

**Supplementary Table S1.** Search terms in PubMed, Embase and Cochrane Library

| PubMed   | Embase   | Cochrane Library  |
|--|--|---|
| ((Anastomotic leak OR anastomotic leakage OR postoperative leak OR postoperative leakage OR esophageal leak OR esophageal leakage OR esophageal fistula OR leakage OR fistula OR leak OR perforation OR upper gastrointestinal tract OR esophagus OR esophageal OR gastric OR stomach OR esophagectomy OR anastomosis)) OR (((Anastomotic Leak"[Mesh]) OR "Esophageal Fistula"[Mesh]) OR "Fistula"[Mesh]) OR "Upper Gastrointestinal Tract"[Mesh]) OR "Esophagus"[Mesh] OR "Stomach"[Mesh]) OR "Esophagectomy"[Mesh]) OR "Anastomosis, Surgical"[Mesh])) AND (((endoscopic vacuum therapy OR endoscopic vacuum assisted closure OR endoluminal vacuum therapy OR vacuum therapy OR vacuum assisted closure OR negative pressure wound therapy OR endoscopic negative pressure therapy OR negative pressure therapy OR endovac therapy OR endo sponge)) OR "Negative-Pressure Wound Therapy"[Mesh])) AND (((treatment outcome OR mortality OR hospital duration OR treatment duration OR complication) OR ("Treatment Outcome"[Mesh] OR "Mortality"[Mesh] OR "Duration of Therapy"[Mesh]))) | (('anastomotic leak' OR 'anastomotic leakage' OR 'postoperative leak' OR 'postoperative leakage' OR 'esophageal leak' OR 'esophageal leakage' OR 'esophageal fistula' OR 'leak' OR 'perforation' OR 'upper gastrointestinal tract' OR 'esophagus' OR 'esophageal' OR 'gastric' OR 'stomach' OR 'esophagectomy' OR 'anastomosis') OR ('anastomosis leakage')/exp OR ('postoperative leak')/exp OR ('esophageal leak')/exp OR ('esophagus fistula')/exp OR ('leakage')/exp OR ('fistula')/exp OR ('perforation')/exp OR ('upper gastrointestinal tract')/exp OR ('esophagus')/exp OR ('stomach')/exp)) AND ((('endoscopic vacuum therapy' OR 'endoscopic vacuum assisted closure' OR 'endoluminal vacuum therapy' OR 'vacuum therapy' OR 'vacuum assisted closure' OR 'negative pressure wound therapy' OR 'endoscopic negative pressure therapy' OR 'negative pressure therapy' OR 'endovac therapy' OR 'endo sponge') OR ('endoscopic vacuum therapy')/exp OR ('endoluminal vacuum therapy')/exp OR ('vacuum assisted closure')/exp OR ('vacuum therapy device')/exp)) AND (((('treatment outcome' OR 'mortality' OR 'hospital duration' OR 'treatment duration' OR 'complication') OR ('treatment outcome')/exp OR ('mortality')/exp OR ('treatment duration')/exp OR ('complication')/exp))) | ((anastomotic leak OR anastomotic leakage OR postoperative leak OR postoperative leakage OR esophageal leak OR esophageal leakage OR esophageal fistula OR leakage OR fistula OR leak OR perforation OR upper gastrointestinal tract OR esophagus OR esophageal OR gastric OR stomach OR esophagectomy OR anastomosis) OR ([Anastomotic Leak] explode all trees) OR ([Esophageal Fistula] explode all trees) OR ([Fistula] explode all trees) OR ([Upper Gastrointestinal Tract] explode all trees) OR ([Esophagus] explode all trees) OR ([Stomach] explode all trees) OR ([Esophagectomy] explode all trees) OR ([Anastomosis, Surgical] explode all trees)) AND ((endoscopic vacuum therapy OR endoscopic vacuum assisted closure OR endoluminal vacuum therapy OR vacuum therapy OR vacuum assisted closure OR negative pressure wound therapy OR endoscopic negative pressure therapy OR negative pressure therapy OR endovac therapy OR endo sponge) OR ([Negative-Pressure Wound Therapy] explode all trees)) AND ((treatment outcome OR mortality OR hospital duration OR treatment duration OR complication) OR ([Treatment Outcome] explode all trees) OR ([Mortality] explode all trees) OR ([Duration of Therapy] explode all trees)) |

**Supplementary Table S2.** Definition of clinical success, detail indication, and cause of mortality in the 29 studies included

| Authors        | Definition of clinical success                     | Detail indication   | Mortality (n) | Cause of mortality  |
|----------------|--|---|---------------|---|
| Palmes 2020    | NA   | Post-op fistula(n=4): 4 Ivor Lewis (29% SCC, 71% EAC)   | 2             | sepsis due to persistent leak (closure fail)  |
| Jung 2019      | closure of defect under endoscopy                  | Post-op leak(n=23): 15 Ivor Lewis, 8 gastrectomy (5 SCC, 17 EAC, 1 NET)<br>Perforation(n=7): 2 endoscopic dilation, 1 TEE, 1 postoperative torquation, 1 endoscopy, 1 Boerhaave, 1 ischemia | 1<br>1        | multi-organ failure after mixed cardiogenic and septic shock (closure fail)<br>underlying advanced esophageal cancer (closure fail) |
| Jeon 2019      | NA   | Post-op leak(n=22): 14 Ivor Lewis, 4 modified McKeown, 2 colon interposition, 2 gastrectomy (19 SCC, 2 EAC, 1 GIST)   | 0             | -   |
| Watson 2019    | closure of defect under endoscopy and esophagogram | Post-op leak(n=2): 2 Ivor Lewis (2 EAC)<br>Post-op fistula(n=1): gastrectomy  | 0             | -   |
| Pinto 2019     | NA   | Post-op leak(n=2): 1 RYGB, 1 sleeve gastrectomy   | 0             | -   |
| Morell 2019    | closure of defect under endoscopy                  | Post-op leak(n=6): 4 RYGB, 2 sleeve gastrectomy   | 0             | -   |
| Min 2019       | closure of defect under endoscopy                  | Post-op leak(n=20): 7 Ivor Lewis, 8 3-field lymph node dissection, 4 McKeown, 1 Transhiatal esophagectomy   | 1             | sepsis due to persistent leak (closure fail)  |
| Loske 2019     | closure of defect under endoscopy                  | Post-op leak(n=1): 1 Billroth-1 gastro-jejunostomy<br>Perforation(n=10): 1 endoscopic dilation, 1 operative drain, 1 surgical papillectomy, 1 ERCP, 6 perforated ulcer                      | 0<br>2        | NA (closure success)  |
| Leeds 2019     | closure of defect under endoscopy or esophagogram  | NA  | NA            | NA  |
| Walsh 2019     | closure of defect under endoscopy and esophagogram | Post-op leak(n=1): 1 Ivor Lewis<br>Perforation(n=1): 1 Boerhaave  | 1<br>0        | aspiration pneumonia (closure success)  |
| Alakkari 2019  | closure of defect under esophagogram               | Post-op leak(n=1): 1 Merendino esophageal reconstruction<br>Perforation(n=1): 1 spontaneous esophageal perforation  | 0<br>0        | -<br>-  |
| Berlth 2018    | closure of defect under endoscopy                  | Post-op leak(n=111)<br>EVT(n=34): 74% Ivor Lewis<br>SEMS(n=77): 88% Ivor Lewis  | 14<br>3<br>11 | 11 sepsis due to persistent leak(closure fail), 3 sepsis due to other cause (closure success)                                       |
| Valli 2018     | closure of defect under endoscopy or esophagogram  | Post-op leak(n=11): 6 esophagogastrostomy, 3 esophagojejunostomy, 1 gastrojejunostomy, 1 sleeve gastrectomy<br>Fistula(n=1): 1 TEE  | 0             |   |
| Still 2018     | closure of defect under endoscopy or esophagogram  | Post-op leak(n=2): anastomosis site leak<br>Perforation(n=9): 8 iatrogenic perforation, 1 Boerhaave,<br>Post-op leak(n=2): 2 bronchoesophageal fistula                                      | 1<br>NA       | persistent leak (closure fail)<br>NA  |
| Pournaras 2018 | closure of defect under endoscopy                  | Post-op leak(n=14): anastomosis site leak<br>Perforation(n=7): 7 iatrogenic perforation   | 0<br>1        | withdrawing consent for further intervention following one EVT  |

|                        |  |   |         |   |
|------------------------|--|---|---------|---|
| <b>Ooi 2018</b>        | closure of defect under endoscopy or esophagogram  | Post-op leak(n=6): 2 esophagectomy, 2 sleeve gastrectomy, 1 total gastrectomy, 1 intra-op injury due to gastric band<br>Perforation(n=4): 2 endoscopic dilation, 1 Boerhaave, 1 TEE | 1<br>1  | sepsis due to persistent leak (closure fail)<br>sepsis due to persistent leak (closure fail)  |
| <b>Noh 2018</b>        | closure of defect under endoscopy and esophagogram | Post-op leak(n=12): 11 Ivor Lewis, 1 esophageal diverticulectomy  | 1       | aspiration pneumonia (closure success)  |
| <b>Loske 2018</b>      | NA   | Post-op leak(n=3): 2 Ivor Lewis, 1 gastrectomy<br>Perforation(n=1): 1 Boerhaave   | 0<br>0  | -<br>-  |
| <b>Laukoetter 2017</b> | closure of defect under endoscopy                  | Post-op leak(n=39): anastomosis site leak<br>Perforation(n=13): 9 iatrogenic perforation, 4 Boerhaave   | 5<br>0  | 1 multiorgan failure due to persistent leak (closure fail), 2 EVT related fatal bleeding (closure success), 1 pneumonia (closure success) |
| <b>Kuehn 2016</b>      | NA   | Post-op leak(n=11): anastomosis site leak<br>Perforation(n=10): 8 iatrogenic perforation, 2 Boerhaave   | 1<br>0  | sepsis due to persistent leak (closure fail)  |
| <b>Hwang 2016</b>      | closure of defect under endoscopy or esophagogram  | Post-op leak(n=18)<br>EVT(n=7): 71% Ivor Lewis<br>SEMS(n=11): 36% Ivor Lewis  | 0<br>2  | cancer progression (closure fail)   |
| <b>Möschler 2015</b>   | NA   | Post-op leak(n=5): 5 thoracoabdominal resection of the esophagus<br>Perforation(n=5): 3 iatrogenic perforation, 2 foreign body  | 2<br>0  | cardiovascular disease (closure success)  |
| <b>Mennigen 2015</b>   | closure of defect under endoscopy and esophagogram | Post-op leak(n=45)<br>EVT(n=15): 100% Ivor Lewis<br>SEMS(n=30): 100% Ivor Lewis   | 1<br>8  | pneumonia (closure success)<br>4 sepsis (closure success), 4 sepsis (closure fail)  |
| <b>Loske 2015</b>      | NA   | Perforation(n=10): 8 iatrogenic perforation, 2 foreign body   | 0       | -   |
| <b>Heits 2014</b>      | closure of defect under endoscopy                  | Perforation(n=10): 4 iatrogenic perforation, 1 foreign body, 5 Boerhaave  | 1       | Heart failure (closure success)   |
| <b>Liu 2014</b>        | NA   | Post-op leak(n=5): 4 Ivor Lewis, 1 McKeown  | 0       | -   |
| <b>Schorsch 2013</b>   | NA   | Post-op leak(n=17): 7 thoracoabdominal esophagogastrectomy, 5 transhiatal esophagogastrectomy, 5 gastrectomy  | 1       | 1 sepsis (closure fail)   |
| <b>Schniewind 2013</b> | closure of defect under endoscopy or esophagogram  | Post-op leak(n=29)<br>EVT(n=17): 100% Ivor Lewis<br>SEMS(n=12): 100% Ivor Lewis   | 2<br>5  | NA<br>NA  |
| <b>Brangewitz 2013</b> | closure of defect under endoscopy or esophagogram  | EVT(n=32): 94% anastomosis site leak<br>SEMS(n=39): 79% anastomosis site leak   | 5<br>11 | NA<br>NA  |

EAC esophageal adenocarcinoma; ERCP, endoscopic retrograde cholangiopancreatography; EVT, endoscopic vacuum therapy; NA, not available; NET, neuroendocrine tumor; RYGB, Roux-en-Y gastric bypass; SEMS, self-expanding metal stent; SCC, squamous cell carcinoma; TEE transesophageal echocardiography

**Supplementary Table S3.** Detail information of the 4 studies included patients with fistula

| Authors     | Definition of fistula  | Detail information                      | Outcome  |
|-------------|--|---|--|
| Palmes 2020 | Tracheoesophageal fistula (TEF) or bronchoesophageal fistula (BEF) | 2 Lt.BEF, 1 Rt.BEF, 1 TEF               | 2 Clinical success<br>2 Clinical fail → sepsis → death |
| Watson 2019 | NA   | 1 gastroesophageal junction fistula     | 1 Clinical success                                     |
| Valli 2018  | NA   | Chronic fistula after TEE               | 1 Clinical fail → sepsis → death                       |
| Still 2018  | NA   | 2 BEF (EVT + bronchial stent placement) | NA   |

EVT, endoscopic vacuum therapy; NA, not available; TEE transesophageal echocardiography

**Supplementary Table S4.** Patients characteristics of studies comparing endoscopic vacuum therapy and self-expanding metal stent

| Study, treatment method, n | Patients, n | Male, n | Age (median, years) | Negative pressure (mmHg) | Oncologic resection, % | Neoadjuvant therapy, % | Etiology :surgical anastomotic leak, % | (Sub-) total esophagectomy, % | Reconstruction type esophagogastrostomy, % | Type of stent              | Defect size (median, mm) |
|----------------------------|-------------|---------|---------------------|--------------------------|------------------------|------------------------|--|-------------------------------|--|----------------------------|--------------------------|
| <b>Brangewitz 2013</b>     |             |         |                     |                          |                        |                        |  |                               |  |                            |                          |
| EVT                        | 32          | 28      | 63 (45-84)          | 125                      | 88                     | 56                     | 94                                     | NA                            | 44   | NA                         | NA                       |
| SEMS                       | 39          | 30      | 62 (32-78)          | NA                       | 74                     | 15                     | 79                                     | NA                            | 69   | Fully covered              | NA                       |
| <b>Schniewind 2013</b>     |             |         |                     |                          |                        |                        |  |                               |  |                            |                          |
| EVT                        | 17          | NA      | NA                  | 70-80                    | NA                     | NA                     | 100                                    | 100                           | NA   | NA                         | NA                       |
| SEMS                       | 12          | NA      | NA                  | NA                       | NA                     | NA                     | 100                                    | 100                           | NA   | NA                         | NA                       |
| <b>Mennigen 2015</b>       |             |         |                     |                          |                        |                        |  |                               |  |                            |                          |
| EVT                        | 15          | 14      | 56 (42-76)          | 100-125                  | 100                    | 73                     | 100                                    | 100                           | 100  | NA                         | NA                       |
| SEMS                       | 30          | 21      | 66 (40-92)          | NA                       | 93                     | 43                     | 100                                    | 100                           | 100  | Fully covered              | NA                       |
| <b>Hwang 2016</b>          |             |         |                     |                          |                        |                        |  |                               |  |                            |                          |
| EVT                        | 7           | 5       | 71 (63-78)          | 125                      | 100                    | NA                     | 100                                    | 71                            | NA   | NA                         | 8.1                      |
| SEMS                       | 11          | 9       | 67 (55-81)          | NA                       | 100                    | NA                     | 100                                    | 36                            | NA   | fully or partially covered | 6.6                      |
| <b>Berlth 2018</b>         |             |         |                     |                          |                        |                        |  |                               |  |                            |                          |
| EVT                        | 34          | 29      | 65 (43-84)          | 125                      | 100                    | 53                     | 100                                    | 74                            | 74   | NA                         | NA                       |
| SEMS                       | 77          | 63      | 64 (43-88)          | NA                       | 100                    | 65                     | 100                                    | 88                            | 88   | Fully covered              | NA                       |

EVT, endoscopic vacuum therapy; NA, not available; SEMS, self-expanding metal stent

**Supplementary Table S5.** Methodological quality

| Authors        | Selection<br>Representativeness | Selection<br>Selection | Selection<br>Ascertainment | Selection<br>Outcome of<br>interest | Comparability<br>Comparability | Outcome<br>Assessment of<br>outcome | Outcome<br>Duration of<br>follow-up | Outcome<br>Adequacy of<br>follow-up | Total Score<br>(maximum:<br>9 stars) |
|----------------|---------------------------------|------------------------|----------------------------|-------------------------------------|--------------------------------|-------------------------------------|-------------------------------------|-------------------------------------|--------------------------------------|
| Palmes 2020    | 0                               | NA                     | *                          | *                                   | NA                             | *                                   | NA                                  | NA                                  | 3                                    |
| Jung 2019      | *                               | NA                     | *                          | *                                   | NA                             | *                                   | *                                   | 0                                   | 5                                    |
| Jeon 2019      | *                               | NA                     | *                          | *                                   | NA                             | *                                   | *                                   | 0                                   | 5                                    |
| Watson 2019    | 0                               | NA                     | *                          | *                                   | NA                             | *                                   | 0                                   | 0                                   | 3                                    |
| Pinto 2019     | 0                               | NA                     | *                          | *                                   | NA                             | *                                   | 0                                   | 0                                   | 3                                    |
| Morell 2019    | 0                               | NA                     | *                          | *                                   | NA                             | *                                   | 0                                   | 0                                   | 3                                    |
| Min 2019       | *                               | NA                     | *                          | *                                   | NA                             | *                                   | *                                   | 0                                   | 5                                    |
| Loske 2019     | 0                               | NA                     | *                          | *                                   | NA                             | *                                   | 0                                   | 0                                   | 3                                    |
| Leeds 2019     | *                               | NA                     | *                          | *                                   | NA                             | *                                   | 0                                   | 0                                   | 4                                    |
| Walsh 2019     | 0                               | NA                     | *                          | *                                   | NA                             | *                                   | 0                                   | 0                                   | 3                                    |
| Alakkari 2019  | 0                               | NA                     | *                          | *                                   | NA                             | *                                   | 0                                   | 0                                   | 3                                    |
| Berlth 2018    | *                               | NA                     | *                          | *                                   | 0                              | *                                   | 0                                   | 0                                   | 4                                    |
| Valli 2018     | 0                               | NA                     | *                          | *                                   | NA                             | *                                   | 0                                   | 0                                   | 3                                    |
| Still 2018     | 0                               | NA                     | *                          | *                                   | NA                             | *                                   | 0                                   | 0                                   | 3                                    |
| Pournaras 2018 | *                               | NA                     | *                          | *                                   | NA                             | *                                   | 0                                   | 0                                   | 4                                    |
| Ooi 2018       | 0                               | NA                     | *                          | *                                   | NA                             | *                                   | 0                                   | 0                                   | 3                                    |
| Noh 2018       | *                               | NA                     | *                          | *                                   | NA                             | *                                   | *                                   | *                                   | 6                                    |
| Loske 2018     | 0                               | NA                     | *                          | *                                   | NA                             | *                                   | 0                                   | 0                                   | 3                                    |
| Laukoetter     | *                               | NA                     | *                          | *                                   | NA                             | *                                   | *                                   | *                                   | 6                                    |
| Kuehn 2016     | *                               | NA                     | *                          | *                                   | NA                             | *                                   | *                                   | *                                   | 6                                    |
| Hwang 2016     | *                               | NA                     | *                          | *                                   | 0                              | *                                   | 0                                   | 0                                   | 4                                    |
| Möschler 2015  | 0                               | NA                     | *                          | *                                   | NA                             | *                                   | 0                                   | 0                                   | 3                                    |
| Mennigen 2015  | *                               | NA                     | *                          | *                                   | 0                              | *                                   | 0                                   | 0                                   | 4                                    |
| Loske 2015     | 0                               | NA                     | *                          | *                                   | NA                             | *                                   | 0                                   | 0                                   | 3                                    |
| Heits 2014     | 0                               | NA                     | *                          | *                                   | NA                             | *                                   | 0                                   | 0                                   | 3                                    |
| Liu 2014       | 0                               | NA                     | *                          | *                                   | NA                             | *                                   | 0                                   | 0                                   | 3                                    |
| Schorsch 2013  | *                               | NA                     | *                          | *                                   | NA                             | *                                   | 0                                   | 0                                   | 4                                    |
| Schniewind     | *                               | NA                     | *                          | 0                                   | *                              | *                                   | 0                                   | 0                                   | 4                                    |
| Brangewitz     | *                               | NA                     | *                          | *                                   | 0                              | *                                   | 0                                   | 0                                   | 4                                    |