Improvement of the multimodality treatment of oesophageal cancer
Courrech Staal, E.F.W.

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Oesophageal cancer treatment in a tertiary referral hospital evaluated by indicators for quality of care

Submitted

Ewout FW Courrech Staal
Karen M Bloemendal
Martine C Bloemer
Berthe MP Aleman
Annemieke Cats
Johanna W van Sandick
Abstract

Background
Studies on quality of care for oesophageal cancer patients usually include only traditional outcome parameters. The aim of the study was to address quality of care in a broader perspective.

Methods
Between 2003 and 2008, 821 oesophageal cancer patients were referred to our institute. Indicators to measure quality of care were defined and comparisons between two time periods were made.

Results
335 patients came for a second opinion only, 382 patients received palliative treatment and 104 (13%) patients underwent potentially curative treatment. The median time between the first hospital visit and start of treatment decreased from 24 days in period I to 18 days in period II ($P=0.03$). Of patients who underwent potentially curative treatment, 81% in period I and 86% in period II were discussed during a weekly multidisciplinary meeting ($P=0.54$). Compliance with the national guideline was comparable in both periods (84% vs. 80%, $P=0.27$). There were non-significant improvements in completion of chemoradiation (85% vs. 91%), postoperative complication rates (57% vs. 33%) and 3-year survival (40% vs. 46%).

Conclusion
By evaluating different dimensions of healthcare quality, we have identified which steps in the multidisciplinary care path need more attention in order to raise the whole level of care.
Introduction

Oesophageal cancer is sixth on the list of cancer mortality causes in the world.¹ In 2008, the incidence in the Netherlands was estimated around 1850 new patients per year.² It has been recommended to concentrate the surgical treatment of oesophageal cancer in high-volume centres. Though an improvement in postoperative mortality is expected, there are doubts about the effectiveness of such measures in raising the whole level of quality of care.³ Quality assurance in the treatment of cancer is gaining importance since many studies have shown variation in outcome. Most quality assurance programmes, however, are predominantly based on traditional outcome parameters such as postoperative mortality rates and survival. A better understanding of the complex clinical processes that lead to either success or failure may have more potential to improve outcome of health care. Preferably, the concentration of oesophageal cancer treatment is accompanied by a national quality assurance program, evaluating the different dimensions of quality of care in all hospitals taking care of oesophageal cancer patients.⁴

At the end of 2005, an evidence-based national guideline for the treatment of oesophageal cancer was published in the Netherlands.⁵ It is unknown whether the implementation of this guideline has influenced the quality of care for oesophageal cancer patients.

The aim of the present study was to evaluate the quality of care for oesophageal cancer patients who were seen at our institute between 2003 and 2005 (period I) or between 2006 and 2008 (period II). Indicators for quality of care were defined.

Materials and Methods

The Netherlands Cancer Institute-Antoni van Leeuwenhoek Hospital (NKI-AVL) in Amsterdam is a tertiary referral centre for patients with oesophageal cancer in the Netherlands.

Study population

Between January 2003 and December 2008, 821 patients with oesophageal cancer were seen at the NKI-AVL outpatient clinic for a second opinion, further staging and/or treatment. This group of patients was retrospectively studied in detail based on data retrieved from hospital records and the electronic hospital information system. Comparisons between two time periods were made, i.e., before (2003-2005) and after (2006-2008) the publication of the national guideline on Staging and Treatment of Oesophageal Cancer in December 2005.
Indicators for quality of care

Indicators for quality of care were defined by review of similar articles in the literature on breast cancer and head and neck cancer\textsuperscript{6,7}, by consultation of the national guideline\textsuperscript{5}, and by consensus between two of the investigators (ECS, JvS). The indicators are listed in Table 1. Compliance with the national guideline was examined exclusively in patients treated at the NKI-AVL.

Diagnostic work-up and Staging

Oesophageal cancer diagnosis was obtained by oesophagogastroduodenoscopy with biopsies, usually at the referring hospital. When necessary, the tumour stage was re-assessed at the NKI-AVL by computed tomography (CT)-scan, external ultrasonography of the neck and/or endoscopic ultrasonography (EUS) with fine needle aspiration on indication. From the year 2004 on, positron emission tomography (PET) was regularly used in oesophageal cancer staging. Tumour node metastasis (TNM) stages were subdivided in four different categories according to the treatment algorithm in the national guideline: T1-2N0M0, T3N0-1M0-1a/T1-2 N1and/orM1a, T4N0-1M0-1a, AnyT-AnyN-M1b.

During a weekly meeting, patients with potentially curable disease were assessed by a multidisciplinary team (MDT) of gastroenterologists, surgeons, radiation oncologists, medical oncologists, radiologists and, in more recent years, nuclear medicine physicians. During this meeting, the results of all diagnostic measures were shown, the patient’s clinical condition was discussed and a treatment plan was proposed. Patients were scored as "discussed" only if documented proof was available that the patient had been discussed at a MDT meeting prior to treatment.

Treatment

Patients in a good general condition with a T1-3N0-1M0-1a tumour received potentially curative treatment, whereas patients with a T4N0-1Mo-1a or AnyT-AnyN-M1b tumour received palliative treatment. Furthermore, there was a group of patients who were seen for a second opinion only.

Potentially curative treatment

For T1-2NoMo oesophageal cancer, standard treatment is surgical resection. For T3No1Mo-1a/T1-2 N1and/orM1a oesophageal carcinomas, surgery is the treatment of choice provided that a microscopically radical resection (R0) can be achieved. According to the national guideline of 2005, neoadjuvant chemoradiotherapy should only be applied in the setting of a clinical study. At the NKI-AVL, however, this has been standard treatment since 1997.\textsuperscript{8-10} After the completion of neoadjuvant chemoradiotherapy, before surgery, the
Table 1: Predefined indicators for quality of care in oesophageal cancer treatment

<table>
<thead>
<tr>
<th>Indicator</th>
<th>Explanation</th>
</tr>
</thead>
<tbody>
<tr>
<td>First care provider at the NKI-AVL*</td>
<td>Type of specialist to whom the patient was referred</td>
</tr>
<tr>
<td>Referral wait†</td>
<td>Interval between the date of making the first appointment and the date of first hospital attendance</td>
</tr>
<tr>
<td>Treatment wait†</td>
<td>Interval between the date of first attendance and the start of treatment of any kind</td>
</tr>
<tr>
<td>Total wait†</td>
<td>Interval between referral date and first treatment date</td>
</tr>
<tr>
<td>Number of appointments†</td>
<td>Number of appointments at the NKI-AVL before the start of treatment</td>
</tr>
<tr>
<td>Number of hospital visits†</td>
<td>Number of visits to the NKI-AVL before the start of treatment</td>
</tr>
<tr>
<td>Multidisciplinary meeting†</td>
<td>Case presentation in the weekly multidisciplinary meeting</td>
</tr>
<tr>
<td>Compliance with the guideline*,‡</td>
<td>Compliance with the national guideline on Staging and Treatment of Oesophageal Cancer</td>
</tr>
<tr>
<td>Difference in stage of disease*,‡</td>
<td>A difference in stage of disease as documented at the referring hospital and that observed at the NKI-AVL</td>
</tr>
<tr>
<td>Discrepancy in type of treatment*,‡</td>
<td>Discrepancy between the treatment as proposed at the referring hospital and the treatment actually given at the NKI-AVL</td>
</tr>
<tr>
<td>Results of chemoradiotherapy†,‡</td>
<td>Toxicity of treatment and completion of regimen</td>
</tr>
<tr>
<td>Results of surgery†,‡</td>
<td>R0 resection, number of removed lymph nodes, surgical reintervention rate, anastomotic leakage rate, in-hospital mortality</td>
</tr>
<tr>
<td>Survival†,‡</td>
<td>1- and 3-year survival</td>
</tr>
</tbody>
</table>

Abbreviations: NKI-AVL, The Netherlands Cancer Institute - Antoni van Leeuwenhoek Hospital; R0: microscopically radical resection

* Indicator defined by consensus between two of the investigators
† Indicators defined by review of similar articles in the literature
‡ Indicators defined by consultation of the national guideline
Chapter 8

188 patients were re-evaluated to monitor the effect of chemoradiation (response evaluation). If possible, surgery was planned 5-6 weeks after the completion of chemoradiotherapy.

Some patients were treated with neoadjuvant chemotherapy alone as part of a phase II study\textsuperscript{11,12}, and several patients received postoperative adjuvant chemoradiation as part of a phase I/II dose finding study.

Chemoradiation without surgery was given to patients with locally advanced tumours who were unfit for major surgery.

Palliative treatment
For patients with a T4 tumour and for those with distant metastases (M1b), the intent of the treatment was palliative. Dysphagia was treated with stent placement and/or radiotherapy. Palliative external radiotherapy consisted mostly of 30-39 Gray in 10-13 fractions. Palliative brachytherapy implied 12 Gray in one fraction. At times, palliative chemotherapy was given.

Second opinion
For patients who came to the NKI-AVL for a second opinion only, a limited set of data was collected including general patient and tumour characteristics, date of oesophageal cancer diagnosis, date of making the first appointment at the NKI-AVL, date of the first hospital attendance, and TNM stage as documented at the referring hospital. Information on the treatment given at the referring hospital was not collected.

Statistical analysis
All analyses were performed using SPSS (Statistical Package for the Social Sciences, Chicago, IL) version 15.0.1. Differences in patient, tumour, and treatment characteristics as well as outcome measurements between the two time periods were assessed using the Mann-Whitney test for continuous variables and the chi-square test or Fisher’s exact test for categorical variables. Waiting times were assessed in terms of median values, since the distributions were highly skewed.

Patients’ survival was calculated from the start of treatment to the date of death or the date of last follow-up by means of life-table analysis. Overall survival calculations included postoperative mortality. $P$-values $< 0.05$ (2-sided) were considered statistically significant.
Results

Reasons for referral
Of the 821 patients, 335 came for a second opinion only (164 versus 171), 382 patients were given palliative treatment (174 versus 208) and 104 patients underwent potentially curative treatment (42 versus 62) (Figure 1). The majority of patients referred for palliative treatment received radiotherapy and/or stent placement (260/382; 68%). With regard to potentially curative treatment, most patients were given chemoradiation with or without surgery (95/104; 91%).

Figure 1: Flow chart of oesophageal cancer patients who presented at the NKI-AVL between 2003 and 2008

Patient and tumour characteristics
Table 2 shows patient and tumour characteristics. There were no significant differences between the two groups with regard to gender, age, tumour location and histology, and TNM stage distribution as documented at our institute. In both time periods, the gastroenterologist was the most common first specialist at the NKI-AVL (65% and 55%, respectively), but in the second period significantly more patients were directly referred to the radiation oncologist (22% vs. 31%, $P=0.03$).

Abbreviations: NKI-AVL: The Netherlands Cancer Institute-Antoni van Leeuwenhoek Hospital
Waiting time statistics

Table 3 shows referral wait, treatment wait, and total wait for both time periods. For all three waiting times, the median number of days decreased significantly.
Table 3: Waiting time statistics

<table>
<thead>
<tr>
<th>Period</th>
<th>2003-2005</th>
<th>2006-2008</th>
<th>Test for difference*</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Curative</td>
<td>Palliative</td>
<td>Second opinion</td>
</tr>
<tr>
<td></td>
<td>(n=42)</td>
<td>(n=174)</td>
<td>(n=164)</td>
</tr>
<tr>
<td>Referral wait</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No. of evaluated patients</td>
<td>30</td>
<td>146</td>
<td>144</td>
</tr>
<tr>
<td>Median (days)</td>
<td>5</td>
<td>6</td>
<td>8</td>
</tr>
<tr>
<td>Interquartile range (days)</td>
<td>2-7</td>
<td>3-7</td>
<td>5-12</td>
</tr>
<tr>
<td>Treatment wait</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No. of evaluated patients</td>
<td>42</td>
<td>164</td>
<td>--</td>
</tr>
<tr>
<td>Median (days)</td>
<td>40</td>
<td>18</td>
<td>N/A</td>
</tr>
<tr>
<td>Interquartile range (days)</td>
<td>29-50</td>
<td>8-33</td>
<td>N/A</td>
</tr>
<tr>
<td>Total wait</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No. of evaluated patients</td>
<td>30</td>
<td>137</td>
<td>--</td>
</tr>
<tr>
<td>Median (days)</td>
<td>45</td>
<td>24</td>
<td>N/A</td>
</tr>
<tr>
<td>Interquartile range (days)</td>
<td>35-58</td>
<td>14-42</td>
<td>N/A</td>
</tr>
</tbody>
</table>

Abbreviations: NKI-AVL: The Netherlands Cancer Institute-Antoni van Leeuwenhoek Hospital; N/A: not assessed

* Test for difference between the two time periods for all patients
**Appointments and hospital visits**

In Table 4, the number of appointments and hospital visits are depicted. For patients who underwent potentially curative treatment, the median number of appointments before the start of treatment increased from 7 to 9 ($P=0.21$), but the number of hospital visits remained the same (6; $P=0.72$). In the second time period, the percentage of patients with less hospital visits than appointments had increased ($P=NS$).

**Table 4: Number of appointments and number of hospital visits before start of treatment**

<table>
<thead>
<tr>
<th>Period</th>
<th>2003-2005</th>
<th>2006-2008</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Curative (n=42)</td>
<td>Palliative (n=164)</td>
</tr>
<tr>
<td>Number of appointments</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Median</td>
<td>7</td>
<td>3</td>
</tr>
<tr>
<td>Interquartile range</td>
<td>5-9</td>
<td>1-5</td>
</tr>
<tr>
<td>Number of hospital visits</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Median</td>
<td>6</td>
<td>2</td>
</tr>
<tr>
<td>Interquartile range</td>
<td>5-8</td>
<td>1-4</td>
</tr>
<tr>
<td>Less hospital visits than appointments</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Number of patients</td>
<td>21 (50%)</td>
<td>51 (31%)</td>
</tr>
</tbody>
</table>

**Multidisciplinary meeting**

There was a non-significant increase in the proportion of patients undergoing potentially curative treatment who were discussed in the weekly MDT meeting between period I (34/42; 81%) and period II (53/62; 86%) ($P=0.54$).

For patients who received palliative treatment, in both time periods a comparable percentage of patients was discussed (20% [35/174] in period I and 19% [40/208] in period II).

**Compliance with the national guideline**

The national guideline on Staging and Treatment of Oesophageal Cancer in the Netherlands has, amongst others, provided algorithms to guide physicians in choosing the type of treatment based on TNM stage and patient’s clinical condition. For 463 patients treated at our hospital, compliance with the national guideline could be assessed and was comparable in both periods (165/197 [84%] in period I vs. 212/266 [80%] in period II, $P=0.27$).
Discrepancies in stage of disease and type of treatment between the referring hospital and the NKI-AVL

In 116 (54%) of the 216 patients who were treated at our institute in the first period, no additional diagnostic work-up was performed. Of the remaining 100 patients, 42 (42%) had a change in TNM stage based on additional examinations and this led to a change in treatment for 24 (24%) patients.

In the second period, 26 (10%) of 270 patients underwent no additional work-up. Forty-two (17%) of the remaining 244 patients had a change in TNM stage based on additional examinations and 49 (20%) patients had a change in treatment.

Table 5: Outcome results of patients who underwent potentially curative treatment

<table>
<thead>
<tr>
<th>Period</th>
<th>2003-2005 (n=42)</th>
<th>2006-2008 (n=62)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Chemoradiation (no. of patients)</td>
<td>39</td>
<td>56</td>
<td></td>
</tr>
<tr>
<td>Grade 3/4 haematological toxicity</td>
<td>8 (21%)</td>
<td>11 (20%)</td>
<td>0.92</td>
</tr>
<tr>
<td>Grade 3/4 non-haematological toxicity</td>
<td>4 (10%)</td>
<td>4 (6%)</td>
<td>0.71</td>
</tr>
<tr>
<td>Completion of planned regimen</td>
<td>33 (85%)</td>
<td>51 (91%)</td>
<td>0.36</td>
</tr>
<tr>
<td>Surgery (no. of patients)</td>
<td>15</td>
<td>27</td>
<td></td>
</tr>
<tr>
<td>R0 resection</td>
<td>14 (93%)</td>
<td>26 (96%)</td>
<td>1.00</td>
</tr>
<tr>
<td>Number of removed lymph nodes</td>
<td>11 (4-16)</td>
<td>12 (1-34)</td>
<td></td>
</tr>
<tr>
<td>Postoperative complication</td>
<td>8 (57%)</td>
<td>9 (33%)</td>
<td>0.21</td>
</tr>
<tr>
<td>Surgical reintervention rate</td>
<td>2 (13%)</td>
<td>3 (11%)</td>
<td>1.00</td>
</tr>
<tr>
<td>Anastomotic leakage rate</td>
<td>0 (0%)</td>
<td>1 (4%)</td>
<td>1.00</td>
</tr>
<tr>
<td>In-hospital mortality</td>
<td>0 (0%)</td>
<td>1 (4%)</td>
<td>1.00</td>
</tr>
<tr>
<td>Survival (no. of patients)</td>
<td>42</td>
<td>62</td>
<td></td>
</tr>
<tr>
<td>Survival</td>
<td></td>
<td></td>
<td>0.70</td>
</tr>
<tr>
<td>Median (months)</td>
<td>22</td>
<td>21</td>
<td></td>
</tr>
<tr>
<td>1-year</td>
<td>69%</td>
<td>65%</td>
<td></td>
</tr>
<tr>
<td>3-year</td>
<td>40%</td>
<td>46%</td>
<td></td>
</tr>
</tbody>
</table>

Abbreviations: R0: Microscopically radical resection

Outcome results

In Table 5, outcome results are given for patients who underwent potentially curative treatment. There was a non-significant increase in the percentage of patients who completed
the planned chemoradiation regimen (from 85% to 91%), as there was a non-significant decrease in postoperative complication rate. In both time periods, the Ro-resection rate was high (93% and 96%, respectively).

Median follow-up for patients in period I was 19 months (interquartile range [IR] 9-45) and for those in period II was 16 months (IR 9-28). There were no differences in survival data between the two time periods (Table 5).

Discussion

We have assessed the quality of care for oesophageal cancer patients who were seen at our institute between 2003 and 2008. Different dimensions of health care quality were evaluated. Results showed that (1) waiting times improved throughout this study period, (2) planning of appointments at the outpatient clinic was more efficient in recent years, (3) assessment at a multidisciplinary meeting was above 80% in patients who received potentially curative treatment, (4) compliance with the national guideline was fair, (5) in a considerable number of patients, there was a discrepancy in type of treatment as proposed at the referring hospital and the treatment actually given, and (6) outcome results of potentially curative treatment were good.

With only 13% of patients undergoing potentially curative treatment, our institute has an unique case-mix of referred oesophageal cancer patients. The distribution of patients between gastroenterologist and radiation oncologist as first consultant specialist was more balanced in the second time period, i.e., more patients were directly seen by the radiation oncologist (22% to 31%). This increase is an improvement in planning of referred patients since a majority of patients in the palliative treatment group received radiotherapy only. Possibly, referral patterns have become better since the attendance of Comprehensive Cancer Centre consultants at oncology meetings of referring hospitals has been intensified.

Although the total number of patients increased over time, waiting times for oesophageal cancer treatment improved significantly. In a study by Robinson et al, referral wait for patients with breast cancer improved after the introduction of a government’s two-week target, but treatment wait increased. In a study on head and neck cancer patients, a consensus pathway for the process of care led to longer waiting times. In our national guideline on Staging and Treatment of Oesophageal Cancer, maximum acceptable waiting times are not specified. In our study, planning of more than one appointment on the same day has been helpful in decreasing the treatment wait from 24 to 18 days.

Findings from a British study suggest that MDT management is associated with improved outcomes after surgery for oesophageal cancer. In our study, a majority of the
patients who received potentially curative treatment was discussed in MDT setting (81% in period I and 86% in period II respectively). Ideally, MDT assessment should ensure effective coordination, the best quality and good continuity of patient care by bringing together key professionals with all the necessary knowledge, skills, and experience.\textsuperscript{14} In daily practice, MDT management is challenging because of different clinical programmes, time pressure, and continuous advances in staging and treatment modalities.\textsuperscript{15} At our institute, we aim at discussing all potentially curable patients at our weekly meeting. And, recently, a multidisciplinary outpatient clinic has been initiated, where patients are seen on the same day by a gastroenterologist, radiation oncologist and surgeon to further improve MDT management.

Wöckel \textit{et al} analyzed the impact of guideline adherence in breast cancer treatment.\textsuperscript{16} They concluded that therapies dispensed in line with guidelines may improve survival for patients with breast cancer. In our study, compliance with proposed treatment modalities according to the national guideline was suboptimal (84\% in period I and 80\% in period II). One of the reasons for non-compliance has been a longstanding in-house protocol for standard preoperative chemoradiotherapy, whereas the national guideline \textemdash in its present form \textemdash leaves room for no neoadjuvant treatment in patients with resectable oesophageal cancer. In the near future, the guideline will be revised at this point, following the results of a Dutch randomized multicentre study.\textsuperscript{17}

Although more patients underwent additional work-up in the second period, the proportion of patients in whom a change in stage of disease was found decreased (42\% vs. 17\%). This could be explained by an increase in diagnostic resources and experience in referring hospitals. In both time periods, around 20\% of patients had a change in treatment plan. Re-assessment of tumour stage and treatment plan is time-consuming for both the patient and the involved medical specialists. Nevertheless, given the importance of correct tumour staging and individual treatment planning, this strategy of evaluating referred patients is to be continued.

Outcome results of chemoradiation and surgery improved over time, although not significantly. Completion of chemoradiation treatment in 85-91\% of patients is in line with the 88-98\% mentioned in the literature.\textsuperscript{10,18} Also, our results of surgical treatment meet the standards in large, high-volume series.\textsuperscript{19,20}

A major limitation of our study was its retrospective design. For example, data on multidisciplinary assessment were retrieved from written patient files. Nowadays, this information is available in the electronic hospital information system. Preferably, there is a prospective registration of quality of care measures in each hospital where oesophageal cancer patients are treated.
The Dutch national guideline on Staging and Treatment of Oesophageal Cancer was published at the end of 2005. As yet, the guideline lacks a set of quality indicators to evaluate its implementation in clinical practice. We suggest that such a set should involve both process and outcome measures, as defined for the purpose of this study (Table 1), including waiting times, multidisciplinary team assessment, and outcome-based criteria for the treatment of oesophageal cancer patients. By evaluating different dimensions of health care quality, one can identify which steps in the multidisciplinary care path need improvement in order to raise the whole level of care for these patients.
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