COLLEGE OF ONCOLOGY

National Clinical Practice Guidelines

Oesophageal Cancer

Version 1.2008

Continue

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This report was supported by the Belgian Healthcare Knowledge Centre. The full scientific report can be consulted at the KCE website (www.kce.fgov.be).

Reference: Peeters M, Lerut T, Vlayen J, Mambourg F, Ectors N, Deprez P, et al. Wetenschappelijke ondersteuning van het College voor Oncologie: een nationale praktijkrichtlijn voor de aanpak van slokdarm- en maagkanker. Good Clinical Practice (GCP). Brussel: Federaal Kenniscentrum voor de Gezonheidszorg (KCE); 2008. KCE reports 75A (D2008/10.273/16).

or

Reference: Peeters M, Lerut T, Vlayen J, Mambourg F, Ectors N, Deprez P, et al. Guidelines pour la prise en charge du cancer oesophagien et gastrique: elements scientifiques à destination du Collège d'Oncologie. Bruxelles: Centre fédéral d'expertise des soins de santé (KCE); 2008. KCE reports 75B (D2008/10.273/17).

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OESOPHAGEAL CANCER

OESOPHAGEAL CANCER

General algorithm

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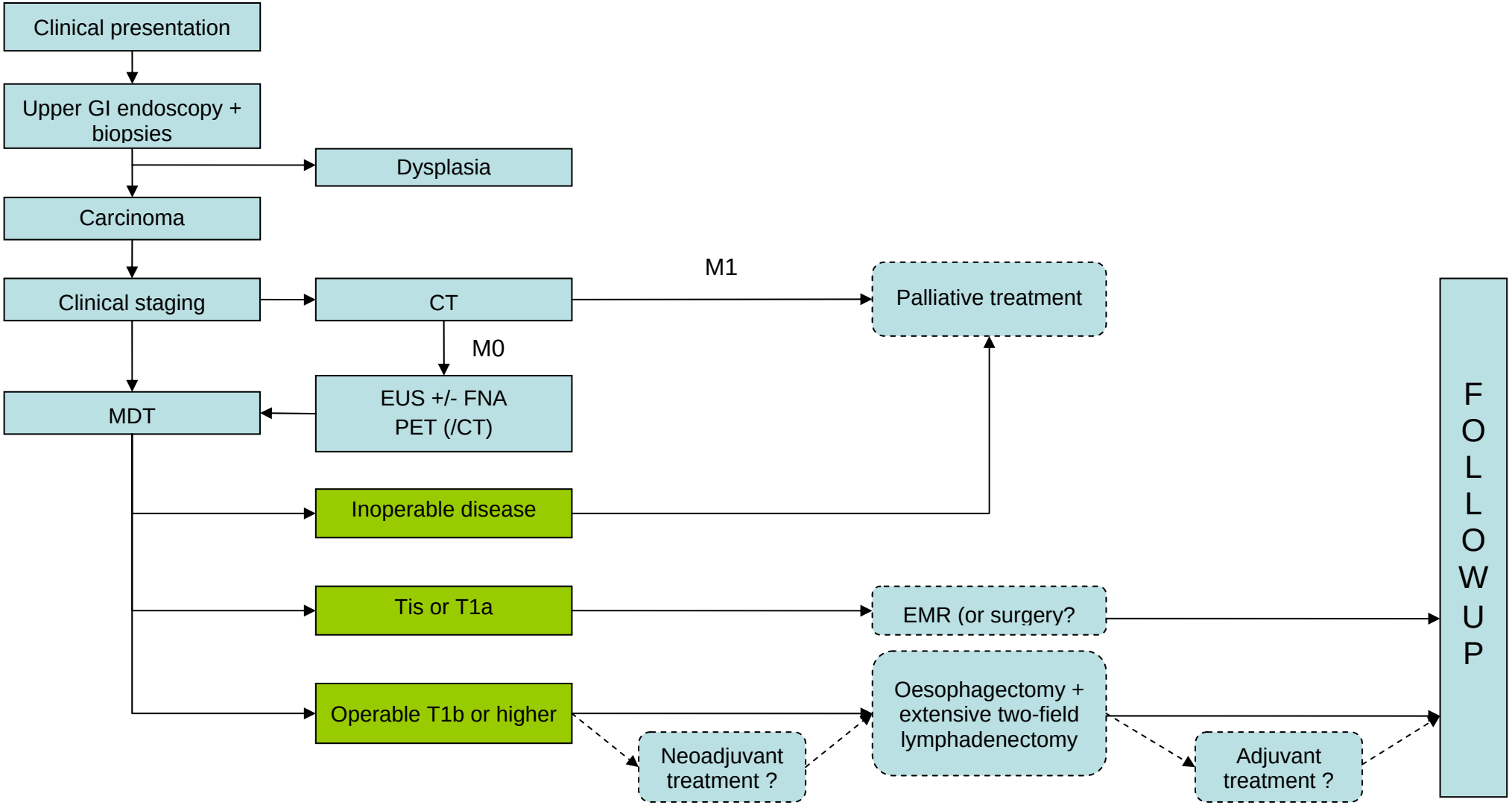

National Guidelines Oesophageal Cancer

INTRODUCTION

This document provides an overview of the clinical practice guidelines for oesophageal cancer. For more in-depth information and the scientific background, we would like to ask the readers to consult the full scientific report at www.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')

The guidelines are based on the best evidence available at the time they are derived (date restriction 2001-2007). The aim of these guidelines is to assist all care providers involved in the care of patients with oesophageal cancer.

SEARCH FOR EVIDENCE

Clinical practice guidelines

Sources

A broad search of electronic databases (Medline, EMBASE), specific guideline websites and websites of oncologic organisations (Table 1) was conducted in July 2007.

In- and exclusion criteria

Both national and international clinical practice guidelines (CPGs) on oesophageal cancer were searched. A language (English, Dutch, French) and date restriction (2001 – 2007) were used. CPGs without references were excluded, as were CPGs without clear recommendations.

Additional evidence

For each clinical question, the evidence – identified through the included CPGs – was updated by searching Medline and the Cochrane Database of Systematic Reviews from the search date of the CPG on (search date August-September 2007).

Grade of recommendation

A grade of recommendation was assigned to each recommendation using the GRADE system (Table 2).

EPIDEMIOLOGY

Oesophageal cancer is the eighth most common cancer in the world and one of the most lethal [1]. Incidence rates of oesophageal cancer show well-known regional disparities. Overall, incidence rates for all types of oesophageal cancer range from four to nine cases per 100.000 males per year (1975 – 1997) in Western countries [2]. Lower incidence rates are

found in Northern Europe (Finland, Norway, and Sweden), whereas the French regions of Burgundy and Calvados have incidence rates of > 14 per 100.000 males per year.

In Belgium, the crude incidence rate of oesophageal cancer rose from 8.8 per 100.000 males in 1997 to 10.8 per 100.000 males in 2003, and from 2.2 per 100.000 females in 1997 to 3.5 per 100.000 females in 2003 (Belgian Cancer Registry, personal communication).

DEFINITIONS

Topographic definitions [11-16]

- If more than 50% of the mass of the tumour is situated in the cardia, the tumour should be considered to be of cardiac origin and classified as a gastric tumour
- If the mass of the tumour is predominantly found in the oesophagus, it should be classified as an oesophageal tumour.
- Tumours of the gastro-oesophageal junction should be classified and have the same concept of treatment as oesophageal tumours.

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.

DIAGNOSIS [47-54]

- Patients presenting with any of the following alarm symptoms within the clinical context of potential oesophageal pathology should be referred for early endoscopy and biopsies: dysphagia, recurrent vomiting, anorexia, weight loss, gastrointestinal blood loss ***(1C recommendation)***.
- Flexible upper gastrointestinal endoscopy with at least biopsies of all suspicious lesions is recommended as the diagnostic procedure of choice in patients with suspected oesophageal cancer ***(1C recommendation)***.
- High-resolution endoscopy (HRE) and chromoendoscopy is not routinely recommended, but may be of value in screening and follow-up of high-risk patients ***(2C recommendation)***.

WORK-UP DYSPLASTIC LESIONS [47,55-58]

- Reduction of risk of progression to adenocarcinoma is not an indication for anti-reflux surgery in patients with Barrett's oesophagus ***(2A recommendation)***.
- In patients with Barrett's oesophagus there should be a structured biopsy protocol with quadrantic biopsies every two centimetres and biopsy of any visible lesion ***(1C recommendation)***.
- Pathologists should follow a classification for reporting dysplasia that the multidisciplinary team is familiar with ***(1C recommendation)***.

- Evaluation of suspected high-grade dysplasia in Barrett's oesophagus biopsies should be undertaken with knowledge of the clinical and endoscopic background ***(1C recommendation)***.
- Patients confirmed with high-grade dysplasia should have careful endoscopic and pathological assessment ***(1C recommendation)***.
- High-resolution endoscopy +/- chromoendoscopy as well as every 1 cm qaudrantic biopsies is recommended in patients with a dysplastic or neoplastic lesion in a Barrett's oesophagus ***(1C recommendation)***.
- Where therapeutic intervention is contemplated on the basis of high-grade dysplasia, the diagnosis should be validated by a second pathologist experienced in this area and further biopsies or eventually diagnostic endoscopic mucosal resection (EMR) should be done if there is uncertainty ***(1C recommendation)***.
- Treatment options for patients with high-grade dysplasia should be discussed at a multidisciplinary meeting with access to the clinical and pathological information ***(expert opinion)***.
- Patients with high-grade dysplasia should be referred to centres or network reference centres with the appropriate endoscopic and surgical expertise and facilities ***(1C recommendation)***.

STAGING [47,56,59-79]

TNM classifcation and TNM stage grouping are presented in table 3 and table 4.

- In patients with oesophageal cancer, CT scan of the chest (including lower neck region) and abdomen with intravenous contrast and gastric distension with oral contrast or water should be performed routinely. The liver should at least be imaged in the arterial and portal venous phase ***(1C recommendation)***.
- Patients with oesophageal or gastro-oesophageal junction cancers who are candidates for any curative therapy should have their tumours staged with endoscopic ultrasonography +/- fine needle aspiration cytology (FNAC) and ultrasonography of the neck ***(1B recommendation)***.
- Fine needle aspiration cytology (FNAC) needs to be interpreted by an experienced pathologist ***(expert opinion)***.
- In patients with oesophageal cancer and an option for curative treatment after conventional staging (CT/endoscopic ultrasonography), PET(/CT) scan may be considered for the staging of lymph nodes (loco-regional, distal or all lymph nodes) and distant sites other than lymph nodes ***(1C recommendation)***.
- The following examinations can be considered for specific indications: MRI, bronchoscopy +/- bronchial ultrasonography (BUS) +/- biopsy, thoracoscopy, or laparoscopy ***(1C recommendation)***.

TREATMENT MUCOSAL CANCER [47,56,80-83]

- Where therapeutic intervention is considered for a supposedly T1a mucosal cancer, the diagnosis should be validated by a second pathologist experienced in this area. Further biopsies or eventually diagnostic endoscopic mucosal resection (EMR) should be done if there is uncertainty ***(1C recommendation)***.
- Treatment options for patients with mucosal cancer should be discussed at a multidisciplinary meeting with access to the clinical and

- pathological information ***(expert opinion)***.
- Superficial oesophageal cancer limited to the mucosa should be treated with endoscopic mucosal resection (EMR), taking into account well-defined criteria relating to stage, size, length of Barrett, histological type, differentiation grade, and lymphovascular invasion ***(1C recommendation)***.
- Mucosal ablative techniques, such as argon plasma coagulation (APC), photodynamic therapy (PDT) or laser, are investigational and should be limited to units with appropriate expertise ***(1C recommendation)***.

TREATMENT OF CANCER BEYOND THE MUCOSA

Neoadjuvant treatment [67,74,84-92]

- Preoperative radiotherapy alone is not recommended for patients with oesophageal cancer ***(2A recommendation)***.
- Neoadjuvant treatment is not routinely indicated for patients with oesophageal cancer ***(2A recommendation)***.
- The need for neoadjuvant treatment should be discussed during a multidisciplinary meeting ***(expert opinion)***.
- Prospective registration of clinical outcomes and adverse events of combined treatment is recommended ***(expert opinion)***.

Surgical treatment [47,56,84,88,93-101]

- Surgical resection is considered standard treatment for patients with resectable oesophageal cancer ***(1A recommendation)***.
- Surgery for oesophageal cancer should be aimed at achieving an R0 resection, and should be considered preferentially through a transthoracic en bloc resection ***(1A recommendation)***.
- Extensive two-field lymphadenectomy should be standard during oesophagectomy to improve staging, local disease control and potentially cure rate ***(1C recommendation)***.
- Three-field lymphadenectomy is strictly investigational ***(2C recommendation)***.
- Oesophageal cancer surgery should be carried out in high volume specialist surgical units by surgeons with experience and/or specialist training in oesophageal and gastro-oesophageal junction cancer ***(1C recommendation)***.

Adjuvant treatment [84,104-107]

- Postoperative adjuvant chemotherapy is not recommended for patients with oesophageal cancer ***(2A recommendation)***.
- Postoperative adjuvant radiotherapy is not recommended for patients with oesophageal cancer ***(2A recommendation)***.
- Postoperative adjuvant chemoradiotherapy is not recommended for patients with oesophageal cancer ***(expert opinion)***.

Non-surgical treatment with curative intent [47,56,93,94,108-111]

- Definitive chemoradiotherapy should be considered in patients with oesophageal cancer who have locally advanced disease that is considered unresectable, in patients who are unfit for surgery, or in patients who decline surgery ***(1A recommendation)***. It can also be

considered for patients with cervical oesophageal cancer in order to preserve the larynx ***(1C recommendation)***.

PALLIATIVE TREATMENT AND METASTATIC DISEASE [47,48,56,112-115]

- Control of obstruction caused by oesophageal cancer should be obtained with stent placement or laser/ argon plasma coagulation (APC) therapy, depending on the local availability and expertise ***(1A recommendation)***.
- Partially covered self-expanding metal stents or plastic expandable stents are the best options for palliation of dysphagia caused by oesophageal cancer ***(1B recommendation)***.
- Laser therapy, argon plasma coagulation (APC) therapy or re-stenting should be considered for control of tumour ingrowth or overgrowth in stented patients ***(1C recommendation)***.
- The use of oesophageal dilatation alone should be avoided ***(2C recommendation)***.
- Oesophagectomy (transthoracic or transhiatal) should not be performed with palliative intent in patients with oesophageal cancer ***(1C recommendation)***.
- Substernal bypass for oesophageal cancer should not be performed with palliative intent ***(1C recommendation)***.
- 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 ***(2A recommendation)***.
- Palliative external-beam radiotherapy or endoluminal brachytherapy should be considered in patients with dysphagia from oesophageal cancer and with the perspective of a more prolonged survival ***(2C recommendation)***.
- Patients with 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 ***(1C recommendation)***.

FOLLOW-UP [47,56]

- It is recommended that the follow-up of patients treated for oesophageal cancer includes a physical examination every three months, and a CT scan every six months in the first year and afterwards annually until the fifth year ***(expert opinion)***.
- 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 ***(expert opinion)***.

RECURRENT DISEASE [116-123]

- In patients with recurrent oesophageal cancer, treatment options should be discussed in the multidisciplinary team ***(expert opinion)***.
- In patients with a local recurrence or new tumour after endoscopic mucosal resection (EMR), treatment options, including local treatment, should be discussed in the multidisciplinary team ***(expert opinion)***.

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Searched guideline websites and websites of oncologic organisations	
Alberta Heritage Foundation For Medical Research (AHFMR)	http://www.ahfmr.ab.ca/
American Society of Clinical Oncology (ASCO)	http://www.asco.org/
American College of Surgeons (ACS)	http://www.facs.org/cancer/coc/
CMA Infobase	http://mdm.ca/cpgsnew/cpgs/index.asp
Guidelines International Network (GIN)	http://www.g-i-n.net/
National Comprehensive Cancer Network (NCCN)	http://www.nccn.org/
National Guideline Clearinghouse	http://www.guideline.gov/
National Cancer Institute	http://www.cancer.gov/
Haute Autorité de Santé (HAS)	http://bfes.has-sante.fr/HTML/indexBFES_HAS.html
BC Cancer Agency	http://www.bccancer.bc.ca/default.htm
Institute for Clinical Systems Improvement (ICSI)	http://www.icsi.org/index.asp
National Health and Medical Research Council (NHMRC)	http://www.nhmrc.gov.au/
Scottish Intercollegiate Guidelines Network (SIGN)	http://www.sign.ac.uk/
New Zealand Guidelines Group (NZGG)	http://www.nzgg.org.nz/
Fédération Nationale des Centres de Lutte Contre le Cancer (FNCLCC)	http://www.fnclcc.fr/sor/structure/index-sorspecialistes.html
National Institute for Health and Clinical Excellence (NICE)	http://www.nice.org.uk/

Grade of Recommendation/ Description	Benefit vs. Risk and Burdens	Methodological Quality of Supporting Evidence	Implications
1A/ Strong recommendation, high quality evidence	Benefits clearly outweigh risk and burdens, or vice versa	RCTs without important limitations or overwhelming evidence from observational studies	Strong recommendation, can apply to most patients in most circumstances without reservation
1B/ Strong recommendation, moderate quality evidence	Benefits clearly outweigh risk and burdens, or vice versa	RCTs with important limitations (inconsistent results, methodological flaws, indirect, or imprecise) or exceptionally strong evidence from observational studies	Strong recommendation, can apply to most patients in most circumstances without reservation
1C/ Strong recommendation, low quality evidence	Benefits clearly outweigh risk and burdens, or vice versa	Observational studies or case series	Strong recommendation, but may change when higher quality evidence becomes available
2A/ Weak recommendation, high quality evidence	Benefits closely balanced with risks and burden	RCTs without important limitations or overwhelming evidence from observational studies	Weak recommendation, best action may differ depending on circumstances or patients' or societal values
2B/ Weak recommendation, moderate quality evidence	Benefits closely balanced with risks and burden	RCTs with important limitations (inconsistent results, methodological flaws, indirect, or imprecise) or exceptionally strong evidence from observational studies	Weak recommendation, best action may differ depending on circumstances or patients' or societal values
2C/ Weak recommendation, low quality evidence	Benefits closely balanced with risks and burden	Observational studies or case series	Very weak recommendation, other alternatives may be equally reasonable

T Primary Tumour

Tx	Primary tumour cannot be assessed
T0	No evidence of primary tumour
Tis	Carcinoma in situ
T1	Tumour invades lamina propria or submucosa
T2	Tumour invades muscularis propria
T3	Tumour invades adventitia
T4	Tumour invades adjacent structures

N Regional Lymph Nodes

Nx	Regional lymph nodes cannot be assessed
N0	No regional lymph nodes metastasis.
N1	Regional lymph node metastasis

M Distant Metastasis

Mx	Distant metastasis cannot be assessed
M0	No distant metastasis
M1	Distant metastasis
	For tumours of lower thoracic oesophagus
	M1a Metastasis in celiac lymph nodes
	M1b Other distant metastasis
	For tumours of upper thoracic oesophagus
	M1a Metastasis in cervical lymph nodes
	M1b Other distant metastasis
	For tumours of lower mid-thoracic oesophagus
	M1a Not applicable
	M1b Non-regional lyph node or other distant metastasis

Stage 0	Tis	N0	M0
Stage I	T1	N0	M0
Stage IIA	T2	N0	M0
	T3	N0	M0
Stage IIB	T1	N1	M0
	T2	N1	M0
Stage III	T3	N1	M0
	T4	Any N	M0
Stage IV	Any T	Any N	M1
Stage IVA	Any T	Any N	M1a
Stage IVB	Any T	Any N	M1b

