Clinical Commissioning Policy: 18F-fluorodeoxyglucose (FDG) positron emission tomography-computed-tomography (PET CT) as part of radical radiotherapy treatment planning for oesophageal cancer (all ages)

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Clinical Commissioning Policy: 18F-fluorodeoxygluose (FDG) positron emission tomography-computer tomography (PET-CT) as part of radical radiotherapy treatment planning for oesophageal cancer (all ages)

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Contents

Policy Statement

NHS England will not routinely commission 18F-FDG-PET CT as part of radical radiotherapy treatment planning for oesophageal cancer in accordance with the criteria outlined in this document.

In creating this policy NHS England has reviewed this clinical condition and the options for its treatment. It has considered the place of this treatment in current clinical practice, whether scientific research has shown the treatment to be of benefit to patients, (including how any benefit is balanced against possible risks) and whether its use represents the best use of NHS resources.

Equality Statement

Promoting equality and addressing health inequalities are at the heart of NHS England's values. Throughout the development of the policies and processes cited in this document, we have:

- given due regard to the need to eliminate discrimination, harassment and victimisation, to advance equality of opportunity, and to foster good relations between people who share a relevant protected characteristic (as cited under the Equality Act 2010) and those who do not share it; and
- given regard to the need to reduce inequalities between patients in access to, and outcomes from healthcare services and to ensure services are provided in an integrated way where this might reduce health inequalities.

Plain Language Summary

About oesophageal cancer

Oesophagael cancer is a cancer of the foodpipe, which carries food from the mouth to the stomach. It is the 13th most common cancer in the United Kingdom (UK), with approximately 9,211 cases diagnosed per year (Cancer Research UK, 2018b). Oesophageal cancer can develop in people of any age and gender, however, it is more commonly diagnosed in older males.

At the time of diagnosis, around 39% of people with the condition are well enough to be able to undergo treatment which aims to cure the cancer (National Oesophago-Gastric Cancer Audit, 2017). These are sometimes called radical treatments or treatments given with curative intent.

About current treatments

Surgery is the most common curative treatment for oesophagael cancer, however, both chemotherapy, radiotherapy and combination therapy (one or more of surgery, chemotherapy and radiotherapy) can also be given as part of a curative treatment plan. The policy relates to radiotherapy given with curative intent, which is sometimes called radical radiotherapy.

Because radiotherapy involves the use of radiation, it is important to carefully plan the treatment. This is to make sure that the right amount of radiation needed to treat the cancer is given exactly where it is needed, minimising the amount of radiation given to healthy body tissues. This process is called radiotherapy treatment planning.

As part of the radiotherapy treatment planning process, people with oesophagael cancer currently have a computerised tomography (CT) scan. The scan shows the cancer and the structures around it and helps ensure the prescribed dose of radiation can be targeted to the cancer.

About the new treatment

PET-CT scans involve the injection of a mildly radioactive substance into the body about an hour prior to the scan taking place. This is so that the scan can show where the substance does and does not accumulate in the body, which can provide important information about how well different body functions are working. The most common substance is 18F-flourodeoxyglucose, this is usually called FDG.

The use of PET-CT to plan radiotherapy treatments may offer a more targeted approach to radiotherapy treatment delivery. More targetted treatment delivery may result in fewer side effects from radiotherapy and reduced need for further treatment.

What we have decided

NHS England has carefully reviewed the evidence for PET-CT, using FDG, as part of radical radiotherapy treatment planning for oesophageal cancer. We have concluded that there is not enough evidence to make the treatment available at this time.

1 Introduction

Oesophagael cancer is a cancer of the foodpipe, which carries food from your mouth to your stomach. At the time of diagnosis, approximately 39% of people with oesophageal cancer are well enough to be able to undergo treatment with curative intent (i.e treatment that aims to cure the cancer) (National Oesophago-Gastric Cancer Audit, 2017).

Surgery is the main curative treatment option for oesophageal cancer, however, in some cases either chemotherapy or radiotherapy may be given in its place. Some people may also have a combination (at least two or more) of surgery, chemotherapy and radiotherapy as part of a curative treatment plan.

It is estimated that radiotherapy forms part of the treatment plan for approximately 40-50% of all oesophageal cancer cases where radical treatment is possible (National Institute of Health and Care Excellence, 2018).

Planning the radiotherapy treatment is integral to ensuring that the cancer gets the prescribed dose of radiation while normal body tissues get as little as possible (Cancer Research UK, 2016b). It is important to be able to define the location and the extent of the cancer that will be subject to radiation; this is called the gross tumour volume. Currently computed tomography (CT) scans are used to plan the radiotherapy treatment for patients with oesophageal cancer and determine the gross tumour volume.

PET-CT combines both a CT scan with a positron emission tomography (PET) scan to provide highly detailed three-dimensional images of the inside of the body. PET-CT scans involve the injection of a radioactive substance (sometimes referred to as a radiotracer), most commonly FDG, into the body about an hour prior to the scan taking place. This substance is detected by the PET-CT scanning machine as it collects in different parts of the body. By analysing the areas where the radiotracer does and doesn't build up, it is possible to work out how well certain body functions are working and identify any abnormalities.

PET-CT scans are particularly helpful for investigating confirmed cases of cancer to determine how far the cancer has spread and/or how well it's responding to treatment. It is thought that PET-CT scans may also have a role in radiotherapy treatment planning, allowing for more accurate determination of the tumour volume (size of the tumour) and the delivery of better-targeted radiotherapy treatment.

2 Definitions

Computed tomography (CT) scan - uses X-rays and a computer to create detailed images of the inside of the body.

Curative treatment - a treatment which aims to remove or destroy the cancer completely.

Gross tumour volume – is a term used to define the location and size of the tumour for radiation therapy.

Leucopenia - a reduction in the number of white blood cells.

Neo-adjuvant treatment - the administration of therapeutic agents before a main treatment, for example using chemotherapy and/or radiotherapy prior to surgery.

Oesophagus - the food pipe which runs between the throat and the stomach.

Radical radiotherapy – radiotherapy used with curative intent.

Radiotherapy – the use of radiation, usually x-rays, to kill cancer cells.

3 Aims and Objectives

This policy considered: PET-CT using FDG, as part of radical radiotherapy treatment planning for oesophageal cancer.

The objectives were to: determine/ ascertain whether:

- compared to radiotherapy planned without PET-CT (using FDG), the effect of PET-CT (using FDG) planned radiotherapy (and chemoradiotherapy) on gross tumour volume (GTV) among patients with established oesophageal cancer due to be treated in a neo-adjuvant or radical manner;
- the effect of reduced GTV on adverse effects from radiotherapy and whether it allows treatment completion;
- compared to radiotherapy planned without PET-CT (using FDG), PET–CT (using FDG) planned radiotherapy resulted in improved outcomes for patients with oesophageal cancer;
- compared to radiotherapy planned without PET-CT (using FDG), the evidence of cost effectiveness of radiotherapy directly planned with PET-CT (using FDG); and
- there is evidence that combined PET-CT (using FDG) for staging/diagnosis and for radiotherapy planning is more cost effective compared to separate PET-CT (using FDG) for these two purposes.

4 Epidemiology and Needs Assessment

Oesophageal cancer is the 13th most common cancer in the UK with 9,211 new cases in 2015 (Cancer Research UK, 2018b). This type of cancer is strongly related to age, with 8 out 10 cases diagnosed in patients over the age of 60 years (Cancer Research UK, 2016). Approximately 70% of cases are diagnosed at a late stage and the prognosis for oesophageal cancer remains poor with a five-year survival of 15% and a ten-year survival of 12% (Cancer Research UK, 2018b). The incident rate is 3.5 times higher in males than females.

The risk factors for oesophageal cancer are largely lifestyle related and include: (i) being over-weight/obese; (ii) smoking or using tobacco; and (iii) alcohol.

Needs assessment

Between 2013–2016, approximately 39% of people with oesophageal cancer had treatment given with curative intent (National Oesophago-Gastric Cancer Audit, 2017). This equates to approximately 3,600 people having curative treatment for

their cancer in England every year. Data from the National Radiotherapy Dataset (RTDS) shows that in 2016/17, approximately 1,450 people had radical radiotherapy treatment for their oesophagael cancer, accounting for approximately 40% of all oesophagael cancers treated with curative intent.

5 Evidence Base

No controlled studies matching the Population, Intervention, Comparison and Outcomes (PICO) inclusion criteria were identified. No evidence was identified comparing the effectiveness of radiotherapy directly planned with FDG PET-CT to radiotherapy without direct FDG PET-CT planning.

Three prospective uncontrolled studies were included in which patients received an FDG PET-CT scan in the treatment position and outcomes from radiotherapy using the FDG PET-CT treatment plan were reported.

Clinical effectiveness

- Three uncontrolled studies used FDG PET-CT to delineate gross tumour volume (GTV). In one study (Ng et al 2017) two potential treatment plans were generated for all patients, one using a CT scan and one an FDG PET-CT scan. Differences between the two treatment plans were reported, based on the assumption that the FDG PET-CT plan represented the true extent of the disease. In most patients the two scanning methods resulted in differences in estimated tumour size and areas identified as requiring treatment, but these differences were not consistent in magnitude or direction. The study did not compare the effectiveness of plans or treatment using different scanning methods. All patients received treatment using the FDG PET-CT treatment plan. In two studies (Yu et al 2015; Lertbutsayanukul et al 2013) the delineation of GTV using FDG PET-CT was used to deliver different levels of radiation dose to different tumour areas (with reduced dose to margins).
- In one study (Ng et al 2017) a clinical complete response to treatment was seen in 50% (95%CI 34 to 66) of 36 patients assessed three months after completion of radiotherapy and a partial response in a further 39% (95%CI 25

to 55). In another study (Lertbutsayanukul et al 2013) pathologic response to neo-adjuvant chemotherapy was assessed in seven patients undergoing surgery. A complete response (on histological examination) was seen in 57% of patients and a further 29% had microscopic residual disease.

- In Ng et al (2017) loco-regional treatment failures (within the radiation treatment field) were observed in 29% of 38 patients who received radiotherapy (median follow-up four years). Regional failure was observed in one of 14 surviving patients in Lertbutsayanukul et al (2013) (median follow-up 12 months).
- One-year overall survival ranged from 69% to 87% in the three studies (Ng et al 2017; Yu et al 2015; Lertbutsayanukul et al 2013). The study with the longest median follow-up (Ng et al 2017) reported four-year overall survival as 37% (95%CI 24 to 57). Ng et al also reported loco-regional failure free survival as 86% (95%CI 75 to 99) at one year and 65% (95%CI 47 to 90) at four years; and relapse free survival (measured from the end of radiotherapy to the date of first relapse at any site or date or death for patients that did not relapse) as 58% (95%CI 44 to 76) at one year and 30% (95%CI 18 to 49) at four years. In addition Lertbutsayanukul et al (2013) reported one-year event-free survival (measured from the date of commencing radiotherapy to the date of loco-regional, systemic cancer recurrence or secondary primary cancer. In patients who did not have surgery, event was determined at time to tumour progression or metastases) as 59% and Yu et al (2015) reported one-year progression free survival (not further defined) as 52%.
- In Lertbutsayanukul et al (2013) 15 patients assessed three months after the completion of radiotherapy all had a partial metabolic response with a mean maximum standard uptake value (the ratio of the image derived radioactivity concentration and the whole body concentration of the injected radioactivity) reduction of 62% (range 37 to 82).

Safety

- The most common severe adverse events in Lertbutsayanukul et al (2013) were leucopenia (59%) and vomiting (24%), and one patient died from oesophageal fistula 186 days after the first day of radiation. In Yu et al (n=25)

severe adverse events occurring during treatment were acute oesophagitis (40%), hematologic toxicity (28%) and nausea and vomiting (24%), and one patient died from oesophageal haemorrhage. The most commonly reported mild to moderate adverse effects were anaemia, platelet decrease, cardiovascular toxicity, dysphagia, pulmonary toxicity, weight loss, vomiting and leucopenia.

- In Lertbutsayanukul et al (2013) the percentage of normal tissue receiving radiation was reported: 26% of normal lung tissue received 20Gy; 48% of normal lung tissue received 10Gy; the average maximum dose to the spinal cord was 40.6Gy and the median dose to the heart was 30.8Gy.
- In Yu et al (2015) there was uninterrupted completion of radiotherapy for 23 of 25 patients. In two patients radiotherapy was interrupted due to bronchiectasis haemoptysis and cold and fever respectively.

Cost-effectiveness

No studies assessing the cost or cost-effectiveness of radiotherapy planned with FDG PET-CT or the cost or cost-effectiveness of combined compared to separate staging and planning PET-CT scans were identified.

6 Documents Which Have Informed this Policy

None.

7 Date of Review

This document will be reviewed when information is received which indicates that the policy requires revision.

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