Functional inoperability of oral and oropharyngeal cancer
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Chapter 3

The surgical dilemma of functional inoperability in oral and oropharyngeal cancer: current consensus on operability with regard to functional results.

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ABSTRACT

Objective. If surgical resection of a tumour results in an unacceptable loss of function, this is defined as functional inoperability. The current survey aims to define the borders of functional inoperability in oral and oropharyngeal carcinoma and evaluate its current use by obtaining opinions from the experts in the field.

Design. A web based survey.

Participants. Dutch head neck surgeons and radiotherapists.

Main outcome measures. Assessment of functional results after tumour resection in twenty-two statements and five cases.

Results. Response on the survey is 93% and the reactions are variable. Reactions vary slightly by the size of the clinic or discipline (radiation oncology versus head and neck surgery). There is agreement about the unacceptable function loss after total glossectomy. There is no absolute consensus about the functional outcome after certain surgical procedures, namely: bilateral maxillectomy, resection of a tonsil and base of tongue carcinoma including removal of the vallecula and epiglottis, and total soft palate resection. Disagreement of operability is also observed for T3 and T4 base of tongue carcinomas based on case descriptions and magnetic resonance images. Assessment of whether one hypoglossal nerve can be preserved is agreed to be a key factor for functional operability.

Conclusion. The term functional inoperability appears to be clinically used by Dutch experts in the decision-making process in advanced head and neck carcinomas. According to the experts who took part in the survey, primary total glossectomy or sacrificing both hypoglossal nerves is an operation that causes too much and therefore unacceptable function loss. In several case scenarios a consensus over operability could not be reached by the experts. The reactions vary per physician, institute and patient. Functional inoperability is variable and difficult to determine, but it is clinically used and therefore important to bring under attention.
INTRODUCTION

Although it is not a widespread used term to describe the impossibility to preserve function after resection of a tumour, head and neck surgical oncologists may use the idea of functional inoperability as one of the important parameters for their therapeutic decisions. The starting point of the present wave of organ preservation treatment protocols is the impossibility to preserve function in advanced laryngeal cancer when a total laryngectomy is deemed necessary. However, the decision to whether or not treat advanced head and neck cancer surgically is mainly dictated by the appraisal of achieving clear margins. Since the availability of advanced reconstruction techniques, chances to achieve clear margins have improved considerably. However, as a result of certain extensive resections the function loss will be so severe that even with the best current reconstruction methods the resulting function loss will not be acceptable. This could be called functional inoperability.

For oral and oropharyngeal cancer, there is evidence that organ preservation protocols have achieved similar locoregional and overall control rates, compared to surgery (although for oral cancer this still remains to be validated). It is important to assess the functional consequences of each treatment in order to have a balanced view on the pros and cons of this approach. Unfortunately, no randomised comparative studies between chemoradiation and surgery in advanced oral and oropharyngeal carcinoma have been performed on oral function or quality of life.

The question that remains is at what stage oral and oropharyngeal cancer can be considered functionally inoperable, i.e. when is the expected postoperative loss of function so severe that treatment in an organ/function preservation protocol is indicated. With the absence of any useful definition of functional inoperability, also given the wide variation of anatomical sites, surgical skills and reconstruction techniques, this study was conducted to establish an expert-based definition (level of evidence 5). We have performed a web-based survey among head neck surgeons and radiotherapists in the Netherlands. The survey aims to consider the opinion of experts in the field about the function loss to be expected after several surgical interventions to reach a consensus that may contribute to further refinement of the definition of this surgical dilemma. We will report the findings of this survey and discuss the problems that arise when describing and defining functional inoperability.
MATERIALS AND METHODS

Participants
A web-based survey was sent to seventy-two head neck surgeons (with basic training in otorhinolaryngology or oral-maxillofacial surgery) and radiotherapists in the Netherlands, participating in the Dutch Head and Neck Cooperative Group. The participants were contacted by mail and/or telephone to achieve the highest possible response rate.

The questionnaire
The questionnaire consists of cases and statements, for the translated survey see appendix A. The questionnaire begins with general questions and a multiple-choice question concerning factors that influence functional inoperability, see figure 1. There are five cases, illustrated by magnetic resonance images (MRI) and clinical information. In each case, the participants are asked whether they regarded the tumour functionally inoperable or not. Apart from the cases there are twenty-one statements. All statements are based on cases with availability optimal (free) flap reconstruction after ablative surgery. In all statements and cases there is also a possibility to opt for ‘neutral’.

RESULTS

Compliance to the survey is 93%, with retrieval of completed questionnaires from 67 experts. The participants are comprised of 43% (n=29) otorhinolaryngologists, 18% (n= 12) oral-maxillofacial surgeons and 22% (n=15) radiotherapists and in 16% (n=11) this is unknown.

All participants are certified as oncological head and neck surgeon or radiotherapist with at least two years of experience and members of the Dutch Head and Neck Cooperative Group. They work in 15 different clinics in the Netherlands. Seven of the participants work in ‘small’ clinics, seeing less than 200 new head/neck cancer patients per year, 51 in ‘medium size’ clinics, seeing 200-300 new head/neck patients per year, 9 in a ‘large’ clinic, seeing more than 300 new head/neck patients per year. Forty-seven of the participants work in university hospitals (8 Dutch and 1 Belgian), 8 in peripheral hospitals, 3 in radiotherapy centres and 9 in specialised oncology centres. All clinics have official Head and Neck tumour boards.

All participants use the term functional inoperability in their current practice. According to the participants the most important factor in determining functional inoperability is total loss of oral and oropharyngeal food transport, see figure 1.
A Dutch survey about functional inoperability

**Figure 1: Factors determining functional inoperability**

<table>
<thead>
<tr>
<th>Factor</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total loss of taste</td>
<td>90%</td>
</tr>
<tr>
<td>Expected therapy loyalty</td>
<td>85%</td>
</tr>
<tr>
<td>Older age</td>
<td>51%</td>
</tr>
<tr>
<td>Severe deterioration of speech</td>
<td>51%</td>
</tr>
<tr>
<td>Comorbidity</td>
<td>43%</td>
</tr>
<tr>
<td>Expectations and wishes of patient</td>
<td>36%</td>
</tr>
<tr>
<td>Cosmetically unacceptable</td>
<td>36%</td>
</tr>
<tr>
<td>Deterioration of oral/oropharyngeal transport to fluid diet</td>
<td>36%</td>
</tr>
<tr>
<td>Total loss of speech</td>
<td>36%</td>
</tr>
<tr>
<td>Total loss of oral/oropharyngeal food transport</td>
<td>36%</td>
</tr>
</tbody>
</table>

The numbers represent the percentage of respondents that felt that the factor influences the operability of oral and oropharyngeal carcinoma.

Ninety per cent of the respondents opted for this factor as a criterion to decide functional inoperability. This is followed by total loss of speech (85%), deterioration of the swallowing function resulting in a fluid diet (51%) and a cosmetically unacceptable result (51%). Expectations and wishes of the patient was considered to be a decisive factor by only 43% and comorbidity by 36%.

**Statements**

In nine statements, reflecting surgical procedures, there was agreement that the tumours were operable (84% to 97%). In figure 2 the statements are shown, reflecting an unacceptable functional result according to more than 50% of the respondents.

Four statements involving total or subtotal glossectomy as first treatment option were considered an argument for functional inoperability by the most: a total glossectomy alone, in combination with a supraglottic or total laryngectomy and a commando procedure with anterior segmental resection of the mandible, resection of anterior floor of mouth and subtotal glossectomy without preserving any of the hypoglossal nerves. See figure 2 for the percentage of respondents that considered these as unacceptable.
Figure 2: Interventions that lead to an unacceptable functional result according to more than half of the respondents

1. Total glossectomy and supraglottic laryngectomy (93%)
2. Total glossectomy + total laryngectomy (84%)
3. Commando procedure: resection of the floor of mouth and subtotal glossectomy sacrificing both hypoglossal nerves (88%)
4. Total soft palate resection (55%)
5. Total mandibulectomy (63%)
6. Resection of tonsil and base of tongue carcinoma with resection of the vallecula and epiglottis (52%)
7. Resection of tonsil and base of tongue carcinoma with dubious chance of saving one hypoglossal nerve and lingual artery (76%)

The numbers represent the percentage of respondents that considered the functional result of the intervention as unacceptable. Only statements are shown that are regarded as functional unacceptable by more than half of all respondents.

In eight of the 21 statements (38%) the opinions varied a lot. In two of these, the majority opted for functional inoperability, see figure 2:

1. Total mandibulectomy (63% considered the functional result as unacceptable);
2. Resection of a tonsil and base of tongue carcinoma extending over the midline with dubious possibility of preserving one hypoglossal nerve and lingual artery (76%).

In three of these eight statements most of the respondents judged the tumour as operable:

1. Resection of the posterior and lateral pharyngeal wall (64% considered this as a functional acceptable result);
2. A commando procedure with subtotal glossectomy (unilateral preservation of the hypoglossal nerve), lateral floor of mouth resection and lateral segmental resection of the mandible with disarticulation (69%);
3. A commando procedure consisting of a subtotal glossectomy with preservation of one hypoglossal nerve, anterior floor of mouth resection and an anterior segmental mandible resection (67%).
The opinions about three of the following hypothetical resections were very divergent:

1. Total soft palate resection (39% operable/55% functionally inoperable/6% neutral)
2. Resection of a tonsil and base of tongue carcinoma with resection of the vallecula and epiglottis (18%/52%/30%);
3. Bilateral maxillectomy (48%/22%/30%).

**Figure 3: T2N0 tongue carcinoma**

Axial and saggital slice of a T2 weighed MRI-scan. The scan shows a base of tongue carcinoma (2.5 x 2.5 cm), extending until the midline.

**Figure 4: T3N0 base of tongue carcinoma**

Axial and saggital slice of a T2 weighed MRI-scan. The scan shows a symmetrical exofytic growing tumour medially in the base of tongue.
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Cases

With regard to the five presented patients, the results were concordant in three. In two cases the opinions varied. In one of these, a 48-year-old man with a T2N0 tongue carcinoma with clinically submucosal extension over the midline, the majority of the respondents (66%) chose for resecting the tumour, see figure 3.

Table 1: Concordant cases of electronic survey on Functional Inoperability

<table>
<thead>
<tr>
<th>MRI</th>
<th>Case Description</th>
<th>Operable (%)</th>
<th>Inoperable (%)</th>
<th>Neutral (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Case 1</td>
<td>63 yrs T4aN2a cheek/inferior alveolar proces</td>
<td>Examination: large ulcerating tumour at the inferior alveolar process, extension to maxilla, not to tongue and mobile to skin, mental nerve intact. MRI: tumour (max. 6cm) with infiltration of the right horizontal part of the mandible and to the lateral floor of mouth, not to the tongue.</td>
<td>81</td>
<td>9</td>
</tr>
<tr>
<td>Case 2</td>
<td>54 yrs T3N2b base of tongue</td>
<td>Examination: a tumour at the base of tongue left, no infiltration to vallecula or contralateral side. MRI: tumour (max 5x2x2,5cm) at the base of tongue left, extension to midline to the right side and to left tonsil, the vallecula is filled up caudally.</td>
<td>7</td>
<td>85</td>
</tr>
<tr>
<td>Case 3</td>
<td>52 yrs T3N0 floor of mouth</td>
<td>Examination: an ulcer (1x1,5cm) at median and left side of the floor of mouth, no deep infiltration of the tongue, root or dorsum of tongue and mobile to the mandible. MRI: tumour (1,5x2,5cm) at the floor of mouth left paramedian, against the mandible that is intact.</td>
<td>97</td>
<td>3</td>
</tr>
</tbody>
</table>
In the other case, a 50-year-old woman with a T3N0 median, exophytic growing base of tongue carcinoma, the majority (72%) considered the tumour as functionally inoperable, see figure 4. In the above described cases the diversity of the answers is probably due to different preoperative assessments of the possibility to spare one hypoglossal nerve. In the other three cases the results were quite concordant. See the summary of the cases in table 1.

In two of the five cases the tumour was considered by the majority as functionally inoperable: the case described in figure 4 and another case describing a T3N2b base of tongue carcinoma, see table 1.

The most frequently mentioned factors that led to this decision, were predicted total loss of swallowing (81%), total loss of speech function (52%), deterioration of swallowing to a fluid diet (22%) and severe deterioration of speech (36%).

There were no significant differences between disciplines regarding answers of the statements. See table 2 for a break-down of the discordant cases.

**Table 2: Discordant statements and cases; a break-down by physician**

<table>
<thead>
<tr>
<th>Functional result acceptable after</th>
<th>Surgeons (n=41)</th>
<th>Radiotherapists (n=15)</th>
<th>P&lt;sup&gt;1&lt;/sup&gt;</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total soft palate resection</td>
<td>Yes 15</td>
<td>5</td>
<td>1.000</td>
</tr>
<tr>
<td></td>
<td>No 24</td>
<td>8</td>
<td></td>
</tr>
<tr>
<td>Resection of tonsil, base of tongue, vallecula, epiglottis</td>
<td>Yes 6</td>
<td>1</td>
<td>0.359</td>
</tr>
<tr>
<td></td>
<td>No 24</td>
<td>11</td>
<td></td>
</tr>
<tr>
<td>Bilateral maxillectomy</td>
<td>Yes 23</td>
<td>4</td>
<td>0.066</td>
</tr>
<tr>
<td></td>
<td>No 9</td>
<td>6</td>
<td></td>
</tr>
<tr>
<td>Case 1, T2N0 tongue carcinoma, see figure 3</td>
<td>Yes 30</td>
<td>12</td>
<td>0.019</td>
</tr>
<tr>
<td></td>
<td>No 5</td>
<td>3</td>
<td></td>
</tr>
<tr>
<td>Case 2, T3N0 tongue carcinoma, see figure 4</td>
<td>Yes 8</td>
<td>7</td>
<td>0.614</td>
</tr>
<tr>
<td></td>
<td>No 28</td>
<td>5</td>
<td></td>
</tr>
</tbody>
</table>

Respondents of whom discipline was unknown were excluded (n=11) for this comparison and so were the ‘neutral’ answers. 1) P-values were calculated in a 2x2 crosstab with Pearson Chi Square test or with Fisher’s exact test as the numbers were too low. The bold value represents significance, meaning p<0.05.

Regarding the functional results after a bilateral maxillectomy the radiotherapists’ answers were more negative, although not significant due to low numbers. Furthermore, there appeared to be a statistically significant difference of opinion between the different disciplines (surgeons versus radiotherapists), for the results of the first case (T2N0 tongue carcinoma, see figure 3); a greater
percentage of surgeons, 68%, consider the tumour as inoperable because of expected function losses, versus 33% of the radiotherapists (p=0.019, see table 2). In these answers, the surgeons considered the function loss due to surgery worse than the radiotherapists.

We also compared the results per different clinic, divided in small, medium and large or in university, satellite hospital or comprehensive cancer centre. The only statistical significance was for the second case, a patient with a T3N0 tongue carcinoma. From university hospitals, 36 out of 47 (76%) considered the tumour as operable, from cancer centre/ radiotherapy centres 5 out of 12 (42%) and from the satellite clinics only 3 out of 8 (38%), a statically significant difference (p=0.011). Regarding the functional results after soft palate resection the results varied but not statistically significant per size of the clinic; 5 out of 7 participants (71%) from small clinics agreed on the operability, 20 out of 51 in the medium clinics (39%) and only 1 out of 9 (11%) from the large clinic.

**DISCUSSION**

*Synopsis of results*

Functional inoperability is currently used for tumour board discussions on selection of patients for organ-sparing therapies e.g. concurrent chemoradiation. Although the term seems (subconsciously) widely accepted in the Netherlands among head and neck surgeons and radiation oncologists, so far no serious attempts have been made to reach consensus on this surgical dilemma. We realise that the issue of functional inoperability is troubling to many, since the definition varies considerably among treating physicians and is related to the expertise of the individual surgeon. Results of our survey showed some differences between clinics and physicians, although difficult to interpret due to small sample sizes.

Although the results of our survey are just a reflection of the points of view of Dutch Head and Neck surgeons and radiotherapists, this could be the first attempt to demarcate a certain clinical condition as functionally inoperable and to reach a level of evidence 5, the expert opinion. Results of our survey show that amongst Dutch experts the most consistent agreement about functional inoperability is when a total glossectomy is required, resecting both hypoglossal nerves and lingual arteries. In nine out of 22 (41%) of the statements there was no agreement about the acceptability of the expected function loss. This diversity illustrates the controversies amongst functional inoperability.
Results after non-surgical therapy in literature
When describing a particular tumour extension as functionally inoperable, it is important to consider the treatment outcome after the alternative therapy: chemoradiation. Despite organ-sparing results of concomitant chemoradiation, the risk of functional consequences is still considerable. The most common long-term complication is dysphagia, caused by damage to the base of tongue and pharyngeal wall after severe mucositis, radiation induced fibrosis, xerostomia and radiation necrosis. Speech, however, appears to be relatively uncompromised and might be better after treatment with chemoradiation compared to surgical therapy.

When choosing for a non-surgical approach, the frequency of salvage surgery has to be kept in mind. In the study of Soo et al. eventually only in 45 % of the chemoradiation arm, the treatment was organ-sparing. After salvage surgery higher complication rate and wound-healing problems may be expected.

The need of multidisciplinary discussion and individualisation
A large number of factors play a role in the functional result after treatment for large oral cavity and oropharynx tumours. Firstly, surgery remains a skill and the ability and experience of the surgeon in large resections and chosen method of reconstruction is a key factor for success of surgical therapy.

Moreover, the clinical experience in an institution, its customary practices and resources, influence the protocols of reconstruction, radiotherapy, dental rehabilitation, speech and swallowing therapy, dietary consultation and other support that are of utmost importance for the functional outcome. Other factors to be taken into account are local availability of as well chemo- and radiotherapy and operation room facilities, waiting time and complication rate of a specific institute.

As illustrated by the cases from the survey and described in the results section, the diagnostic accuracy and clinical assessment of the physicians is also very important. In our cases, the experts disagreed about the operability of the tumour in two of the five cases, presumably because they had different opinions about the infiltration of the tumour and how much tongue tissue had to be removed. Further research in exploring other diagnostic tools is necessary. It may be assumed that future imaging techniques implementing both organ mobility and tumour extension may give us more insight into the functional operability of the lesion. Additionally, high resolution multi slice computed tomography images may provide more information about the course of the hypoglossal nerve and the lingual artery and their relation to the tumour.
Apart from tumour- and doctor-related factors, there are several patient related factors: willingness to accept morbidity, age of the patient, comorbidities, expected therapy compliance and social situation influence the outcome of functional status. Comorbidities are proven as factors that have an impact on the patient perceived quality of life and on the functional outcome after surgical therapy. The preferences and expectations of a patient should be taken into account with the highest priority to achieve the best treatment result and satisfaction of the patient. In our opinion this is one of the most important factors in the decision-making process.

Therefore, we think a clear guideline for functional inoperability is not manageable and would not be accurate. Nevertheless, the reached consensus among Head and Neck oncology experts in the Netherlands on judging primary total glossectomy as representative for functional inoperability is a first step towards answering a quite problematic question. We recommend thorough discussion among the multidisciplinary group of clinicians to decide the best treatment course, especially taking into account every patient’s individual perceptions and expectations, as all factors and nuances are to be captured neither in guidelines nor in protocols.

Future perspectives
This survey reflects only the opinions of Dutch experts and as opinions regarding the treatment choice differ worldwide, it is our goal to perform a similar survey internationally. Moreover, the opinions of the patients-self, but also of experienced speech therapists, nurses and physiotherapists would be interesting to evaluate, because they follow patients longitudinally along their treatment.

Attempting to resect the tumour with ‘negative’ margins has always been the main surgical goal. However, discussion arises of what margin of surrounding tissue should be removed. Some support the ‘more is better’ theory, but the approach using very narrow surgical margins with adjuvant radiotherapy has resulted in equal if not better oncological control. The recent upcoming of minimally invasive techniques such as transoral laser ablation and robotic surgery using the Da Vinci robot are therapies that might influence the concept of functional inoperability in the future. Newer surgical techniques may enable large tumours to be excised with less surrounding tissue and thus less function loss.

Furthermore, advancements in imaging techniques could possibly define the margins of functional inoperability better. For example, a cine MRI made during swallowing, may enable the imaging of the elasticy and fixation of tissues and tumour, therewith improving the prediction of the postoperative function. The ultimate solution would be a model in which per individual patient the postoperative function can be assessed, so the patient can self-decide.
CONCLUSION

The term functional inoperability appears to be clinically used by Dutch experts in the decision-making process in advanced head and neck carcinomas. In their opinion, primary total glossectomy or sacrificing both hypoglossal nerves is an operation that causes significant and therefore unacceptable function loss. In several tumour extensions there is no consensus about the functional operability. It varies per physician, institute and patient. Functional inoperability is variable and difficult to determine, but it is clinically used and therefore important to bring under attention.
REFERENCES


