

Diagnostic evaluation, surgical technique, and perioperative management after esophagectomy: consensus statement of the German Advanced Surgical Treatment Study Group

Daniel Palmes · Matthias Brüwer · Franz G. Bader ·
Michael Betzler · Heinz Becker · Hans-Peter Bruch ·
Markus Büchler · Heinz Buhr · B. Michael Ghadimi ·
Ulrich T. Hopt · Ralf Konopke · Katja Ott ·
Stefan Post · Jörg-Peter Ritz · Ulrich Ronellenfitch ·
Hans-Detlev Saeger · Norbert Senninger ·
German Advanced Surgical Treatment Study Group

Received: 6 May 2011 / Accepted: 7 June 2011 / Published online: 29 June 2011
© Springer-Verlag 2011

Abstract

Purpose Correct diagnosis, surgical treatment, and perioperative management of patients with esophageal carcinoma remain crucial for prognosis within multimodal treatment procedures. This study aims to achieve a consensus regarding current management strategies in esophageal cancer by questioning a panel of experts from the German Advanced Surgical Treatment Study (GAST) group, comprised of 9 centers specialized in esophageal surgery, with a combined total of >220 esophagectomies per year.

Materials and methods The Delphi method, a systematic and interactive, evidence-based approach, was used to obtain consensus statements from the GAST group regarding ambiguities and disparities in diagnosis, patient selection, surgical technique, and perioperative management of patients with esophageal carcinoma. After four rounds of surveys, agreement was measured by Likert scales and defined as full (100% agreement), near ($\geq 66.6\%$ agreement), or no consensus ($< 66.6\%$ agreement).

D. Palmes (✉) · M. Brüwer · N. Senninger
Department of General and Visceral Surgery,
University of Münster,
Waldeyerstrasse 1,
48149 Münster, Germany
e-mail: palmes@uni-muenster.de

H. Becker · B. M. Ghadimi
Department of General and Visceral Surgery,
Göttingen University Medical Center,
Göttingen, Germany

F. G. Bader · H.-P. Bruch
Department of Surgery, University of Schleswig Holstein,
Campus Lübeck,
Lübeck, Germany

U. T. Hopt
Department of General and Visceral Surgery,
University of Freiburg,
Freiburg im Breisgau, Germany

M. Betzler
Department of Surgery, Alfried Krupp Hospital,
Essen, Germany

R. Konopke · H.-D. Saeger
Department of General, Thoracic and Vascular Surgery,
School of Medicine, Dresden University of Technology,
Dresden, Germany

M. Büchler · K. Ott
Department of Surgery, University of Heidelberg,
Heidelberg, Germany

H. Buhr · J.-P. Ritz
Department of General, Vascular and Thoracic Surgery,
Charité—Campus Benjamin Franklin,
Berlin, Germany

S. Post · U. Ronellenfitch
Department of Surgery, Medical Faculty Mannheim,
University Medical Centre Mannheim, Heidelberg University,
Mannheim, Germany

Results Full or near consensus was obtained for essential aspects of esophageal cancer staging, proper surgical technique, perioperative management and indication for primary surgery, and neoadjuvant treatment or palliative treatment. No consensus was achieved regarding acceptability of minimally invasive technique and postoperative nutrition after esophagectomy.

Conclusion The GAST consensus statement represents a position paper for treatment of patients with esophageal carcinoma which both contributes to the development of clinical treatment guidelines and outlines topics in need of further clinical studies.

Keywords Consensus statement · Esophageal carcinoma · Multimodal treatment · Delphi method · German Advanced Surgical Treatment Study Group

Introduction

Over the past years, treatment of esophageal carcinoma (EC) has fundamentally changed, resulting in a sophisticated multidisciplinary approach combining surgery, chemotherapy, and radiotherapy [1]. At present, ambiguities and disparities remain in patient selection, diagnosis, indication for neoadjuvant treatment, favored surgical technique, and perioperative management. To collate and disseminate information regarding these aspects and create a clinical consensus statement, a consensus panel was convened by the German Advanced Surgical Treatment Study (GAST) group. The GAST group is comprised of 9 centers specialized in esophageal surgery with a combined total of >220 (median 25 per center, range 11–45) esophagectomies per year. A modified Delphi method, a rigorous and standardized approach to minimize bias and facilitate consensual position, was employed. The resulting consensus statement reflects the opinions of an organized group of experts, reviews the current literature, and outlines specific areas of controversy and ambiguity that call for additional study.

Materials and methods

To formulate consensus statements, the Delphi method was utilized. This systematic and interactive forecasting method

enables equal input from each panel member and reduces undue influence of a minority of participants [2]. The consensus statement development process consisted of expert panel appointment, survey development, four rounds of panel surveys including discussion of ambiguous items requiring clarification, and repeat of the survey with ensuing final analysis and interpretation.

The panel consisted of 17 experts in 9 centers specialized in EC surgery. After panel recruitment, a qualitative group survey was conducted to help determine the focus of the consensus statement. This survey concentrated on areas of controversy, knowledge gaps, variances in practice, and disparities of opinion. Topics for the clinical consensus statement were brainstormed and refined, including:

1. Diagnostic evaluation (including patient selection for neoadjuvant treatment)
2. Surgical technique
3. Perioperative management
4. Treatment of anastomotic complications

The first qualitative group survey employed free text responses to open-ended questions that covered the following categories: (1) diagnostic evaluation (patient selection for primary surgery and neoadjuvant treatment vs. palliative treatment, response control after neoadjuvant treatment, and treatment of high/cervical EC), (2) proper surgical technique (antibiotic prophylaxis, patient-positioning and surgical access, technique of esophagogastrotomy, and pyloric drainage), (3) perioperative management (anesthesiological requirements, timing of extubation, management of nasogastric tube and enteral nutrition, and routine control of anastomosis), and (4) management of anastomotic complications (diagnosis and stage-adjusted treatment). After reviewing the responses, targeted questions including statements were formulated. Once each panelist had completed the survey, the responses were summarized and reviewed, and a new panel survey was designed in order to reconcile any statements that were found to have no consensus or to be irrelevant. After three rounds of panel surveys, a three-point Likert scale was introduced containing the categories “agree”, “disagree”, and “neutral” [2]. For the Likert scales, a full consensus was defined as a 100% agreement, near consensus as a $\geq 66.6\%$ agreement, and no consensus as a $< 66.6\%$ agreement.

Results and discussion

Topic 1: Patient selection and diagnostic evaluation

Initial diagnostics and imaging techniques for EC staging

Statement	Agreed	Neutral	Disagreed	Result
Mandatory initial diagnostics and imaging techniques in patients with EC include endoscopy, endoscopic ultrasound, tumor biopsy, CT scanning of thorax and abdomen, and bronchoscopy in case of suprabifurcal squamous cell carcinoma.	100%	0%	0%	Full consensus

Preoperative endoscopy should investigate parameters of surgical importance, e.g., upper and lower cancer demarcation, distance of hiatus and mucosal esophagus–cardia border from the frontal dental line in centimeter, as well as extent of Barrett’s mucosa and upper esophageal sphincter in upper esophageal third cancer [3]. Endoscopic ultrasound represents the method of choice for detecting local tumor infiltration and peritumoral lymphadenopathy. Although tending to be operator-dependent and its accuracy appears to be limited in tumors with a diameter >5 mm or that are located at the esophagogastric junction, it shows the highest sensitivity when compared to CT and FDG–PET–CT [4–6]. Detection of distant metastasis should be performed by conventional CT scanning of thorax and

abdomen. Although there is strong evidence that 18F FDG uptake correlates with the presence of viable tumor mass, functional imaging techniques, such as PET or PET–CT, are not yet part of the standard diagnostic work-up in patients with esophageal carcinoma and should only be used in the setting of clinical trials [5, 7]. Fiberoptic bronchoscopy should be performed in patients with EC located at or above the level of the tracheal bifurcation (i.e., suprabifurcal esophageal cancer), which is frequently complicated by its spread into the airways [8]. Further, potentially pre-existing bronchopulmonary infections can be detected early on by preoperative bronchoscopy, thus decreasing the incidence of pulmonary complications after esophagectomy [9].

Indication for primary surgical resection, neoadjuvant chemotherapy followed by surgery, and definite radiochemotherapy

Statement	Agreed	Neutral	Disagreed	Result
Primary surgical resection with radical esophagectomy and lymphadenectomy should be performed in patients with non-metastatic, resectable EC (cT1-2 N0 M0).	88.9%	11.1%	0	Near consensus
Neoadjuvant treatment followed by surgery is beneficial in patients with advanced but resectable, non-metastatic EC (>cT2 and/or Np0 and M0) who respond well to neoadjuvant treatment.	77.8%	22.2%	0	Near consensus
Definite radiochemotherapy represents a treatment option for cervical EC (<5 cm distance to upper esophageal sphincter) that are not eligible for R0 resection.	77.8%	11.1%	11.1%	Near consensus
Patients with resectable EC and signs of lymph node metastasis of the coeliac trunk should be treated by neoadjuvant treatment followed by surgery.	100%	0	0	Full consensus

Radical esophagectomy and lymphadenectomy is currently the only well-established curative treatment modality in patients with resectable, non-metastatic EC, if complete R0 resection of the esophagus can be achieved. Primary surgery should be performed in patients with non-metastatic, resectable EC (cT1-2 N0 M0) who are fit enough to undergo major surgery [10, 11]. Palliative esophagectomy currently represents an unusual and rare treatment option, mostly used in patients with interventionally unmanageable risks (e.g., bleeding, perforation) or contra-indications for radiochemotherapy.

Whether neoadjuvant treatment followed by surgery improves survival in patients with esophageal carcinoma is currently under discussion [10]. While some meta-analyses report improved survival after neoadjuvant therapy in the subgroup of well-responding patients, it is established that neoadjuvant treatment increases morbidity and surgical risk [12–15]. To take into account these risks and

the inconclusive clinical studies, neoadjuvant treatment and the following surgery should currently only be carried out for patients in good general condition with advanced but resectable, non-metastatic EC (>cT2 and/or Npos and M0). It should be noted that lymph node metastases at the coeliac trunk (formally M1a) should be treated as regional lymph node metastases [16–19]. If necessary, staging laparoscopy should be performed to confirm the diagnosis or rule out a peritoneal carcinosis.

The concept of definitive radiochemotherapy for EC should currently be regarded as preliminary and is subject to further studies [10, 20, 21]. Patients with cervical esophageal squamous cell carcinoma (<5 cm distance to the upper esophageal sphincter) may benefit from definitive radiochemotherapy. However, this treatment option competes with limited resection and reconstruction by a free jejunal graft which is associated with low mortality but represents a complex surgical procedure [22].

Neoadjuvant treatment regimen

Statement	Agreed	Neutral	Disagreed	Result
Neoadjuvant treatment of advanced EC (>cT2 and/or Npos and M0) should be performed either by chemotherapy in case of adenocarcinoma or by radiochemotherapy in case of squamous cell carcinoma.	66.7%	22.2%	11.1%	Near consensus
No valid method for response control to neoadjuvant treatment is currently available preoperatively. Instead, restaging should be performed 1–2 weeks after completion of neoadjuvant treatment to exclude distant metastases before surgery.	77.8%	11.1%	11.1%	Near consensus
Response or non-response to neoadjuvant treatment is defined by histological examination of the resected specimen. Adjuvant treatment is performed in case of non-response.	77.8%	11.1%	11.1%	Near consensus
4–6 weeks should be allowed between completion of neoadjuvant treatment and surgery to reduce the risk of wound healing disorders and to improve the general preoperative condition of the patient.	66.7%	11.1%	22.2%	Near consensus
Further studies are necessary to define (1) the standard method for response control, (2) the timing of response control, (3) the definition of response vs. non-response, and (4) the treatment approach in responders and non-responders.	77.8%	22.2%	0	Near consensus

According to current studies, it is not yet possible to conclusively assess whether neoadjuvant treatment followed by surgery improves survival in EC patients. A detailed review of the literature regarding neoadjuvant radio- and/or chemotherapy followed by surgery vs. surgery alone has been done elsewhere [10]. The authors conclude that squamous cell carcinoma patients seem to benefit from neoadjuvant radiochemotherapy vs. neoadjuvant radiotherapy or surgery alone [14, 15, 23, 24]. However, this small survival benefit is achieved at the cost of increased surgical risk and increased morbidity [25–27]. For patients with adenocarcinoma of the esophagus, neoadjuvant chemotherapy and radiochemotherapy improve survival [28] and neoadjuvant radiochemotherapy is

associated with increased complication rates vs. neoadjuvant chemotherapy alone [12].

There is currently no universally accepted, reproducible, and reliable method for response assessment after neoadjuvant treatment of EC. This is due in part to differing neoadjuvant therapy regimens, differing methods for response assessment, e.g., CT scan, endoscopy, endoscopic ultrasound or PET–CT, and differing time frames for response control [6, 29, 30]. This leads to varying definitions of “response” and “non-response” and translates to variations in the decision of whether or not to continue neoadjuvant treatment. As long as no standards are available regarding neoadjuvant treatment and method and timing of response control, response to neoadjuvant

treatment should only be evaluated by histological examination of resected specimens. In case of non-response, adjuvant treatment should be performed postoperatively, possibly using a different therapy regimen. Restaging should be carried out 1–2 weeks after completion of neoadjuvant treatment in order to exclude distant metastasis before surgery. However, some studies show that non-responders do not profit from adjuvant treatment, even if the therapy regimen is different to the neoadjuvant treatment, making a reliable method for response control highly desirable [31].

The best time for surgery after neoadjuvant treatment has not been established yet. Neoadjuvant treatment can cause esophagitis or delayed wound healing; therefore, the risk of

surgical complications can be increased when surgery is performed immediately after neoadjuvant treatment [26]. On the other hand, the biologic effect of neoadjuvant treatment appears to influence the extent of surgery, for example, through downsizing [28]. Therefore, the GAST group recommends surgery during a time slot of 4–6 weeks after completion of neoadjuvant treatment.

Nonetheless, the formally reached “near consensus” regarding all statements concerning the neoadjuvant treatment regimen should not obscure the fact that further studies are absolutely necessary to define a standard method and time frame for response control and the appropriate treatment approach for responders and non-responders.

Palliation of EC

Statement	Agreed	Neutral	Disagreed	Result
Palliation of EC should be performed by chemotherapy and/or radiotherapy in an individually tailored approach. Esophageal obstruction should be treated endoluminally, e.g., by dilatation or stenting. When necessary, enteral intake should be enabled through a PEG tube or jejunal catheter.	100%	0	0	Full consensus

In patients with unresectable or inoperable EC (due to local invasion, distant metastasis, and medical comorbidities), quality of life will take precedence over long-term prognosis. EC palliation should be performed by chemotherapy and radiotherapy in an individual approach, achieving locoregional control and prolonging survival in some patients [32]. Restoration and maintenance of the ability to swallow, as well as control of pain and bleeding, represent the primary objectives for best supportive care in

these patients [33]. Esophageal obstruction should be treated by endoluminal therapy, e.g., by dilatation, stent, laser ablation, or photodynamic therapy. Enteral food intake should be ensured by PEG tube or jejunal catheter [32, 33]. Palliative esophagectomy also provides palliation in the setting of EC but should be restricted to patients with severe complications (e.g., perforation or incontrollable tumor bleeding) due to its increased risk of morbidity and mortality in relation to non-surgical palliative options.

Topic 2: Surgical technique

Statement	Agreed	Neutral	Disagreed	Result
Perioperative antibiotic prophylaxis should be performed using the combination of a 2nd generation cephalosporin and nitroimidazole if necessary (e.g., in case of reconstruction using a colonic conduit) and should be repeated after 2.5 h.	66.7%	33.3%	0	Near consensus
In open surgery (e.g., Ivor Lewis esophagectomy), the patient is placed in a “screw position” in order to perform laparotomy and thoracotomy in one step.	11.1%	33.3%	55.6%	No consensus
Open surgery comprises a median laparotomy and right thoracotomy within the 6th (5th–7th) intercostal space and—if necessary—left cervical access.	77.8%	22.2%	0	Near consensus
Minimally invasive esophagectomy represents a complex and technically challenging procedure that can be equivalent to standard techniques concerning oncologic quality and complication rates when carried out in specialized centers.	44.5%	22.2%	33.3%	No consensus
For intrathoracic anastomosis, the stapler end-to-side anastomosis is the first choice over a hand-sewn full-thickness anastomosis, e.g., in case of a short conduit. Minimally invasive intrathoracic and cervical anastomoses should be done by hand-sewn full-thickness end-to-end technique.	66.7%	33.3%	0	Near consensus

(continued)

Statement	Agreed	Neutral	Disagreed	Result
Pylorus drainage in patients undergoing esophagogastrectomy with gastric conduit reconstruction should be omitted.	100%	0	0	Full consensus
Postoperative gastric emptying disorders are transient and should be conservatively managed.	77.8%	22.2%	0	Near consensus

Perioperative antibiotic prophylaxis should be performed using a second generation cephalosporin (e.g., cephuroxime 1.5 g intravenously) and—if a colon interponate is used—in combination with a nitroimidazole (e.g., metronidazol 0.5 g intravenously). Antibiotics should be reapplied after 2.5 h.

Radical esophagectomy with mediastinal and abdominal lymphadenectomy currently represents the only well-established treatment modality for patients with non-metastatic, resectable EC [10, 11]. Among the variety of surgical approaches for esophageal resection, the Ivor Lewis esophagectomy seems superior compared to the transhiatal approach [34]. This procedure combines a laparotomy with a right thoracotomy to carry out esophagogastric resection, mediastinal and celiac lymphadenectomy, and reconstruction with either a gastric or colonic conduit. If the patient is placed in the “screw position” (a 30° tilt of the body to the left side), laparotomy and thoracotomy can be performed in one step and total operation time can be reduced. Dependent on tumor localization and entity, a median laparotomy, right thoracotomy (fifth to seventh intercostal space) and, if necessary, a left cervical access can be effected using this position. However, no consensus has been achieved since some centers preferred a supine position for the abdominal part in the first step and moved the patient to a left lateral decubitus position for right thoracotomy in the second step. Even in patients with Siewert classification type I adenocarcinoma, an abdomino-thoracic access should be preferred since several studies have shown increased 5-year survival rates in comparison to the transhiatal route, presumably due to more extended lymphadenectomy [35, 36]. The extent of lymphadenectomy for EC routinely comprises a two-field lymphadenectomy with lymph node dissection of the mediastinum and upper abdominal compartment [37]. In contrast, a three-field lymphadenectomy is frequently performed in Japan which achieves a higher rate of R0 resections but is associated with greater morbidity [37, 38].

Minimally invasive esophagectomy is a complex and technically challenging procedure that is performed in only a few medical centers worldwide [1]. Randomized trials have shown that laparoscopic and/or thoracoscopic esophagectomy can be equivalent to open esophagectomy in terms of morbidity, mortality, and survival when carried out in appropriately experienced surgical centers [39–41]. However, according to the GAST group, it has yet to be established whether minimally invasive esophagectomy can be accepted as equal to open surgery. This may be due to the fact that currently only few centers of the GAST group routinely employed minimally invasive techniques for esophagectomy. It is recommended to perform the laparoscopic part in supine position and the thoracoscopic resection in ventral position. Minimally invasive intrathoracic anastomoses should be carried out in hand-sewn full-thickness end-to-end technique [40, 41].

Reconstruction after esophagectomy should be performed using a gastric conduit as the first choice or alternatively by a colonic interponate using the posterior mediastinal route [10, 42]. Intrathoracic anastomosis can be performed either by stapler (e.g., end-to-side anastomosis using a circular stapler) or by hand-suture full-thickness (e.g., end-to-end anastomosis in case of a short conduit). Currently, hand-sewn and stapler anastomotic techniques are regarded as equivalent concerning the rate of postoperative anastomotic leaks and stenosis [42–45]. Cervical anastomosis should preferentially be performed by a hand-sewn end-to-end anastomosis (full-thickness). However, there is increasing evidence that a cervical stapler anastomosis is associated with less insufficiency and a superior functional result in comparison to hand-sewn anastomoses [46, 47].

Pylorus drainage in patients undergoing esophagogastrectomy with gastric conduit reconstruction should be avoided, as gastric emptying is not improved and reflux of bilioduodenal juice is increased. Postoperative gastric emptying disorders should, moreover, be conservatively

managed by prokinetic agents or botox injection and, if necessary, by endoscopic dilatation of the pylorus [48].

Topic 3: Perioperative management

Statement	Agreed	Neutral	Disagreed	Result
Anesthesiological management for esophagectomy should contain thoracic epidural analgesia, goal-oriented fluid management, and protective ventilation during one-lung anesthesia.	100%	0	0	Full consensus
Patients should be extubated as early as possible within 24 h postoperatively.	100%	0	0	Full consensus
Provided that the gastric conduit is sufficiently emptying, the nasogastric tube must be removed as early as possible in order to avoid microaspiration.	66.7%	11.1%	11.1%	Near consensus
Food intake should be commenced gradually starting with the 4th postoperative day.	55.5%	22.2%	11.1%	No consensus
No routine check of anastomosis is necessary before beginning peroral food intake.	55.6%	11.1%	33.3%	No consensus

Anesthesiological management can contribute to a reduction of respiratory failure and anastomotic leakage after esophageal surgery by the use of thoracic epidural analgesia, protective ventilation strategies, prevention of aspiration, and judicious fluid management [49]. Thoracic epidural anesthesia improves microcirculation of the gastric conduit and is associated with a decreased occurrence of anastomotic leakage [50, 51]. Fluid overload should be avoided because it may delay recovery of gastrointestinal function, impair wound and anastomotic healing, as well as coagulation and cardiac and respiratory function [49, 52].

Patients should be extubated as early as possible within 24 h postoperatively since prolonged postoperative ventilation exposes patients to potential barotrauma, aspiration, nosocomial infection, and sedation-related side effects [53]. Furthermore, bronchoscopy prior to extubation can contribute to decrease the incidence of bronchopulmonary infections [9].

After esophagectomy, patients have a high risk of aspiration due to excision of the lower esophageal sphincter, denervation of the stomach, and sometimes paralysis of the recurrent laryngeal nerve [54]. Routine postoperative nasogastric decompression of the gastric conduit may protect against macro-aspiration and decrease the risk of anastomotic leakage from distension-induced gastric conduit ischemia [49]. On the other hand, the nasogastric tube may itself lead to impaired hypopharyngeal function and microaspiration, pneumonia, and patient discomfort [55–57]. Therefore, the nasogastric tube should be removed as early as possible, usually during the first

postoperative day after esophagectomy, provided that the gastric conduit is sufficiently emptying.

No consensus was reached concerning postoperative nutrition after esophagectomy. Although early postoperative enteral nutrition has a number of advantages over total parenteral nutrition, it has been traditionally avoided after esophagectomy in order to minimize anastomotic strain and reduce the inherent risks of postoperatively impaired gastrointestinal motility [58, 59]. However, current studies show that enteral nutrition is a safe route for nutrient delivery as early as 6 h postoperatively and that the surgical certainty of esophagoenteric anastomoses makes an early oral enteral feeding possible [58, 60–62]. Another option represents a Witzel feeding jejunostomy at the time of laparotomy or the placement of a nasojejunal tube for early postoperative enteral nutrition [63, 64]. Both methods are not free of complications, such as the appearance of catheter dislodgements, perijejunostomic leaks in case of a feeding jejunostomy, or microaspiration when a nasojejunal tube is used [64]. Gradual begin of feeding after esophagectomy represents a compromise comprised of short-term parenteral nutrition combined with 400 ml of fluids given orally within the first 4 days postoperatively. During this time, decrease of the transient gastric emptying disorders due to the preceding vagotomy can be anticipated. Beginning with day 5, oral nutrition can be gradually escalated to solid foods.

Likewise, no consensus was reached concerning a “routine” check of the anastomosis after esophagectomy before starting enteral nutrition. Although a “routine” check of the anastomosis has been proven to be a little

sensitive for detection of anastomotic leakage, it can be performed by simple and low-risk methods, e.g., by swallowing methylene blue [48]. Clinical symptoms, such as pain, increased temperature, reduced vigilance,

drainage quality, arrhythmia, and increasing inflammatory laboratory parameters, should be used for the screening of anastomotic insufficiency rather than a routine control [65].

Topic 4: Treatment of anastomotic complications

Statement	Agreed	Neutral	Disagreed	Result
Endoscopy and application of a contrast agent is the method of choice for diagnosing anastomotic leaks after esophagectomy.	100%	0	0	Full consensus
1° intrathoracic anastomotic leaks (small fistula, sufficiently drained, no mediastinitis, or sepsis) should be conservatively treated by antibiotics and enteral nutrition via a tri-lumen esophageal tube.	100%	0	0	Full consensus
2° intrathoracic anastomotic leaks (large area leakage with sufficient gastric tube perfusion and drainage, incipient signs of mediastinitis or sepsis) should be treated by a covered self-expanding esophageal stent, antibiotics, and nutrition via a jejunal tube.	100%	0	0	Full consensus
3° intrathoracic anastomotic leaks (large insufficiency with impaired perfusion or necrosis of the gastric tube and mediastinitis or sepsis) should be treated by surgery.	88.9%	11.1%	0	Near consensus
Cervical anastomotic leaks should be treated by wound drainage.	88.9%	0	11.1%	Near consensus

When suspecting anastomotic insufficiency after esophagectomy, the primary diagnostic goals are determination of the leak's size, status of the conduit's perfusion, and morphology—control of sufficient drainage and testing for sepsis parameters. Endoscopy in combination with a contrast agent (e.g., gastrographin) represents the method of choice for detecting anastomotic leaks after esophagectomy because it delivers information about leak size, conduit perfusion, and leak morphology [66]. If indicated, further diagnostics, such as bronchoscopy, CT or X-ray, and sepsis screening by laboratory parameters (e.g., C-reactive protein, procalcitonin), can additionally be performed.

Intrathoracic anastomotic leaks can be divided into three categories of severity: A first-degree insufficiency is characterized by a small fistula which is sufficiently drained. The patient has no mediastinitis or sepsis. Treatment is conservative with antibiotic treatment (e.g., a combination of penicillin and a beta-lactamase inhibitor) and enteral nutrition via a tri-lumen esophageal tube which should be preferred over total parenteral nutrition [59]. In some patients, innovative approaches, such as the application of a Vicryl plug or EndoVac treatment, can also be recommended [67–69]. A second-degree insufficiency is characterized by a large area leakage with a sufficient gastric tube perfusion and drainage but incipient signs of mediastinitis and sepsis. Treatment by a covered, self-expanding esophageal stent is recommended in combina-

tion with antibiotic treatment and temporary nutrition via a tri-lumen esophageal probe. The esophageal stent should be removed after 6 weeks [70]. A third-degree insufficiency is characterized by a large insufficiency combined with impaired gastric tube perfusion and possibly gastric tube necrosis as well as clinical signs of mediastinitis and sepsis. Immediate surgical treatment is necessary either with esophageal discontinuity or if possible trimming of the gastric conduit for re-anastomosis [71].

Cervical anastomotic insufficiencies occur in 25–45% of all anastomoses and are predominantly comprised of fistulas and first-degree insufficiencies. They can be successfully treated in most patients by wound drainage, optionally in combination with fibrin gluing or clipping. Only in cases of mediastinitis is an esophageal discontinuity with secondary reconstruction necessary [72].

Conclusion

Modern treatment of EC is characterized by a sophisticated and multidisciplinary approach. Using the Delphi method, the GAST group has combined clinical experience with scientific evidence on the treatment of this disease. Full or near consensus was reached in almost all topics, thus defining a basis for current treatment and the development of future treatment guidelines, e.g., S1–S3 guidelines. However, the numerous topics without full consensus

emphasize the need for further studies, this being especially true for the field of neoadjuvant treatment, minimally invasive esophagectomy, and postoperative nutrition of patients with EC.

Conflicts of interest None.

References

- Schuchert MJ, Luketich JD, Landreneau RJ (2010) Management of esophageal cancer. *Curr Probl Surg* 47(11):845–946
- Jones J, Hunter D (1995) Consensus methods for medical and health services research. *BMJ* 311(7001):376–380
- Colombo-Benkmann M, Wöinkel T, Palmes D et al (2006) Surgical endoscopy compared to non-surgical endoscopy in patients with esophageal cancer. Is it any better? 27. Deutscher Krebskongress (abstract)
- Lowe VJ, Booya F, Fletcher JG et al (2005) Comparison of positron emission tomography, computed tomography, and endoscopic ultrasound in the initial staging of patients with esophageal cancer. *Mol Imaging Biol* 7(6):422–430
- Choi J, Kim SG, Kim JS et al (2010) Comparison of endoscopic ultrasonography (EUS), positron emission tomography (PET), and computed tomography (CT) in the preoperative locoregional staging of resectable esophageal cancer. *Surg Endosc* 24(6):1380–1386
- Thurau K, Palmes D, Franzius C et al (2011) Impact of PET–CT on primary staging and response control on multimodal treatment of esophageal cancer. *World J Surg* 35(3):608–616
- Noble F, Bailey D, SWCIS Upper Gastrointestinal Tumour Panel et al (2009) Impact of integrated PET/CT in the staging of oesophageal cancer: a UK population-based cohort study. *Clin Radiol* 64(7):699–705
- Riedel M, Hauck RW, Stein HJ et al (1998) Preoperative bronchoscopic assessment of airway invasion by esophageal cancer: a prospective study. *Chest* 113:687–695
- Ott K, Bader FG, Lordick F et al (2009) Surgical factors influence the outcome after Ivor-Lewis esophagectomy with intrathoracic anastomosis for adenocarcinoma of the esophagogastric junction: a consecutive series of 240 patients at an experienced center. *Ann Surg Oncol* 16(4):1017–1025
- Kranzfelder M, Büchler P, Friess H (2009) Surgery within multimodal therapy concepts for esophageal squamous cell carcinoma (ESCC): the MRI approach and review of the literature. *Adv Med Sci* 54(2):158–169
- van Heijl M, van Lanschot JJ, Koppert LB et al (2008) Neoadjuvant chemoradiation followed by surgery versus surgery alone for patients with adenocarcinoma or squamous cell carcinoma of the esophagus (CROSS). *BMC Surg* 8:21
- Gebski V, Burmeister B, Smithers BM et al (2007) Survival benefits from neoadjuvant chemoradiotherapy or chemotherapy in oesophageal carcinoma: a meta-analysis. *Lancet Oncol* 8(3):226–234
- Lorenzen S, Brücher B, Zimmermann F et al (2008) Neoadjuvant continuous infusion of weekly 5-fluorouracil and escalating doses of oxaliplatin plus concurrent radiation in locally advanced oesophageal squamous cell carcinoma: results of a phase I/II trial. *Br J Cancer* 99(7):1020–1026
- Fiorica F, Di Bona D, Schepis F et al (2004) Preoperative chemoradiotherapy for oesophageal cancer: a systematic review and meta-analysis. *Gut* 53(7):925–930
- Urschel JD, Vasan H (2003) A meta-analysis of randomized controlled trials that compared neoadjuvant chemoradiation and surgery to surgery alone for resectable esophageal cancer. *Am J Surg* 185(6):538–543
- Rice TW, Blackstone EH, Rusch VW (2010) 7th edition of the AJCC Cancer Staging Manual: esophagus and esophagogastric junction. *Ann Surg Oncol* 17(7):1721–1724
- Seto Y, Fukuda T, Yamada K et al (2008) Celiac lymph nodes: distant or regional for thoracic esophageal carcinoma? *Dis Esophagus* 21(8):704–707
- Wittekind C, Tannapfel A (2010) The current TNM system for gastrointestinal tumors part I. *Pathologe* 31(5):344–347
- Schomas DA, Quevedo JF, Donahue JM et al (2010) The prognostic importance of pathologically involved celiac node metastases in node-positive patients with carcinoma of the distal esophagus or gastroesophageal junction: a surgical series from the Mayo Clinic. *Dis Esophagus* 23(3):232–239
- Bedenne L, Michel P, Bouché O et al (2007) Chemoradiation followed by surgery compared with chemoradiation alone in squamous cancer of the esophagus: FFC09102. *J Clin Oncol* 25(10):1160–1168
- Stahl M, Stuschke M, Lehmann N et al (2005) Chemoradiation with and without surgery in patients with locally advanced squamous cell carcinoma of the esophagus. *J Clin Oncol* 23(10):2310–2317
- Ott K, Lordick F, Molls M et al (2009) Limited resection and free jejunal graft interposition for squamous cell carcinoma of the cervical oesophagus. *Br J Surg* 96(3):258–266
- Malthaner R, Wong RK, Spithoff K et al (2010) Preoperative or postoperative therapy for resectable oesophageal cancer: an updated practice guideline. *Clin Oncol (R Coll Radiol)* 22(4):250–256
- Arnott SJ, Duncan W, Gignoux M et al (2005) Oesophageal Cancer Collaborative Group. Preoperative radiotherapy for esophageal carcinoma. *Cochrane Database Syst Rev* 19(4):CD001799
- Heise JW, Heep H, Frieeling T et al (2001) Expense and benefit of neoadjuvant treatment in squamous cell carcinoma of the esophagus. *BMC Cancer* 1:20
- Urschel JD, Vasan H, Blewett CJ (2002) A meta-analysis of randomized controlled trials that compared neoadjuvant chemotherapy and surgery to surgery alone for resectable esophageal cancer. *Am J Surg* 183(3):274–279
- Malthaner RA, Wong RK, Rumble RB et al (2004) Neoadjuvant or adjuvant therapy for resectable esophageal cancer: a clinical practice guideline. *BMC Cancer* 24(4):67
- Allum WH, Stenning SP, Bancewicz J et al (2009) Long-term results of a randomized trial of surgery with or without preoperative chemotherapy in esophageal cancer. *J Clin Oncol* 27(30):5062–5067
- Schneider PM, Metzger R, Schaefer H et al (2008) Response evaluation by endoscopy, rebiopsy, and endoscopic ultrasound does not accurately predict histopathologic regression after neoadjuvant chemoradiation for EC. *Ann Surg* 248:902–908
- Sloof GW (2006) Response monitoring of neoadjuvant therapy using CT, EUS, and FDG PET. *Best Pract Res Clin Gastroenterol* 5:941–957
- Kelsen DP, Winter KA, Gunderson LL et al (2007) Long-term results of RTOG trial 8911 (USA Intergroup 113): a random assignment trial comparison of chemotherapy followed by surgery compared with surgery alone for esophageal cancer. *J Clin Oncol* 25(24):3719–3725
- Weigel TL, Frumiento C, Gaumintz E (2002) Endoluminal palliation for dysphagia secondary to esophageal carcinoma. *Surg Clin North Am* 82(4):747–761
- Javle M, Ailawadhi S, Yang GY et al (2006) Palliation of malignant dysphagia in esophageal cancer: a literature-based review. *J Support Oncol* 4(8):365–373

34. Wolff CS, Castillo SF, Larson DR et al (2008) Ivor Lewis approach is superior to transhiatal approach in retrieval of lymph nodes at esophagectomy. *Dis Esophagus* 21(4):328–333
35. Omloo JM, Lagarde SM, Hulscher JB et al (2007) Extended transthoracic resection compared with limited transhiatal resection for adenocarcinoma of the mid/distal esophagus: five-year survival of a randomized clinical trial. *Ann Surg* 246:992–1000
36. Omloo JM, Law SY, Launois B et al (2009) Short and long-term advantages of transhiatal and transthoracic oesophageal cancer resection. *Eur J Surg Oncol* 35(8):793–797
37. Pennathur A, Zhang J, Chen H et al (2004) The "best operation" for esophageal cancer? *Ann Thorac Surg* 89(6):S2163–S2167
38. Igaki H, Tachimori Y, Kato H (2004) Improved survival with upper and/or middle mediastinal lymph node metastasis of squamous cell carcinoma of the lower thoracic esophagus treated with 3-field dissection. *Ann Surg* 239:483–490
39. Santillan AA, Farma JM, Meredith KL et al (2008) Minimally invasive surgery for esophageal cancer. *J Natl Compr Canc Netw* 6(9):879–884
40. Nagpal K, Ahmed K, Vats A et al (2010) Is minimally invasive surgery beneficial in the management of esophageal cancer? A meta-analysis. *Surg Endosc* 24(7):1621–1629
41. Sgourakis G, Gockel I, Radtke A et al (2010) Minimally invasive versus open esophagectomy: meta-analysis of outcomes. *Dig Dis Sci* 55(11):3031–3040
42. Urschel JD, Blewett CJ, Bennett WF et al (2001) Handsewn or stapled esophagogastric anastomoses after esophagectomy for cancer: meta-analysis of randomized controlled trials. *Dis Esophagus* 14(3–4):212–217
43. Korolija D (2008) The current evidence on stapled versus hand-sewn anastomoses in the digestive tract. *Minim Invasive Ther Allied Technol* 17(3):151–154
44. Law S, Fok M, Chu KM (1997) Comparison of hand-sewn and stapled esophagogastric anastomosis after esophageal resection for cancer: a prospective randomized controlled trial. *Ann Surg* 226(2):169–173
45. Luechakitattisak P, Kasetsunthorn S (2008) Comparison of hand-sewn and stapled in esophagogastric anastomosis after esophageal cancer resection: a prospective randomized study. *J Med Assoc Thai* 91(5):681–685
46. Kondra J, Ong SR, Clifton J (2008) A change in clinical practice: a partially stapled cervical esophagogastric anastomosis reduces morbidity and improves functional outcome after esophagectomy for cancer. *Dis Esophagus* 21(5):422–429
47. Cooke DT, Lin GC, Lau CL et al (2009) Analysis of cervical esophagogastric anastomotic leaks after transhiatal esophagectomy: risk factors, presentation, and detection. *Ann Thorac Surg* 88(1):177–184
48. Palmes D, Weilinghoff M, Colombo-Benkmann M et al (2007) Effect of pyloric drainage procedures on gastric passage and bile reflux after esophagectomy with gastric conduit reconstruction. *Langenbecks Arch Surg* 392(2):135–141
49. Ng JM (2008) Perioperative anesthetic management for esophagectomy. *Anesthesiol Clin* 26(2):293–304
50. Michelet P, Roch A, D'Journo XB et al (2007) Effect of thoracic epidural analgesia on gastric blood flow after oesophagectomy. *Acta Anaesthesiol Scand* 51:587–594
51. Lazar G, Kaszaki J, Abraham S et al (2003) Thoracic epidural anesthesia improves the gastric microcirculation during experimental gastric tube formation. *Surgery* 134:799–805
52. Neal JM, Wilcox RT, Allen HW et al (2003) Near-total esophagectomy: the influence of standardized multimodal management and intraoperative fluid restriction. *Reg Anesth Pain Med* 28:328–334
53. McKeivith JM, Pennefather SH (2010) Respiratory complications after oesophageal surgery. *Curr Opin Anaesthesiol* 23:34–40
54. Atkins BZ, Shah AS, Hutcheson KA et al (2004) Reducing hospital morbidity and mortality following esophagectomy. *Ann Thorac Surg* 78:1170–1176
55. Shackcloth MJ, McCarron E, Kendall J et al (2006) Randomized clinical trial to determine the effect of nasogastric drainage on tracheal acid aspiration following oesophagectomy. *Br J Surg* 93:547–552
56. Nguyen NT, Slone J, Wooldridge J et al (2009) Minimally invasive esophagectomy without the use of postoperative nasogastric tube decompression. *Am Surg* 75:929–931
57. Sato T, Takayama T, So K et al (2007) Is retention of a nasogastric tube after esophagectomy a risk factor for postoperative respiratory tract infection? *J Infect Chemother* 13(2):109–113
58. Gabor S, Renner H, Matzi V et al (2005) Early enteral feeding compared with parenteral nutrition after oesophageal or oesophagogastric resection and reconstruction. *Br J Nutr* 93(4):509–513
59. Baker A, Wooten LA, Malloy M (2011) Nutritional considerations after gastrectomy and esophagectomy for malignancy. *Curr Treat Options Oncol* 12(1):85–95
60. Kamei H, Hachisuka T, Nakao M et al (2005) Quick recovery of serum diamine oxidase activity in patients undergoing total gastrectomy by oral enteral nutrition. *Am J Surg* 189(1):38–43
61. Jiang K, Cheng L, Wang JJ (2009) Fast track clinical pathway implications in esophagogastrectomy. *World J Gastroenterol* 15(4):496–501
62. Cerfolio RJ, Bryant AS, Bass CS (2004) Fast tracking after Ivor Lewis esophagogastrectomy. *Chest* 126(4):1187–1194
63. Wani ML, Ahangar AG, Lone GN (2010) Feeding jejunostomy: does the benefit outweigh the risk (a retrospective study from a single centre). *Int J Surg* 8(5):387–390
64. Gupta V (2009) Benefits versus risks: a prospective audit. Feeding jejunostomy during esophagectomy *World J Surg* 33(7):1432–1438
65. Deitmar S, Anthoni C, Palmes D et al (2009) Are leukocytes and CRP early indicators for anastomotic leakage after esophageal resection? *Zentralbl Chir* 134(1):83–89
66. Hölscher AH, Fetzner UK, Bludau M et al (2011) Complications and management of complications in oesophageal surgery. *Zentralbl Chir* (in press)
67. Wedemeyer J, Schneider A, Manns MP et al (2008) Endoscopic vacuum-assisted closure of upper intestinal anastomotic leaks. *Gastrointest Endosc* 67(4):708–711
68. Truong S, Böhm G, Klinge U et al (2004) Results after endoscopic treatment of postoperative upper gastrointestinal fistulas and leaks using combined Vicryl plug and fibrin glue. *Surg Endosc* 18(7):1105–1108
69. Ahrens M, Schulte T, Egberts J et al (2010) Drainage of esophageal leakage using endoscopic vacuum therapy: a prospective pilot study. *Endoscopy* 42(9):693–698
70. Tuebergen D, Rijcken E, Mennigen R et al (2008) Treatment of thoracic esophageal anastomotic leaks and esophageal perforations with endoluminal stents: efficacy and current limitations. *J Gastrointest Surg* 12(7):1168–1176
71. Barkley C, Orringer MB, Iannettoni MD et al (2003) Challenges in reversing esophageal discontinuity operations. *Ann Thorac Surg* 76(4):989–994
72. Siewert JR, Stein HJ, Bartels H (2004) Anastomotic leaks in the upper gastrointestinal tract. *Chirurg* 75(11):1063–1070