor Lewis esophagectomy via two ports provides equivalent perioperative outcomes to open. *Indian J Cancer* 2015; 51: 25.

70 Tan JT, Zhong JH, Yang Y, Mao NQ, Liu DS, Huang DM et al. Comparison of postoperative immune function in patients with thoracic esophageal cancer after video-assisted thoracoscopic surgery or conventional open esophagectomy. *Int J Surg* 2016; 30: 155–160.

71 Xie MR, Liu CQ, Guo MF, Mei XY, Sun XD, Xu MQ. Short-term outcomes of minimally invasive Ivor-Lewis esophagectomy for esophageal cancer. *Ann Thorac Surg* 2014; 97: 1721–1727.

72 Guo M, Xie B, Sun X, Hu M, Yang Q, Lei Y. A comparative study of the therapeutic effect in two protocols: video-assisted thoracic surgery combined with laparoscopy versus right open transthoracic esophagectomy for esophageal cancer management. *Chinese-German Journal of Clinical Oncology* 2013; 12: 68–71.

73 Willer BL, Worrell SG, Fitzgibbons RJ, Mittal SK. Incidence of diaphragmatic hernias following minimally invasive versus open transthoracic Ivor Lewis McKeown esophagectomy. *Hernia* 2012; 16: 185–190.

74 Liu XH, Hu Y, Li KK, Wang YJ, Jiang YG, Guo W. Intraoperative conversion does not affect the oncological outcomes of minimally invasive esophagectomy for treatment of esophageal cancer. *Surg Endosc* 2018; 32: 4517–4526.

75 Seesing MFJ, Gisbertz SS, Goense L, Van Hillegersberg R, Kroon HM, Lagarde SM et al. A propensity score matched analysis of open versus minimally invasive transthoracic esophagectomy in the Netherlands. *Ann Surg* 2017; 266: 839–846.

76 Meng F, Li Y, Ma H, Yan M, Zhang R. Comparison of outcomes of open and minimally invasive esophagectomy in 183 patients with cancer. *J Thorac Dis* 2014; 6: 1218–1224.

77 Li T, Zhao Y, Wu B, Ning ML, Zhao DW, Ye XF. Effects of laparo-thoracoscopic surgery and open surgery on pulmonary infection in elderly patients with esophageal cancer. *Int J Clin Exp Med* 2018; 11: 7104–7110.

78 Kauppi J, Nelskylä K, Huuhtanen R, Salo J, Räsänen J, Silvio E. Open versus minimally invasive esophagectomy: clinical outcomes for locally advanced esophageal adenocarcinoma. *Surg Endos* 2014; 29: 2614–2619.

79 Bakhos CT, Fabian T, Oyasiji TO, Gautam S, Gangadharan SP, Kent MS et al. Impact of the surgical technique on pulmonary morbidity after esophagectomy. *Ann Thorac Surg* 2012; 93: 221–227.

80 Tapias LF, Mathisen DJ, Wright CD, Wain JC, Gaissert HA, Muniappan A et al. Outcomes with open and minimally invasive Ivor Lewis esophagectomy after neoadjuvant therapy. *Ann Thorac Surg* 2016; 101: 1097–1103.

81 Sihag S, Wright CD, Wain JC, Gaissert HA, Lanuti M, Allan JS et al. Comparison of perioperative outcomes following open versus minimally invasive Ivor Lewis esophagectomy at a single, high-volume centre. *Eur J Cardiothorac Surg* 2012; 42: 430–437.

82 Izumi Y, Ryotokuji T, Suzuki T, Miura A, Kato T, Egashira H et al. Minimally invasive esophagectomy:
Minimally invasive transthoracic oesophagectomy

801

evaluation of mediastinal lymphadenectomy for T1b thoracic esophageal cancer. *Esophagus* 2011; 8: 267–272.

83 Huang HT, Wang F, Shen L, Xia CQ, Lu CX, Zhong CJ. Comparison of thoracolaparoscopic esophagectomy with cervical anastomosis with McKeown esophagectomy for middle esophageal cancer. *World J Surg Oncol* 2015; 13: 1–12.

84 Mu JW, Gao SG, Xue Q, Mao YS, Wang DL, Zhao J et al. Comparison of short-term outcomes and three year survival between total minimally invasive McKeown and dual-incision esophagectomy. *Thorac Cancer* 2017; 8: 80–87.

85 Kauppila JH, Helminen O, Kytö V, Gunn J, Lagergren J, Silvio E. Short-term outcomes following minimally invasive and open esophagectomy: a population-based study from Finland and Sweden. *Ann Surg Oncol* 2018; 25: 326–332.

86 Dolan JP, Kaur T, Diggs BS, Luna RA, Schipper PH, Tieu BH et al. Impact of comorbidity on outcomes and overall survival after open and minimally invasive esophagectomy for locally advanced esophageal cancer. *Surg Endosc* 2013; 27: 4094–4103.

87 Parameswaran R, Veeramootoo D, Krishnadas R, Cooper M, Berresford R, Wajed S. Comparative experience of open and minimally invasive esophageogastric resection. *World J Surg* 2009; 33: 1868–1875.

88 Mei X, Xu M, Guo M, Xie M, Liu C, Wang Z. Minimally invasive Ivor-Lewis esophagectomy is a feasible and safe approach for patients with oesophageal cancer. *ANZ J Surg* 2016; 86: 274–279.

89 Zhang X, Yang Y, Ye B, Sun Y, Guo X, Hua R et al. Minimally invasive esophagectomy is a safe surgical treatment for locally advanced pathologic T3 esophageal squamous cell carcinoma. *J Thorac Dis* 2017; 9: 2982–2991.

90 Ye B, Zhong CX, Yang Y, Fang WT, Mao T, Ji C-Y et al. Lymph node dissection in esophageal carcinoma: minimally invasive esophagectomy vs open surgery. *World J Gastroenterol* 2016; 22: 4750.

91 Goosenen JAH, Slaman AE, van Dieren S, Gisbertz SS, van Berge Henegouwen MI. Incidence and treatment of symptomatic diaphragmatic hernia after esophagectomy for cancer. *Ann Thorac Surg* 2018; 106: 199–206.

92 Thirunavukarasu P, Gabriel E, Attwood K, Kukar M, Hochwald SN, Nurkin SJ. Nationwide analysis of short-term surgical outcomes of minimally invasive esophagectomy for malignancy. *Int J Surg* 2016; 25: 69–75.

93 Chen X, Yang J, Peng J, Jiang H. Case-match analysis of combined thoracoscopic–laparoscopic versus open esophagectomy for esophageal squamous cell carcinoma. *Int J Clin Exp Med* 2015; 8: 13516–13523.

94 Wang W, Zhou Y, Feng J, Mei Y. Oncological and surgical outcomes of minimally invasive versus open esophagectomy for esophageal squamous cell carcinoma: a matched-pair comparative study. *Int J Clin Exp Med* 2015; 8: 15983–15990.

95 Mamidanna R, Bottle A, Aylin P, Faiz O, Hanna GB. Short-term outcomes following open versus minimally invasive esophagectomy for squamous cell carcinoma of the esophagus: a population-based national study. *Ann Surg* 2012; 255: 197–203.

96 Nafeux P, Moons J, Cooosemans W, Decaluwé H, Decker G, De Leyn P et al. Minimally invasive esophagectomy: a valuable alternative to open esophagectomy for the treatment of early oesophageal and gastro-oesophageal junction carcinoma. *Eur J Cardiothorac Surg* 2011; 40: 1455–1465.

97 Iwashashi M, Nakamori M, Nakamura M, Ojima T, Katsuda M, Iida T et al. Clinical benefits of thoracoscopic esophagectomy in the prone position for esophageal cancer. *Surg Today* 2014; 44: 1708–1715.

98 Gao Y, Wang Y, Chen L, Zhao Y. Comparison of three-field and minimally-invasive esophagectomy for esophageal cancer. *Interact Cardiovasc Thorac Surg* 2011; 12: 366–369.

99 Fei X, Liao J, Wang D, Xie N, Zhou G. Comparison of long-term outcomes of minimally invasive esophagectomy and open esophagectomy for esophageal squamous cell carcinoma. *Int J Clin Exp Med* 2016; 9: 14 361–14 368.

100 Li J, Shen Y, Tan L, Meng M, Wang H, Xi Y et al. Is minimally invasive esophagectomy beneficial to elderly patients with esophageal cancer? *Surg Endosc* 2015; 29: 925–930.

101 Li KK, Wang YJ, Liu XH, Wang RW, Jiang YG, Guo W. Propensity-matched analysis comparing survival after hybrid thoracoscopic–laparotomy esophagectomy and complete thoracoscopic–laparoscopic esophagectomy. *World J Surg* 2019; 43: 853–861.

102 Daiko H, Fujita T. Laparoscopic assisted versus open gastric pull-up following thoracoscopic esophagectomy: a cohort study. *Int J Surg* 2015; 19: 61–66.

103 Bonavina L, Scolari F, Aiolfi A, Bonitta G, Sironi A, Saino G et al. Early outcome of thoracoscopic and hybrid esophagectomy: propensity-matched comparative analysis. *Surgery* 2016; 159: 1073–1081.

104 Mao T, Fang W, Gu Z, Guo X, Ji C, Chen W. Comparison of perioperative outcomes between open and minimally invasive esophagectomy for esophageal cancer. *Thorac Cancer* 2015; 6: 303–306.

105 Yamashita K, Watanabe M, Mine S, Toihata T, Fukudome I, Okamura A et al. Minimally invasive esophagectomy attenuates the postoperative inflammatory response and improves survival compared with open esophagectomy in patients with esophageal cancer: a propensity score matched analysis. *Surg Endosc* 2018; 32: 4443–4450.

106 Kinjo Y, Kurita N, Nakamura F, Okabe H, Tanaka E, Kataoka Y et al. Effectiveness of combined thoracoscopic–laparoscopic esophagectomy: comparison of postoperative complications and midterm oncological outcomes in patients with esophageal cancer. *Surg Endosc* 2012; 26: 381–390.

107 Lee JM, Cheng JW, Lin MT, Huang PM, Chen JS, Lee YC. Is there any benefit to incorporating a laparoscopic procedure into minimally invasive esophagectomy? *The
impact on perioperative results in patients with esophageal cancer. World J Surg 2011; 35: 790–797.

108 Yanasoot A, Yolsuriyanwong K, Ruangsin S, Laohawiriyakamol S, Sunpaweravong S. Costs and benefits of different methods of esophagectomy for esophageal cancer. Asian Cardiovasc Thorac Ann 2017; 25: 513–517.

109 Smithers BM, Gotley DC, Martin I, Thomas JM. Comparison of the outcomes between open and minimally invasive esophagectomy. Ann Surg 2007; 245: 232–240.

110 Zingg U, Smithers BM, Gotley DC, Smith G, Aly A, Clough A et al. Factors associated with postoperative pulmonary morbidity after esophagectomy for cancer. Ann Surg Oncol 2011; 18: 1460–1468.

111 Chao YK, Hsieh MJ, Liu YH, Liu HP. Lymph node evaluation in robot-assisted versus video-assisted thoracoscopic esophagectomy for esophageal squamous cell carcinoma: a propensity-matched analysis. World J Surg 2018; 42: 590–598.

112 Park IK, Kim YT, Kang CH, Lee HJ, Park S, Hong Y. Comparison of robot-assisted esophagectomy and thoracoscopic esophagectomy in esophageal squamous cell carcinoma. J Thorac Dis 2016; 8: 2853–2861.

113 He H, Wu Q, Wang Z, Zhang Y, Chen N, Fu J et al. Short-term outcomes of robot-assisted minimally invasive esophagectomy for esophageal cancer: a propensity score matched analysis. J Cardiothorac Surg 2018; 13: 1–7.

114 Weksler B, Sharma P, Moudgil N, Chojnacki KA, Rosato EL. Robot-assisted minimally invasive esophagectomy is equivalent to thoracoscopic minimally invasive esophagectomy. Dis Esophagus 2012; 25: 403–409.

115 Deng HY, Huang WX, Li G, Li SX, Luo J, Alai G et al. Comparison of short-term outcomes between robot-assisted minimally invasive esophagectomy and video-assisted minimally invasive esophagectomy in treating middle thoracic esophageal cancer. Dis Esophagus 2018; 31: 1–7.

116 Weksler B, Sullivan JL. Survival after esophagectomy: a propensity-matched study of different surgical approaches. Ann Thorac Surg 2017; 104: 1138–1146.

117 Jeong DM, Kim JA, Ahn HJ, Yang M, Heo BY, Lee SH. Decreased incidence of postoperative delirium in robot-assisted thoracoscopic esophagectomy compared with open transthoracic esophagectomy. Surg Laparosc Endosc Percutan Tech 2016; 26: 516–522.

118 Osaka Y, Tachibana S, Ota Y, Suda T, Makuuti Y, Watanabe T et al. Usefulness of robot-assisted thoracoscopic esophagectomy. Gen Thorac Cardiovasc Surg 2018; 66: 225–231.

119 Wang HB, Guo Q, Li YH, Sun ZQ, Li TT, Zhang WX et al. Effects of minimally invasive esophagectomy and open esophagectomy on circulating tumor cell level in elderly patients with esophageal cancer. World J Surg 2016; 40: 1655–1662.

120 Wu X, He J, Jiang H, Song X, Tang X, Shen J et al. Fully thoracoscopic versus conventional open resection for esophageal carcinoma: a perioperative comparison. Thorac Cancer 2013; 4: 369–372.
Supporting information

Additional supporting information can be found online in the Supporting Information section at the end of the article.