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EVIDENCE-BASED CURRENT SURGICAL PRACTICE

Current Status of Management of Malignant Disease: Current Management of Esophageal Cancer

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Abstract
Objective The objective of this study is to outline the evidence regarding the surgical management of esophageal cancer and provide a single institutional outline regarding its implementation.
Background Esophageal cancer is a major cause of cancer-related morbidity and mortality worldwide. Surgery continues to play an important role in its management and offers the best chance for cure in localized and locally advanced disease. However, considerable controversy exists regarding the optimum treatment strategy in this patient population. Furthermore, despite advances in operative and perioperative care and the advent of minimally invasive approaches, the majority of patients succumb to distant metastases after curative intent resection. This failure highlights the importance of multimodal, stage-directed therapy in the management of patients with newly diagnosed esophageal tumors.
Methods Herein, we provide a comprehensive, evidence-based review of the diagnostic workup and locoregional and systemic treatment options available to esophageal cancer patients. The evidence supporting perioperative chemotherapy versus chemoradiotherapy is outlined and discussed. In addition, we highlight our institutional approach to the diagnostic evaluation, operative selection strategy, and perioperative treatment regimen selection based on the stage of presentation. Finally, we discuss the role of enhanced recovery in the postoperative management of this complex group of patients.
Conclusions Esophageal cancer remains a devastating disease with high mortality. Favorable outcomes mandate a multimodal, stage-directed treatment approach.

Keywords Esophageal cancer · Chemotherapy · Chemoradiotherapy · Endoscopic mucosal resection · Endoscopic submucosal dissection · Adenocarcinoma · Squamous cell carcinoma · Esophagectomy · Enhanced recovery pathway · Minimally invasive esophagectomy

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Introduction

Esophageal cancer is currently the 8th most common malignancy worldwide with approximately 465,000 cases annually. It is the 6th leading cause of cancer death, responsible for approximately 400,000 deaths per annum.[1–3] Worldwide, squamous cell carcinoma (SCC) accounts for the bulk of disease burden and mortality. Conversely, adenocarcinoma (ADC) is the predominant histologic subtype in the western world. ADC of the esophagus and proximal stomach are the fastest rising malignancies in North America, with an increase in incidence of approximately 10 % in the last decade. Additional subtypes include neuroendocrine tumors, melanoma, lymphoma, and sarcoma, which comprise less than 1–2 % of esophageal malignancies.[1,2] Treatment responses differ according to the histologic subtype of the underlying neoplasm and tumor stage, highlighting the importance of accurate diagnosis and staging[1,2,4,5] and an approach that takes histological subtype into consideration.

Treatment strategies for esophageal malignancies can conceptually be divided along two axes: locoregional treatment (surgery and radiotherapy) and systemic therapy (chemotherapy).[1,2,4,5] Surgery continues to play an important role in achieving locoregional control in patients with esophageal carcinoma and offers the best chance for cure in localized and locally advanced disease. However, despite improvements in surgical technique and the advent of minimally invasive approaches, the majority of patients succumb to distant metastases after curative intent resection. This failure highlights the importance of multimodal therapy in the management of patients with a newly diagnosed esophageal malignancy.[6–10] This review will concentrate on the endoscopic, surgical, and adjuvant therapeutic advances for esophageal cancer, highlighting the stage-directed therapeutic approach for this malignancy and the differing responses to various adjuvant therapies depending on histologic subtype. Our institutional approach to the management of patients with esophageal carcinoma is outlined in Fig. 1.

Symptoms and Clinical Evaluation

Given the late symptomatic manifestations of esophageal carcinoma, many patients present with advanced disease. Progressive dysphagia, initially to solids and then liquids, is the overwhelming typical symptomatic presentation. Although several dysphagia scores have been described,[11] we find the 5-point scale validated by Bergquist et al.[12] to be the most clinically useful (0=no symptoms, 1=dysphagia to solids, 2=dysphagia to semi-solids, 3=dysphagia to liquids, 4=dysphagia to saliva). Significant weight loss is frequently an associated finding.

Diagnosis and Staging

Currently, upper GI endoscopy is the diagnostic modality of choice in North America. It permits effective visualization of the esophagus along its entire length as well as the esophagogastric junction via retroflexion of the endoscope within the stomach. In addition, EGD permits the acquisition of tissue for pathologic diagnosis. Finally, a clear delineation of the tumor location is required for operative planning, particularly for esophagogastric junction cancers according the classification proposed by Rudiger Siewert (see treatment below).[1,2,13,14]

Following diagnosis, accurate staging is imperative in order for the selection of an appropriate treatment plan. Esophageal and esophagogastric junction (EGJ) cancers are staged according to the TNM classification as outlined by the 7th

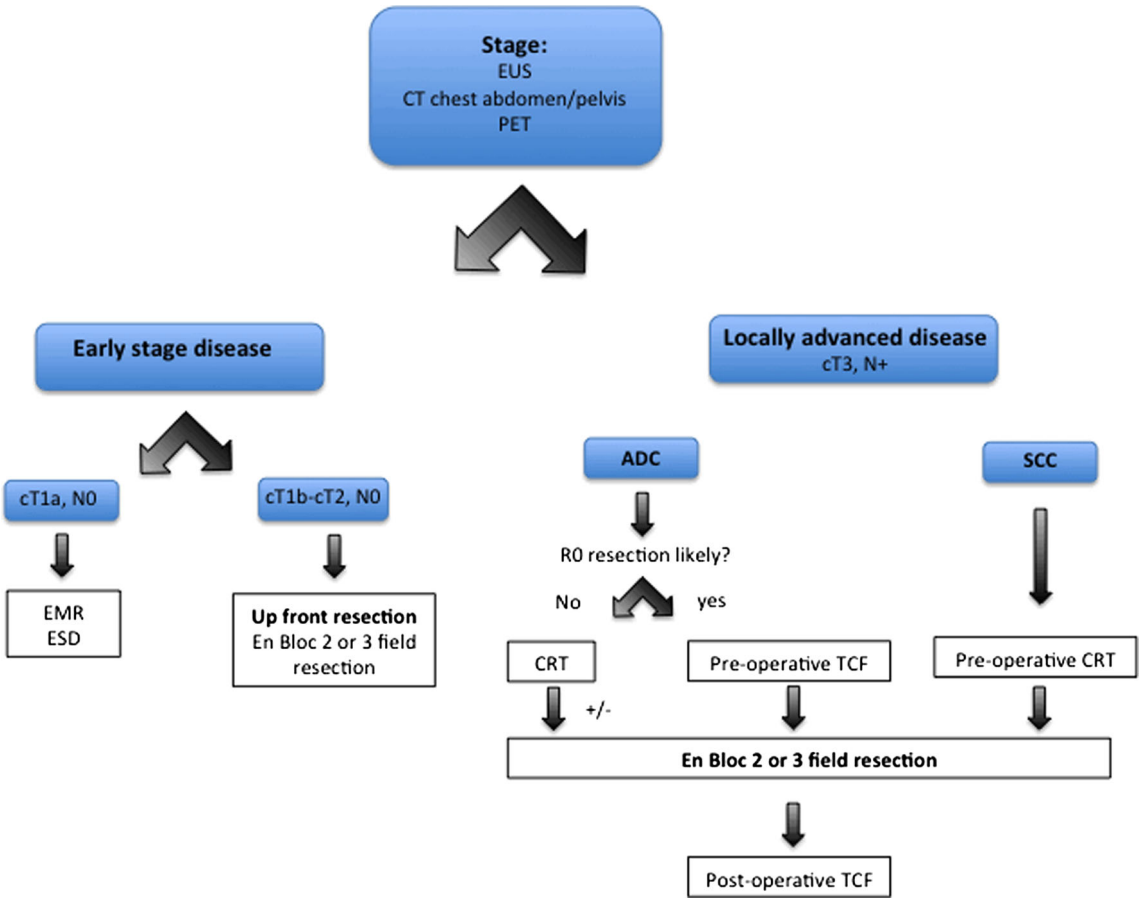

Fig. 1 Schematic approach to the management of patients with esophageal cancer

edition of the American Joint Committee on Cancer /Union for International Cancer Control (AJCC/UICC) staging manuals. This is currently based on histology with ADC and SCC each being staged according to their own system.[15] The modalities of choice include endoscopic ultrasound (EUS), routine CT scan of the chest, abdomen and pelvis, and positron emission tomography (PET) in selected patients.

Clinical T staging is best achieved by EUS. It provides the most detailed description of the depth of tumor involvement of the esophagus/EGJ. T1a tumors are intramucosal in nature.[1,14] T1b cancers invade the submucosa, T2 tumors involve the muscularis propria, T3 lesions invade beyond this layer, and T4 lesions invade adjacent structures. The overall sensitivity and specificity of this modality in the determination of cT stage have been reported as 81.6 and 99.4 % for T1 lesions, 81.4 and 96.3 % for T2 lesions, 91.4 and 94.4 % for T3 lesions, and 92.4 and 97.4 % for T4 lesions, respectively.[1,14] Overall EUS is least reliable in T2 lesions, with 10 % of tumors understaged and 17 % overstaged, respectively.[1,14,16] The routine use of EUS in patients with significant dysphagia is debatable. Not only is EUS assessment beyond the tumor frequently not possible without dilation (and not-insignificant risk of perforation) due to the larger caliber endoscope but also EUS offers little to the treatment paradigm in these patients who are almost universally at least cT3. Given the very high rate of occult lymph node (LN) metastasis in cT3N0 esophageal cancer, most centers treat cT3 lesions with the same multimodal therapy irrespective of LN status. In our experience, EUS offers the greatest opportunity for altering treatment in patients with non-bulky localized lesions (cT2N0 vs T2N1—determining neo-adjuvant therapy versus up front resection—see below) or early disease (T1a vs T1b/T2—determining endoscopic resection versus surgical resection).

EUS is also useful in the identification and analysis of periesophageal and celiac lymph nodes. Nodal size and echogenicity patterns can identify nodes suspicious for tumor involvement. In combination with selective FNA of suspicious nodes, the sensitivity and specificity of EUS have been reported as 92 and 93 %, respectively.[1,14] In patients with early disease identified on EUS (uT1N0), more accurate T staging of the cancer can be performed with endoscopic resection (EMR or ESD), as the difference between pT1a and pT1b may alter treatment strategies (see below—endoscopic therapies).

Initial CT provides a rapid assessment of the operability of disease. While it provides limited information regarding cT stage, visualization of fat planes between the esophagus and adjacent structures excludes cT4 disease. CT scan does provide valuable information regarding cN stage. Enlargement of intra-abdominal and intrathoracic lymph nodes greater than 1 cm in the short axis is suggestive of tumor involvement. In the detection of nodal disease, CT demonstrates a sensitivity and specificity of 59 and 81 %, respectively.[1,14] CT demonstrates a sensitivity of 37–66 % in the detection of distant metastasis. Patients with locally advanced disease (cT3-N+) harbor distant metastases in approximately 30 % of cases.

FDG-PET demonstrates a high sensitivity in the detection of primary lesions in both ADC and SCC (>95 %).[1,14,17] However, its greatest utility is in the detection of metastases. Approximately 92–100 % of esophageal cancers demonstrate FDG uptake and are apparent on positron emission tomography (PET) CT. The overall sensitivity and specificity of this modality in the detection of M1 disease are reported as 69 and 73 %, respectively.[1,14] However, because only approximately 25 % of tumors with signet ring histology demonstrate avidity on PET scan, care must be taken in interpreting negative findings in such patients.[17]

Treatment, Outcomes, and Complications

Early Stage Localized Disease

Early malignancies of the esophagus consist of localized tumors with limited penetration of the esophageal wall (cT1-2 N0). Very early T stage esophageal cancers (ADC and SCC) can be effectively treated by organ-sparing endoscopic resection techniques with equivalent oncologic outcomes as esophagectomy.[8,9,18] To justify endoscopic resection, two main criteria must be met: (1) very low risk of lymph node metastasis and (2) the lesion must be amenable to en bloc resection. Accurate pretreatment T and N staging is increased with endoscopic ultrasound and diagnostic endoscopic mucosal resection (EMR). Despite this, the rate of occult lymph node metastasis for cT1a is between 3 and 10 % and for cT1b, approximately 25 %. To aid in decision-making regarding endoscopic versus surgical resection of T1 malignancies, we have previously identified several endoscopic and pathologic predictors that can be employed to determine the risk of occult lymph node metastases in esophageal adenocarcinoma.[19] These include depth, differentiation, size, and the presence of lymphovascular invasion (LVI). Of these, the presence of LVI is the strongest predictor of lymph

Table 1 Predictors of lymph node metastasis in patients with early esophageal adenocarcinoma. Adapted from Lee et al.[19]

Variable	Odds ratio (95 % CI)
Size, per cm	1.35 (1.07, 1.71)
Depth	
T1b[a]	1.62 (0.65, 4.02)
Differentiation	
Moderate[b]	2.60 (0.53, 12.85)
Poor[b]	2.53 (0.48, 13.32)
Lymphovascular invasion	7.50 (3.30, 17.07)

[a] Versus T1a tumors

[b] Versus well-differentiated tumors

node metastasis, associated with a rate of at least 15 % (Table 1). Therefore, endoscopic resection can safely be recommended in patients with cT1a lesions, well differentiated, and without LVI (LN metastasis rate of less than 1 %). Endoscopic resection of T1b lesions with LVI and poorly differentiated tumors can be performed, albeit with a higher risk of occult LN metastasis.

The two main techniques for endoscopic resection include EMR and endoscopic submucosal dissection (ESD). EMR is technically more facile; however, one can only resect up to 0.5–1 cm at one time. This results in piecemeal resection of larger lesions and a local recurrence rate of up to 30 %.[7,8] ESD allows en bloc resection of any size esophageal lesion but is technically more demanding and requires specialized equipment passed through the operating channel of a standard gastroscope.[9] Clinical T2N0 disease is associated with a not-insignificant rate of occult lymph node metastasis (up to 50 %).[19] This precludes endoscopic techniques, and such patients are treated with surgical resection.

In keeping with the high proportion of lymph node-positive disease in T2N0 disease, considering preoperative therapy for this patient population is not unreasonable. However a recent multi-institutional review of treated cT2N0 tumors revealed that accurate staging is difficult in this patient population, with approximately 40 % of patients being overstaged and an additional 40 % understaged.[20] This issue is further complicated by the recently published FFCD 9901 trial that examined this specific question with a trial comparing neo-adjuvant chemoradiotherapy (CRT) (CF-based) to surgery alone[21] in stages 1–2 lesions. Not only did neo-adjuvant CRT not increase survival but also was associated with a 6-fold increase in postoperative mortality. Therefore in localized disease (stages 1–2), the use of neo-adjuvant therapy (particularly CRT) should be employed with some discretion. Although up-front surgical resection for stages 1–2 esophageal cancers is an acceptable standard of care, we typically recommend neo-adjuvant therapy (CT) for young patients with the highest a priori risk of occult LN metastasis (larger tumors, lymphovascular invasion, poorly differentiated grade).

Locally Advanced Disease

Resection alone for locally advanced disease (cT3 or N+) is associated with low overall survival. These poor outcomes have prompted a large number of adjuvant and neo-adjuvant trials with studies supporting both neo-adjuvant (or perioperative) chemotherapy and neo-adjuvant chemoradiotherapy as acceptable standards of care. However in the west, due to historically low incidence of this disease, esophageal squamous cell carcinoma was frequently combined with adenocarcinoma in these trials to optimize accrual.[22,23] This is unfortunate, as response to treatment varies significantly between these two histologies, most notably the increased radiosensitivity of SCC compared to ADC. Furthermore, histologically consistent trials, primarily with adenocarcinoma, have frequently included malignancies on both sides of the diaphragm.[24,25] Thus, esophageal adenocarcinoma is frequently accrued into gastric adenocarcinoma trials, and vice versa. Differences in response rates of ADC between distal gastric and EGJ or esophageal ADC have been noted; however, these tend to be relatively low compared to the differential response of SCC and ADC to radiotherapy. Although controversial, it is our preference to treat the similar histologies with similar treatment irrespective of location with respect to the diaphragm. The selection of one standard of care over another (chemotherapy versus chemoradiotherapy) requires a careful and critical analysis of the available literature on the topic, which is highlighted in the following two sections.

Case for Neo-adjuvant Chemoradiotherapy

To date, there has been a total of eight large randomized controlled trials (>100 patients) comparing preoperative chemoradiotherapy to surgery alone for esophageal cancer (Table 2).[26–33] As mentioned above, most are of mixed histologies (SCC and ADC). Although an Irish trial examining preop CRT in esophageal ADC [31] was positive, the very poor results for the surgery alone arm (6 %, 3-year survival) was not in keeping with international benchmark standards questioning the surgical quality and validity of the trial. Unfortunately, this flawed trial is heavily weighted in most meta-analyses on the subject, jeopardizing the validity of the results and conclusions. Subsequent trials with CRT (mostly cisplatin- and 5FU-based) were primarily negative, and what is particularly notable from all these trials is that the pathologic complete response (pCR) rate for CRT hovers around a consistent 25 % level. More recently, a Dutch study comparing CRT+surgery versus surgery alone revealed a statistically significant benefit with a relatively modern and tolerable systemic cytotoxic regimen (weekly Carbo-taxol).[30] This study included mixed histologies (approx. 75 % ADC and 25 % SCC), and closer examination of the results demonstrates a clear difference in response rates. Indeed, the pCR rate for SCC is nearly twice that for ADC (again at 25 %), and the survival data reveals that the positive results are truly driven by the SCC cases. Given an R0 resection rate of 92 % in the CRT group versus 69 % in the surgery alone group, much of the benefit from CRT may come from its downsizing effect, increasing the likelihood of curative surgery. In patients with early-stage disease (stages I, II), the risks associated with CRT may not be offset by the benefit from downsizing smaller tumors. This hypothesis is supported by the results of the recent trial by Mariette et al., in which patients with early-stage resectable cancer were randomized to treatment with preoperative CRT or surgery alone. CRT offered no benefit with respect to R0 resection rate (93.8 vs 92.1 %) or survival (47.5 vs 53 %) compared to surgery alone. To the contrary, such patients experienced significantly higher rates of in-hospital mortality (11.1 vs 3.4 %).[30,33] Nevertheless, based

Table 2 Randomized trials comparing chemoradiotherapy and surgery versus surgery alone in the treatment of esophageal cancer patients; $p<0.05$. Adapted from Sjoquist et al.[10]

Trial	*N*	Histology	Chemotherapy	RT (Gy)	pCR (%)	R0 (%)	Survival
Walsh[31]		ADC	Cisplatin, 5FU	40	25	NA	3 years (%)
CT-RT-Sx	58						32*
Sx	55						6
Bosset[26]		SCC	Cisplatin	37	26	NA	Median (months)
CT-RT-Sx	143						18.6
Sx	149						18.6
Urba[29]		SCC, ADC	Cisplatin, 5FU, Vinblastine	45	28	90	3 years (%)
CT-RT-Sx	50					90	30*
Sx	50						16
Lee[19]		SCC	Cisplatin, 5FU	45.6	43		Median (months)
CT-RT-Sx	51					100	27.3
Sx	50					87.5	28.2
Burmeister[38]		SCC, ADC	Cisplatin, 5FU	35	16		Median (months)
CT-RT-Sx	128					80*	22.2
Sx	128					59	19.3
Tepper[28]		SCC, ADC	Cisplatin, 5FU	50.4	33	NR	5 years (%)
CT-RT-Sx	30						39*
Sx	26						16
CROSS[30]		SCC, ADC	Carboplatin, paclitaxel	41.4	29		5 years (%)
CT-RT-Sx	178					92*	47*
Sx	188					69	34
Mariette[33]		SCC, ADC	Cisplatin, 5FU	45	33.3		3 years (%)
CT-RT-Sx	98					93.8	47.5
Sx	97					92.1	53

CT chemotherapy, *RT* radiotherapy, *Sx* surgery, *SCC* squamous cell carcinoma, *ADC* adenocarcinoma, *5FU* 5-fluorouracil, *pCR* pathologic complete response

on the results of the CROSS trial, neo-adjuvant CRT is an accepted standard of care for locally advanced esophageal carcinoma, with clear benefit for SCC and somewhat less enthusiasm for ADC.[30]

Case for Neo-adjuvant Chemotherapy

Given that distant disease is the major mode of failure after curative intent surgical resection of esophageal cancer, it makes sense that enhanced systemic control with systemic cytotoxic chemotherapy would be investigated to address this issue. Indeed, there have been innumerable studies into adjuvant or neo-adjuvant chemotherapy primarily with cisplatin-based therapies (Table 3). Although an accepted standard of care in many parts of Asia (based on the positive SCC trials from the Japanese Clinical Oncology Group initiatives), the enthusiasm for chemotherapy alone in North America was dampened by the negative Kelsen trial.[22,34] This mixed histology study with a large number of patients (>400) likely suffered not only from the addition of SCC with ADC but also by a low R0 resection rate in both arms (approx. 60 %), questioning adequate local control and surgical quality. More recently, there have been two positive large European trials concentrating on esophageal and EGJ adenocarcinomas employing a similar cisplatin/5FU regimen[23,25] thus establishing preoperative chemotherapy as an acceptable standard for esophageal adenocarcinoma. However, these studies still suffer from the use of relatively outdated chemotherapeutic doublet regimens. Indeed in the metastatic setting, triplets have a greater efficacy over doublets. The MAGIC trial investigating perioperative epirubicin, cisplatin, and 5FU (ECF) initially was designed for gastric cancer; however, to increase accrual, EGJ and distal adenocarcinoma were added eventually representing approximately 25 % of the final study population.[24] This study was strongly positive in support of neo-adjuvant ECF and, on subset analysis, particularly so for EGJ adenocarcinomas. Further refinement of systemic cytotoxic chemotherapy with the addition of taxanes (e.g., docetaxel, 5FU, cisplatin) in the preoperative setting has garnered in a new era in the management of esophageal/EGJ adenocarcinomas, as this regimen has been associated with a very high 5-year survival (above 50 %) and complete resection (R0=95 %) for locally advanced disease,[35] while achieving a very low rate of local or regional recurrence.[36]

Although the literature for neo-adjuvant chemotherapy for esophageal ADC is very strong, there is some resistance for adopting this approach in North America. Studies examining a

Table 3 Randomized trials comparing chemotherapy and surgery versus surgery alone in the treatment of esophageal cancer patients. Adapted from Palta et al.[55], *$p<0.05$

Trial	*N*	Histology	Chemotherapy	R0 (%)	Survival
MRC[23]		SCC, ADC	Cisplatin, 5FU		Median (months)
CT	400			60	17
Sx	402			54	13
RTOG 8911[22]		SCC, ADC	Cisplatin, 5FU		Median (months)
CT	213			63	14.9
Sx	227			59	16.1
MAGIC[24]		ADC	Epirubicin, Cisplatin, 5FU	NA	5 years (%)
CT	250				36*
Sx	253				23
FFCD[25]		ADC	Cisplatin, 5FU		5 years (%)
CT	113			84	38*
Sx	111			74	24

CT chemotherapy, *RT* radiotherapy, *Sx* surgery, *SCC* squamous cell carcinoma, *ADC* adenocarcinoma, *5FU* 5 fluorouracil

direct comparison between CT and CRT prior to surgery for esophageal cancer are complicated by very low accrual and inadequate power and are unlikely to answer the question as to which is preferable (Table 4).[37,38] Irrespective, there is ample literature to support both CT and CRT in the neo-adjuvant setting, and the decision on which is preferable will depend on local institutional preferences and patient mix. At our institution, we prefer to offer neo-adjuvant CRT to locally advanced squamous cell carcinoma.[36] For locally advanced adenocarcinoma, we favor taxane-based CT triplets (docetaxel, cisplatin, 5-fluorouracil) based on very positive results from local trials.[35]

Surgical Technique

The choice of surgical approach in esophagectomy is based on tumor location and the surgeon's perceived ability to obtain a curative R0 resection and adequate lymphadenectomy (>25 lymph nodes). Because positive resection margins are one of the strongest predictors of mortality in esophagectomy, we perform intraoperative microscopic margin analysis.[39,40] Results of the intraoperative margin analysis ultimately determine the location of the anastomosis and may alter the surgical plan such that an R0 resection can be obtained. In addition, we favor the use of a modified radical lymphadenectomy (pleura to pleura and spine to pericardium) in the chest and a D2 dissection in the abdomen given our preference for CT as opposed to CRT in the neo-adjuvant setting.[41] Furthermore, data indicates a survival advantage following extended lymphadenectomy, particularly in EGJ tumors.[41]

In general, Ivor-Lewis esophagectomy (either via MIE or open access) is our preferred approach for tumors below the carina (distal esophageal or EGJ types 1 and 2). For tumors with a high suspicion for lymph node involvement in the neck (bulky, mid, or proximal thoracic esophageal tumor), we advocate a 3-field esophagectomy. In our unit, a single-incision left thoracoabdominal approach is reserved for patients with bulky EGJ type 3 tumors with limited proximal extent of mucosal and nodal disease. For patients with smaller type 2 or 3 tumors with very limited esophageal involvement, an entirely transabdominal approach (laparoscopic or open) with proximal gastrectomy can be performed with excellent oncologic and physiologic outcomes (acceptable reflux) as we have demonstrated.[42] Current evidence does not support one anastomotic technique (hand-sewn versus stapled) over

Table 4 Randomized trials comparing chemoradiotherapy and surgery versus chemotherapy and surgery alone in the treatment of esophageal cancer patients. *$p<0.05$. Adapted from Sjoquist et al.[10]

Trial	*N*	Histology	Chemotherapy	Chemoradiotherapy	pCR (%)	R0 (%)	Survival
Stahl[37]		ADC	Cisplatin, 5FU	Induction—cisplatin, 5FU			3 years (%)
CT-RT	60			Concurrent—cisplatin, etoposide (30 Gy)	15.6*	72	47.4
CT	59				2	69	27.7
Burmeister[38]		ADC	Cisplatin, 5FU	Cisplatin			Median (months)
CT-RT	39			5FU (35 Gy)	31*	84.6	32
CT	36				8	80.5	29

CT chemotherapy, *RT* radiotherapy, *Sx* surgery, *SCC* squamous cell carcinoma, *ADC* adenocarcinoma, *5FU* 5 fluorouracil, *pCR* pathologic complete response

another with respect to anastomotic leak (AL). However, there is some evidence suggesting higher stricture rates associated with stapled versus hand-sewn anastomoses.[43] Accordingly, we favor a tension-free hand-sewn technique with a well-vascularized gastric conduit. Irrespective of approach, access, or anastomotic technique, a pyloric drainage procedure is recommended based on several excellent randomized trials from the University of Hong Kong group.[43,44]

The most significant complications arising following esophagectomy include infectious pulmonary complications, anastomotic leak, and conduit necrosis. The overall incidence of complications following esophagectomy is estimated to reach as high as 50 % with an overall mortality of 9 %.[45,46] However, in high volume centers, the mortality can be reduced to a reasonable rate of 2–3 %.[45–48]

Postoperative infections may also be associated with increased rates of distant metastasis for a number of malignancies including esophageal cancer.[49,50] This observation further highlights the critical need to reduce their occurrence. Along these lines, a number of postoperative strategies aimed at minimizing postoperative infectious complications have been put forward. These include MIE and enhanced recovery after surgery (ERAS).[47,51]

MIE approaches are considered for nearly all patients provided en bloc resection and adequate lymphadenectomy are feasible. The oncologic adequacy of MIE is currently under debate.[47] The recently published TIME trial suggests equivalent LN retrieval rates between open esophagectomy and MIE.[52] However, overall LN retrieval rates were below the accepted minimum in both MIE and open groups.[52] Similarly, comparison of R0 resection rates between open and MIE techniques is based on few high-quality studies.[47] This being said, data does exist to support the use of MIE even in more advanced esophageal tumors, which demonstrates excellent R0 resection rates and lymph node retrieval.[53] Thus, the decision on whether or not to apply an MIE approach should be dependent on the operator's perceived ability to provide an adequate oncologic resection. In general, we reserve MIE for benign lesions or early (cT1-2, N0) tumors. In addition, MIE may provide short-term advantages related to decreased rates of pulmonary complications, intraoperative blood loss, and hospital length of stay.[47]

ERAS entails the implementation of a written, evidence-based, multimodal, stepwise approach to the postoperative management of surgical patients. Such pathways entail early enteral feeding, removal of indwelling catheters and early mobilization, ambulation, and hospital discharge and have been shown to reduce complications and hospital length of stay following a number of oncologic surgeries. We have shown that ERAS principles can be applied to complex procedures such as esophagectomy with excellent clinical results[51] and institutional cost savings.[54]

Conclusions

Esophageal cancer remains a devastating disease, which mandates a multimodal, stage-directed treatment approach in order to achieve favorable outcomes. Early stage disease (cT1, N0) is amenable to curative endoscopic management in selected patients with a low risk of regional lymph node metastasis. However, patients with more advanced disease (cT2) demonstrate unacceptably high rates of lymph node metastasis, precluding endoscopic management. Accordingly, these individuals should be offered up-front surgery or neoadjuvant therapy prior to surgery in select cases. Patients with locally advanced disease (cT3, N+) require systemic therapy in the preoperative period. Although we favor chemotherapy for the management of adenocarcinoma, current evidence also supports the use of CRT in the preoperative period. Regardless of the preoperative regimen selected, the surgical approach employed should permit en bloc resection with extended lymphadenectomy in order to maximize the survival benefit associated with surgery in this patient population. Following surgery, vigilance for the development of complications is required in order to mitigate their impact on morbidity and mortality. Implementation of an enhanced recovery pathway facilitates the care of such complex patients and may reduce the incidence of complications and hospital length of stay.

The flow diagram presented highlights the proposed esophageal carcinoma treatment algorithm at the McGill University Health Centre. Abbreviations: EUS, endoscopic ultrasound; CT, computed tomography; PET, positron emission tomography; EMR, endoscopic mucosal resection; ESD, endoscopic submucosal dissection; ADC, adenocarcinoma; SCC, squamous cell carcinoma; CRT, chemoradiotherapy; carbo-taxol 45 Gy; TCF taxotere, cisplatin, 5FU.

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