COLLEGE OF ONCOLOGY

National Clinical Practice Guidelines

Oesophageal Cancer

Version 2.2012

Oesophageal Cancer Guidelines Expert Panel

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Reference: Lerut T, Stordeur S, Verleye L, Vlayen J, Boterberg T, De Hertogh G, De Mey J, Deprez P, Flamen P, Pattyn P, Van Laethem J-L, Peeters M. Update van de praktijkrichtlijn voor slokdarm- en maagkanker. Good Clinical Practice (GCP). Brussel: Federaal Kenniscentrum voor de Gezonheidszorg (KCE); 2012. KCE reports 179A. D/2012/10.273/32).

or

Reference: Lerut T, Stordeur S, Verleye L, Vlayen J, Boterberg T, De Hertogh G, De Mey J, Deprez P, Flamen P, Pattyn P, Van Laethem J-L, Peeters M. Actualisation des recommandations cliniques pour le cancer de l'oesophage et de l'estomac. Good Clinical Practice (GCP). Bruxelles: Centre Fédéral d'Expertise des Soins de Santé (KCE). 2012. KCE Report 179B. D/2012/10.273/33.

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[1] Attended the open meeting [2] Gave feedback by email

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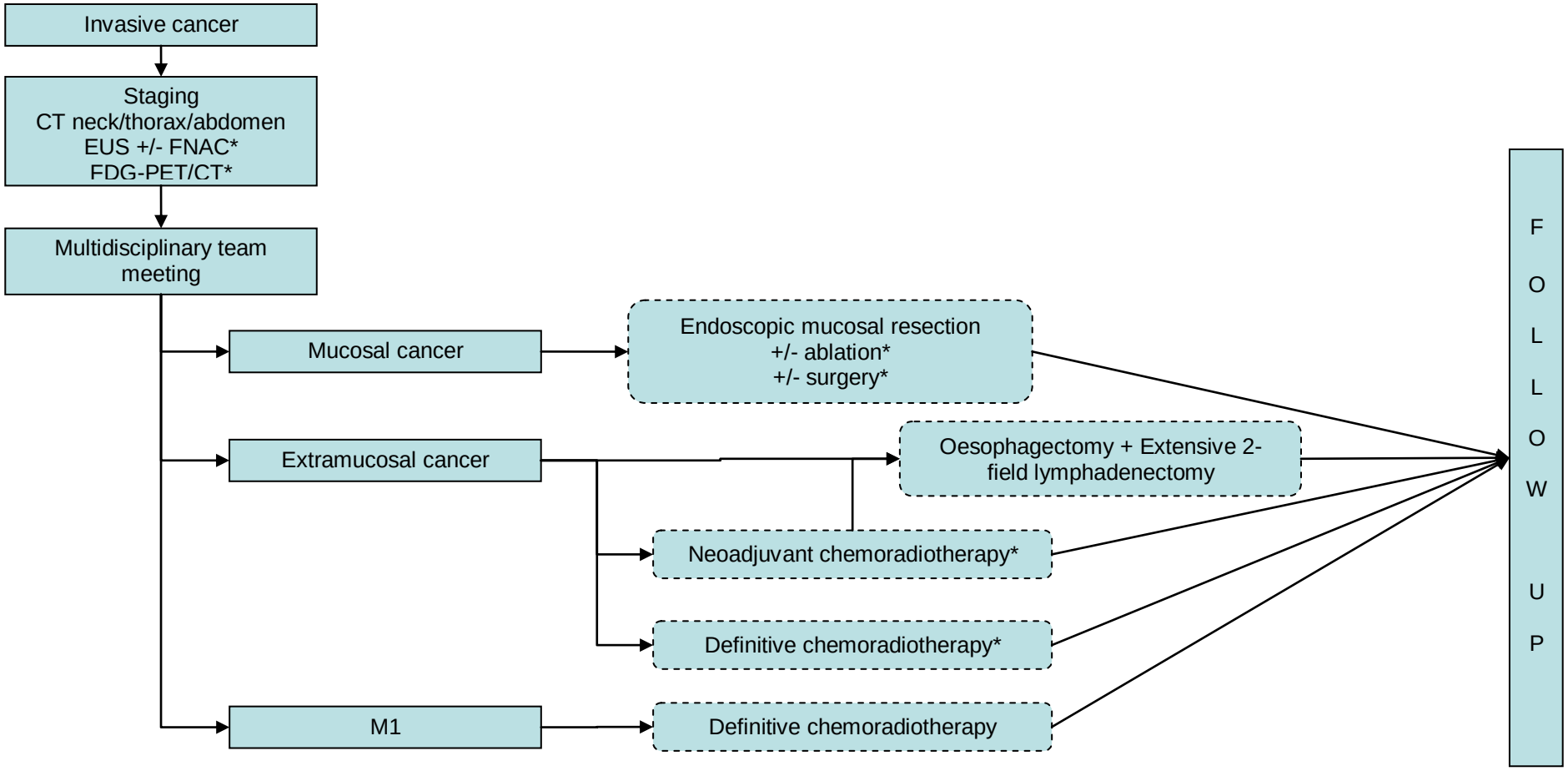
Flowchart: clinical recommendations for oesophageal cancer



* Option to be discussed at the MDT meeting

National Guidelines Oesophageal Cancer

INTRODUCTION [1]

This document presents the updated clinical practice guidelines on oesophageal cancer which was first published in 2008 [1]. It covers a broad range of topics: diagnosis, staging, treatment and follow-up of patients with confirmed invasive oesophageal cancer.

Importantly, the following topics that were part of the previous version were not included in the update:

- work-up of pre-invasive lesions, i.e. Barett's oesophagus and dysplastic lesions, including high-grade dysplasia
- treatment of gastric lymphoma
- treatment of gastrointestinal stromal tumors (GIST)

For more in-depth information and the scientific background, we would like to ask the readers to consult the full scientific report at https://kce.fgov.be.

The guidelines are developed by a panel of experts (see 'expert panel') comprising clinicians of different specialties and were reviewed by relevant professional associations (see 'external reviewers and validators').

The aim of these guidelines is to assist all care providers involved in the care of patients with oesophageal cancer.

EPIDEMIOLOGY [2-8]

Oesophageal cancer is the eighth most common cancer in the world (about 481 000 new cases in 2008 worldwide) and one of the most lethal (6th most common cause of death from cancer worldwide). Incidence rates of oesophageal cancer show well-known regional disparities, with the highest incidence rates in Southern Africa (Age Standardised Rate [ASR] 22.3 per 100 000 men and 11.7 per 100 000 women in 2008) and the lowest rates in Western Africa (ASR 1.4 per 100 000 men in 2008). In Europe, crude incidence rates for all types of oesophageal cancer ranged from 0.7 cases per 100 000 in Cyprus to 13.3 cases per 100 000 in the UK in 2008.

In Belgium, the crude incidence rate of oesophageal cancer in males rose between 2004 and 2006 from 12.4 to 13.6 per 100 000 males, where after it slightly decreased to 12.9 per 100 000 males in 20098. In females, the crude incidence rate varied between 4.1 and 4.7 per 100 000 females in the period 2004-2009. Similar trends are reported for the age standardised incidence.

SEARCH FOR EVIDENCE [9-12]

Sources

Systematic reviews and meta-analyses were searched in the following databases: OVID Medline and PreMedline, EMBASE, Cochrane Database of Systematic Reviews, Database of Abstracts of Reviews of Effects (DARE), Health Technology Assessment (HTA) database. RCTs

were searched in OVID Medline, PreMedline, EMBASE and CENTRAL, while diagnostic accuracy studies were searched in OVID Medline, PreMedline and EMBASE.

A date limit was set from August 2007 (i.e. the search date of the previous version) until 2011.

Grade of recommendation

A grade of recommendation was assigned to each recommendation using the GRADE system (Appendix 1).

EXTERNAL REVIEW

The guidelines prepared by the expert panel were circulated to the relevant professional associations (see 'external reviewers'). Each association was asked to assign two key persons to discuss the recommendations during an open meeting. As a preparation of the meeting all invited experts were asked to score each recommendation on a 5-point Likert-scale to indicate their agreement with the recommendation, with a score of '1' indicating 'completely disagree', '2' indicating 'somewhat disagree', '3' indicating 'unsure', '4' indicating 'somewhat agree', and '5' indicating 'completely agree' (the experts were also able to answer 'not applicable' in case they were not familiar with the underlying evidence). In case an expert disagreed with the recommendation (score '1' or '2'), (s)he was asked to provide appropriate evidence. All scores were then anonymized and summarized into a median score, minimum score, maximum score and % of 'agree'-scores (score '4' and '5') to allow a targeted discussion. The recommendations were then discussed during a face-to-face meeting on March 30th 2012. Based on this discussion a final draft of the recommendations was prepared.

As part of the standard KCE procedures, an external scientific validation of the report was conducted by three independent experts. Following this validation procedure, some recommendations were finally adapted if strong arguments supported a change in the formulation.

DEFINITIONS

Topographic definitions [13-16]

- A tumour of which the epicentre is within 5 cm of the GOJ and extending into the oesophagus is to be classified as an oesophageal tumour.
- Tumours with an epicentre in the stomach greater than 5 cm from the GOJ or those within 5 cm of the GOJ without extension in the oesophagus are to be classified as a gastric tumour.

Early lesions [17-46]

- There is no consensus about the definition of Barrett's oesophagus.
- Several classifications are available for dysplasia. For the physician, the used classification should be clinically relevant.

Early versus locally-advanced invasive disease

- Definitions of early and locally-advanced cancer are not uniform and controversial. Therefore, to avoid discussion, an attempt will be made

to define the eligible population for our recommendations as accurate as possible.

STAGING [47-87]

Conclusions of the literature update

- The rate of correctly staged tumours (T-stage) is higher with EUS than with CT, but the latest generation of scanners (64- and 256-slice) were poorly evaluated (low level of evidence; Tranchemontagne 2009).
- For the detection of regional lymph node metastases, EUS is most sensitive, whereas CT and PET are more specific tests. The examiner experience explains the high variability in the performance outcomes obtained with EUS. FNA substantially improves the sensitivity and specificity of EUS in evaluating the N-stage (low level of evidence; Tranchemontagne 2009).
- For the evaluation of distant metastases, PET has probably a higher sensitivity than CT. Combining these two modalities could be of clinical value, with PET detecting possible metastases and CT confirming or excluding their presence and precisely determining the location(s). The high specificity of PET/CT is useful to exclude positive non-peritumoural lymph nodes and metastasis (low level of evidence; Tranchemontagne 2009).
- Laparoscopy has a higher specificity for M-staging in comparison with CT, but carries a higher risk of morbidity (low level of evidence; CBO 2005). The available evidence does not allow to conclude about the clinical value of thoracoscopy.
- Few studies are available on the diagnostic accuracy of MRI for the staging of oesophageal cancer (low level of evidence; SIGN 2006, CBO 2005).

Final recommendations

- All patients diagnosed with oesophageal cancer should be discussed at a multidisciplinary meeting ***(strong recommendation, low level of evidence)***.
- In patients with newly diagnosed oesophageal cancer, CT scan of the neck (including lower neck region), thorax and abdomen should always be performed ***(strong recommendation, low level of evidence)***.
- Endoscopic ultrasonography (EUS), combined with fine needle aspiration cytology (FNAC) if technically feasible, should be considered to evaluate locoregional invasion (T and N stage) and presence of positive celiac lymph nodes in patients with oesophageal cancer ***(strong recommendation, low level of evidence)***.
- PET/CT should be considered for M staging if a patient with T2-4 N+ oesophageal cancer is a candidate for a curative treatment after CT and EUS ***(strong recommendation, low level of evidence)***.
- The following examinations can be considered for specific indications: MRI, bronchoscopy +/- bronchial ultrasonography (BUS) +/- biopsy, thoracoscopy, or laparoscopy ***(weak recommendation, low level of evidence)***.

Good clinical practice

- Multi-detector, multi-planar reformatted CT scan should be performed with IV contrast. The liver should at least be imaged in the arterial and portal venous phase.

TREATMENT OF MUCOSAL CANCER [47-48,88-91]

Conclusions of the literature update

- Despite low quality evidence, endoscopic treatments seem to reduce the morbidity and mortality associated with oesophagectomy. However, there is no evidence demonstrating the superiority of one particular endoscopic treatment (low level of evidence; McCann 2011).
- In patients with superficial oesophageal cancer (T1a), treatment with endoscopic mucosal resection is equally effective as surgery, but associated with less complications (low level of evidence; SIGN 2006, CBO 2005).
- The clinical effectiveness of mucosal ablative techniques in patients with superficial oesophageal cancer is insufficiently proven (low level of evidence; SIGN 2006, CBO 2005).

Final recommendations

- Endoscopic mucosal resection (EMR) should be performed whenever possible for a T1a oesophageal cancer, aiming at staging and curative resection. If the staging and R0 resection is pathologically confirmed, this procedure can be considered therapeutic, taking into account other well-defined criteria relating to size, length of Barrett, histological type, differentiation grade and lymphovascular invasion. In case the staging and R0 resection is not confirmed, surgery can be considered ***(strong recommendation, low level of evidence)***.
- (Destructive) mucosal ablative techniques cannot be recommended as a curative option for patients with T1a oesophageal cancer and should be limited to centres with appropriate expertise ***(strong recommendation, low level of evidence)***.

Good clinical practice

- The diagnosis of T1a oesophageal cancer should be validated by an experienced pathologist.

TREATMENT OF CANCER BEYOND THE MUCOSA

Neoadjuvant treatment [92-98]

Conclusions of the literature update

- Preoperative radiotherapy is not associated with an improved survival compared to surgery alone in patients with operable oesophageal cancer (moderate level of evidence; Malthaner 2005, Arnott 2010).
- There is no strong evidence for a survival benefit of neoadjuvant chemotherapy over surgery alone in patients with oesophageal carcinoma (low level of evidence; Boughrassa 2009).
- Preoperative chemotherapy is associated with a higher likelihood of R0 resection, without increasing postoperative morbidity or 30-day mortality (low level of evidence; Kranzfelder 2011)
- Preoperative chemotherapy increases neither complications nor postoperative mortality (low level of evidence; Boughrassa 2009, Ando 2011)
- There is evidence for a survival benefit of neoadjuvant chemoradiotherapy over surgery alone in patients with oesophageal carcinoma, irrespective of the histological type (low level of evidence; Sjoquist 2011). The complete histological response rates observed

after this treatment suggest that it could contribute to improving disease-free survival (low level of evidence; Boughrassa 2009). The highest potential benefit was only observed in a minority of patients with a complete response.

- Preoperative chemoradiotherapy is associated with a higher likelihood of R0 resection, without increasing postoperative morbidity or 30-day mortality (low level of evidence; Kranzfelder 2011)
- A clear advantage of neoadjuvant chemoradiotherapy over neoadjuvant chemotherapy has not been established (low level of evidence; Sjoquist 2011).

Final recommendations

- If, after multidisciplinary discussion, neoadjuvant treatment is considered for a locally-advanced oesophageal or junction tumour, neoadjuvant chemoradiotherapy is preferred ***(strong recommendation, low level of evidence)***.

Response assessment and restaging [6965,100-105]

Conclusions of the literature update

- For the evaluation of treatment response, EUS combined with FNA has only a moderate diagnostic value. However, this method is harmful and, in some cases, cannot be performed because of the lesion location (low level of evidence, Ngamruengphong 2010).
- PET performed early in the course or after the neoadjuvant therapy may be able to predict response with low to moderate diagnostic accuracy (low level of evidence; Chen 2011, Kwee 2010, Ngamruengphong 2010)
- CT has insufficient value for early response assessment in patients with potentially curable oesophageal cancer who are treated with neoadjuvant chemoradiotherapy (low level of evidence; Van Heijl 2011).
- There is insufficient evidence to draw conclusions about the diagnostic accuracy of EUS, PET/CT and CT for restaging of patients with oesophageal cancer after neoadjuvant treatment.

Final recommendations

The use of PET and EUS (with or without FNAC) for the assessment of treatment response early in the course of, or after neoadjuvant treatment should be restricted to clinical studies and requires a central prospective registration of all cases ***(weak recommendation, low level of evidence)***.

Surgical treatment [47-48,92,96,99,106-128]

Conclusions of the literature update

- Overall survival after primary CRT or standard multimodality treatment for patients with operable locally advanced oesophageal squamous cell cancer is equivalent (moderate level of evidence; Bedenne 2007, Stahl 2005, Chiu 2005).
- There are indications that surgery preceded by CRT for patients with locally advanced oesophageal squamous cell cancer is associated with a better local progression-free survival than primary CRT (low level of evidence; Stahl 2005).

- Standard multimodality treatment is associated with a higher treatment-related mortality than primary CRT (moderate level of evidence; Bedenne 2007, Stahl 2005).
- There is no significant overall survival benefit with transthoracic oesophagectomy compared to transhiatal oesophagectomy. However, extended transthoracic oesophagectomy for type I oesophageal adenocarcinoma shows a trend towards better 5-year survival. Moreover, an extended transthoracic oesophagectomy is more beneficial for patients with a limited number of positive lymph nodes (< 8) in the resection specimen (moderate level of evidence; Omloo 2007).
- Transthoracic and transhiatal techniques led to similar results in terms of postoperative mortality (regardless of histological tumour type) and in terms of cardiac or infectious complications (low level of evidence; Boughrassa 2011).
- The weakness of the available evidence on the efficacy of the different invasive and minimally invasive techniques hampers to conclude on the superiority of minimally invasive oesophagectomy in terms of short-term and oncological outcomes. Minimally invasive oesophagectomy remains under development (low level of evidence; Boughrassa 2011, Sgourakis 2010).
- Available data are insufficient to conclude on the clinical benefit of extending lymph node dissection to the cervical region (low level of evidence; Boughrassa 2011).
- Centralization of oesophageal cancer surgery in dedicated high-volume centres, which also combine other favourable characteristics (infrastructure, specialization of medical professionals, outcome measures), could lead to better outcomes in this patient group (low level of evidence; Wouters 2011).
- Identifying best practices in patient selection, treatment strategies, technical procedures, and perioperative care are also important to improve the quality of care in patients with oesophageal cancer (low level of evidence; Wouters 2011).

Final recommendations

- Oesophageal cancer surgery should be carried out in high-volume specialist centres with experience and/or specialist training in oesophageal and gastro-oesophageal junction cancer ***(strong recommendation, low level of evidence)***.
- For patients with resectable oesophageal cancer beyond the mucosa, surgery (+/- neoadjuvant chemoradiotherapy) is considered standard (***strong recommendation, high level of evidence)***.
- Surgery for oesophageal cancer should be aimed at achieving an R0 resection, and should be considered preferentially through a transthoracic en bloc resection ***(strong recommendation, high level of evidence)***.
- Minimally invasive oesophagectomy is under development and is not recommended in routine practice ***(weak recommendation, low level of evidence)***.
- Extensive two-field lymphadenectomy should be standard during oesophagectomy to improve staging, local disease control and potentially cure rate ***(strong recommendation, low level of evidence)***.
- Three-field lymphadenectomy during oesophagectomy should be restricted to clinical studies ***(weak recommendation, low level of evidence)***.

Adjuvant treatment [92,129-135]

Conclusions of the literature update

- Postoperative chemotherapy is not associated with a survival benefit compared to surgery alone in patients with oesophageal cancer (low level of evidence; Malthaner 2005).
- Postoperative radiotherapy is not associated with a survival benefit compared to surgery alone in patients with oesophageal cancer (low level of evidence; Malthaner 2005).
- No direct evidence from randomized trials is available comparing postoperative chemoradiotherapy with surgery alone in patients with oesophageal cancer.
- Postoperative chemoradiotherapy is not associated with a survival benefit compared to postoperative chemotherapy in patients with oesophageal cancer (low level of evidence; Malthaner 2005).

Final recommendations

- Adjuvant treatment is not routinely recommended for patients with oesophageal cancer ***(strong recommendation, low level of evidence)***.

Non-surgical treatment with curative intent [47-48,106-108,136-142]

- Overall survival after primary CRT or standard multimodality treatment for patients with operable locally advanced oesophageal squamous cell cancer is equivalent (moderate level of evidence; Bedenne 2007, Stahl 2005, Chiu 2005).
- There are indications that surgery preceded by CRT for patients with locally advanced oesophageal squamous cell cancer is associated with a better local progression-free survival than primary CRT (low level of evidence; Stahl 2005).
- Standard multimodality treatment is associated with a higher treatment-related mortality than primary CRT (moderate level of evidence; Bedenne 2007, Stahl 2005).
- Primary concomitant chemoradiotherapy is associated with a survival benefit compared to radiotherapy alone in patients with locally advanced oesophageal cancer (moderate level of evidence; Wong 2006, Zhao 2005, Liu 2010).
- Treatment with primary concomitant chemoradiotherapy is associated with important toxicity compared to radiotherapy alone (moderate level of evidence; Wong 2006, Zhao 2005, Liu 2010).
- Primary sequential chemoradiotherapy is not associated with a survival benefit compared to radiotherapy alone in patients with locally advanced oesophageal cancer (moderate level of evidence; Wong 2006).

Final recommendations

- Definitive concomitant chemoradiotherapy should be considered in patients with locally advanced oesophageal cancer of any histological type ***(strong recommendation, moderate level of evidence)***:
    - If the tumour is considered unresectable;
    - If the patient is unfit for surgery;
    - If the patient declines surgery.
- In patients with resectable squamous cell carcinoma of the oesophagus who have locally advanced disease, definitive concomitant

chemoradiotherapy should be restricted to clinical studies ***(strong recommendation, moderate level of evidence)***.

- Definitive concomitant chemoradiotherapy can be considered for patients with cervical oesophageal cancer in order to preserve the larynx ***(weak recommendation, low level of evidence)***.

TREATMENT OF METASTATIC DISEASE [48,108,143-157]

Conclusions of the literature update

- Argon plasma coagulation (APC) therapy combined with photodynamic therapy (PDT) or with high dose rate brachytherapy is efficient to increase the dysphagia-free period after treatment and is safe and well tolerated (moderate level of evidence; Rupinski 2011).
- Partially covered self-expanding metal stents (SEMS) or plastic expandable stents reduce the number of reinterventions, but are associated with a lower overall survival than other treatment modalities (laser therapy, thermotherapy ablation (TTA) or brachytherapy) (moderate level of evidence; Sgourakis 2010).
- The use of palliative surgery in patients with oesophageal cancer is associated with high morbidity and decreased quality of life (low level of evidence; Scottish Intercollegiate Guidelines Network 2006).
- Capecitabine and oxaliplatin are as effective as fluorouracil and cisplatin with respect to overall survival. Toxic effects are not negligible and can reduce the quality of life (high level of evidence; Cunningham 2008).
- The use of external-beam radiotherapy or high dose rate (HDR) brachytherapy for the palliation of dysphagia and pain is supported by RCTs and observational studies. The addition of EBRT to HDRBT improved dysphagia-relief experience in 1 RCT (moderate level of evidence; Rosenblatt 2010).

Final recommendations

- Control of obstruction caused by oesophageal cancer should be obtained with stent placement, or laser therapy or argon plasma coagulation (APC) therapy, depending on the local availability and expertise ***(strong recommendation, high level of evidence)***.
- Partially covered self-expanding metal stents or plastic expandable stents are the best options for palliation of dysphagia caused by oesophageal cancer ***(strong recommendation, moderate level of evidence)***.
- Ablative therapies or restenting should be considered for control of tumour ingrowth or overgrowth in stented patients ***(strong recommendation, low level of evidence)***.
- The use of oesophageal dilation alone should be avoided ***(weak recommendation, low level of evidence)***.
- Oesophagectomy (transthoracic or transhiatal) should not be performed with palliative intent in patients with oesophageal cancer ***(strong recommendation, low level of evidence)***.
- Substernal bypass for oesophageal cancer should not be performed with palliative intent ***(strong recommendation, low level of evidence)***.
- In patients with locally advanced or metastatic cancer of the oesophagus, chemotherapy or chemoradiotherapy are treatment

options that should be discussed in the multidisciplinary team ***(weak recommendation, high level of evidence)***.

- Palliative external-beam radiotherapy or endoluminal brachytherapy should be considered in patients with dysphagia from oesophageal cancer and with a longer life expectancy ***(strong recommendation, low level of evidence)***.
- Patients with advanced oesophageal cancer should have access to a specialist palliative care team, in particular in relation to comfort and symptom control, nutrition and quality of life ***(strong recommendation, low level of evidence)***.

SUPPORTIVE CARE [47-48,158]

- The KCE is currently developing a guideline on the supportive care of cancer patients. Specific recommendations on the treatment of chemotherapy- and radiotherapy-related adverse events, exercise treatment, psychosocial support and pain treatment will be available.

FOLLOW-UP [47-48,159-160]

Conclusions of the literature update

- Frequency, type and duration of follow-up is not supported by strong evidence and is consensus-based (very low level of evidence; CBO 2005, SIGN 2006).
- Nurse-led follow-up at home does not adversely affect quality of life or satisfaction of patients compared with standard follow-up by clinicians at the outpatient clinic (low level of evidence; Verschuur 2009).
- Based on one diagnostic accuracy study, PET/CT seems to have a good sensitivity to detect recurrence, at the cost of a high rate of false positive findings (low level of evidence; Roedl 2008).

Final recommendations

- It is recommended that the follow-up of patients treated for oesophageal cancer includes a physical examination and blood analysis every three months, with targeted imaging if needed. A CT scan can be considered every six months in the first year and then annually until the fifth year ***(weak recommendation; very low level of evidence)***.
- Patients treated with endoscopic mucosal resection (EMR) should have a follow-up endoscopy after three months, then every six months in the first two years, and then annually ***(weak recommendation; very low level of evidence)***.

TREATMENT OF RECURRENT DISEASE [161-168]

Conclusions of the literature update

- For patients confronted with a local recurrence of oesophageal cancer, treatments options include local treatment or multimodality treatment (very low level of evidence; Kunisaki 2007, Natsugoe 2006, Yamashita 2005, Nomura 2000).

Final recommendations

- In patients with recurrent oesophageal cancer, treatment options should be discussed in the multidisciplinary team ***(strong recommendation, very low level of evidence)***.

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Appendix 1: GRADE system

Levels of evidence according to the GRADE system

Quality level	Definition	Methodological Quality of Supporting Evidence
High	We are very confident that the true effect lies close to that of the estimate of the effect	RCTs without important limitations or overwhelming evidence from observational studies
Moderate	We are moderately confident in the effect estimate: the true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different	RCTs with important limitations (inconsistent results, methodological flaws, indirect, or imprecise) or exceptionally strong evidence from observational studies
Low	Our confidence in the effect estimate is limited: the true effect may be substantially different from the estimate of the effect	RCTs with very important limitations or observational studies or case series
Very low	We have very little confidence in the effect estimate: the true effect is likely to be substantially different from the estimate of the effect	

Strength of recommendations according to the GRADE system

Grade	Definition
Strong	The desirable effects of an intervention clearly outweigh the undesirable effects *(the intervention is to be put into practice)*, or the undesirable effects of an intervention clearly outweigh the desirable effects *(the intervention is not to be put into practice)*
Weak	The desirable effects of an intervention probably outweigh the undesirable effects *(the intervention probably is to be put into practice)*, or the undesirable effects of an intervention probably outweigh the desirable effects *(the intervention probably is not to be put into practice)*

Appendix 2: TNM classification and stage grouping (7th edition)

cTNM Clinical Classification

T – Primary tumour

Tx Primary tumor cannot be assessed

T0 No evidence of primary tumor

Tis Carcinoma in situ/high-grade dysplasia

T1 Tumour invades lamina propria, muscularis mucosae, or submucosa

- T1a Tumour invades lamina propria or muscularis mucosae
- T1b Tumour invades submucosa

T2 Tumour invades muscularis propria

T3 Tumour invades adventitia

T4 Tumour invades adjacent structures

- T4a Tumour invades pleura, pericardium, or diaphragm
- T4b Tumour invades other adjacent structures such as aorta, vertebral body, or trachea

N – regional lymph nodes

Nx Regional lymph nodes cannot be assessed

N0 No regional lymph node metastasis

N1 Metastasis in 1-2 regional lymph nodes

N2 Metastasis in 3-6 regional lymph nodes

N3 Metastasis in 7 or more regional lymph nodes

M – Distant metastasis

M0 No distant metastasis

M1 Distant metastasis

pTNM Pathological Classification

The pT and pN categories correspond to the T and N categories.

pN0 Histological examination of a regional lymphadenectomy specimen will ordinarily include 6 or more lymph nodes. If the lymph nodes are negative, but the number ordinarily examined is not met, classify as pN0.

Stage grouping

Stage 0	Tis	N0	M0
Stage IA	T1	N0	M0
Stage IB	T2	N0	M0
Stage IIA	T3	N0	M0
Stage IIB	T1, T2	N1	M0
Stage IIIA	T4a	N0	M0
	T3	N1	M0
	T1, T2	N2	M0
Stage IIIB	T3	N2	M0
Stage IIIC	T4a	N1,N2	M0
	T4b	Any N	M0
	Any T	N3	M0
Stage IV	Any T	Any N	M1