



Patient experienced side effects and adverse events after cancer treatment - Patient initiated research

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Abstract

Background In the literature radiation of head and neck cancer (HNC) is followed by late side effects for more than a third of the patients. However, nearly all patients seem to experience side effects. The aim was to collect the multitude of these experiences through a patient-developed detailed questionnaire.

Methods 77 of 117 patients responded to a validated questionnaire from the Danish HNC patient network, age 61 (32 - 90) with 5 years (0 to 32) post treatment period.

Results 99% of the patients experienced at least one side effect, 67% more than twenty symptoms categorised into mouth complains, swallowing and eating problems, affected speaking ability, pain and fatigue during their daily living. Ten years survival was the only significant prognostic factor OR 0.13 (CI 0.02-0.81). Only swallowing and eating problems were significantly reduced over time ($p=0.048$) and in relation to calendar period (0.049), but not with increasing age.

Conclusion The patients experienced pronounced sequelae, independent of gender, age and treatment/intervention.

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Clin Health Promot 2011;1:5-8.

Introduction

Head and neck cancer is 6th worldwide and among the ten most frequent cancers in Denmark with about 1000 new cases each year (1). Head and neck cancer encompasses a variety of specific diagnosis defining the treatment modality. Since 2003 the treatment strategy has been standardized in national guidelines. In 2008 fast track pathways were guaranteed by a political decision for this patient group as well as other groups of cancer patients in Denmark. The most common treatment is radiation therapy, either alone or in combination with surgical intervention. Several side effects have been described after radiation therapy, the most common being dysphagia, xerostomia and hoarseness (2). The patients are informed that the symptoms are most pronounced two weeks after the end of radiation therapy reducing to about one to two thirds over the years (3). Relevant tools have been developed to

measure the side effects focusing on objectivity and the observer's registration of the patient's experience (4-8). However, patient complains and consequences in a broader perspective are not included in these tools. The patients' own description of their experience indicates more and longer-lasting symptoms, which may require more detailed information and especially improved counselling on how to handle these in daily life.

Therefore it was relevant to collect these experiences through a detailed questionnaire developed by patients with neck and oral cavity cancer (NOC).

Patients and methods

The patients

The patients originated from a network of 117 patients with NOC, which is a network under the Danish Cancer Association; a patient-driven organisation aiming at providing a platform for



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exchange of experiences and advices among patients as well as lectures from health professionals and others relevant to the treatment and rehabilitation of head and neck cancer patients.

Development of the questionnaire

The detailed questionnaire was based on brainstorming sessions among the patients at a network meeting. When the questionnaire was developed, it was decided not to ask questions about psychological, social and sexual conditions, which are derived from the side effects. In stead the decision was made only to ask to direct side effects. Two questions were included, however, which touch on social conditions (“to eat in the company of others” and “to be understood when you speak”). The questions were then categorized in themes and formulation/wording and appropriate scales were chosen in collaboration with health professionals. It was validated among a group of patients with NOC cancer and adjusted according to the comments and experiences.

The final questionnaire ‘regarding lasting side effects after radiation therapy due to cancer in neck and mouth’ contain 79 questions detailing problems regarding pain, speech, swallowing, taste, fatigue, infection, and others (Appendix) was sent to the members of NOC Network.

Ethical considerations

There were no ethical barriers in this study, which was initiated, decided and performed by the members of the patient network themselves. The questionnaires were sent to the members without personal identification or number, and the responses were therefore completely anonymous. Because of anonymity, there were no personal reminders sent out. Participation was voluntary, so filling in and submitting the questionnaire, was understood as acceptance of publication.

The members were generally informed at the meetings and written information was distributed with the questionnaire declaring the intent of publicizing the results.

Analysis

Chi2 test and logistic regression analysis was performed among the categories to identify prognostic factors over time (age, survival and calendar year) and presented by odds ratio (OR) and confidence

intervals not including the value one was considered. The changes in sequelae over time were evaluated, P value below 0,05 was considered significant.

Results

The questionnaire yielded a response rate of 66% (77/120).

The median age of patients was 61 years (range 32 to 90) with median of 5 years post treatment (range 0 to 32). Respondents were 58% female and 42% male with 90% treated at one of two hospitals in the capital region. Patient characteristics are given in Table 1.

Table 1 Characteristics of patients from the survey
Given as median (range), frequencies (%) or numbers

	Women n=45	Men n=32	Total n =77
Age (years)	60 (32 to 86)	62 (47 to 90)	61 (32 to 90)
Follow-up (years)	4 (0 to 32)	5 (0 to 11)	5 (0 to 32)
Irradiation			
Unilateral	33 %	19%	27 %
Bilateral	67 %	81%	73%
Location of cancer			
Oral cavity/palate/tongue	14	9	23 (30%)
Salivary gland	4	0	4 (5%)
Neck/vocal chord/ pharynx	5	4	9 (12%)
Naso-pharynx	4	1	5 (6%)
Thyroid gland	0	1	1 (1%)
Lymph nodes/tonsils	17	12	29 (38%)
Unknown primary	1	2	3 (4%)
Unspecified	0	3	3 (4%)

The patient reported side effects are summarised in Figure 1. 99% patients experienced at least one side effect, 67% more than twenty symptoms categorised into mouth complains, swallowing and eating problems, affected speaking ability, pain and fatigue during their daily living. Analysis was performed to identify prognostic factors with 10 years survival as the only significant prognostic factor OR 0.127 (CI 0.020-0.807).

Only swallowing and eating problems were significantly reduced over time ($p=0.048$) and in relation to calendar period (0.049), but not with increasing age.

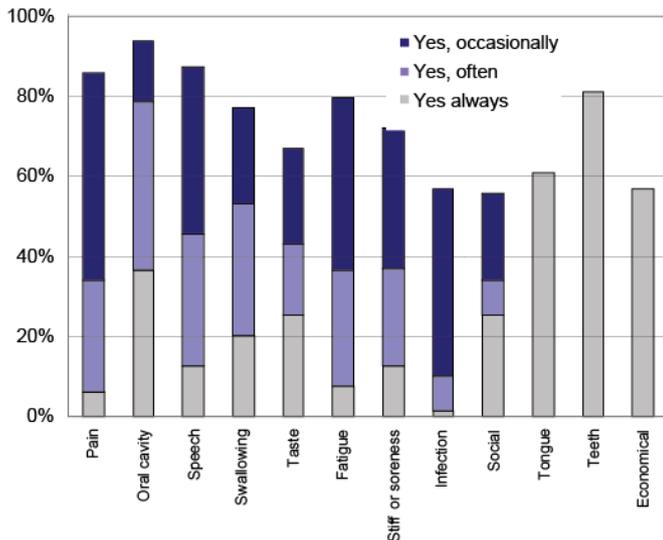
Discussion

We found that the frequency of side effects was very high and had no clear relation to the cancer site, bilateral or unilateral radiation therapy, gender or age. A few symptoms were reduced over time. But the side



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Figure 1 Patient experienced side effects
Grouped according to origin and theme



effects were distributed all over the patient group and exceeds other reviews and studies by comparison (2;9-13). The reason why difficulties with eating and swallowing were reported as reduced over time, could result from patients getting used to the problems over time – and adapt. They may choose food they are able to eat and the adapted way of eating, by drinking water to down food for example, becomes the norm.

Direct comparison with other studies is difficult due to differences in reporting and categorisation, but our patient-developed study shows more pronounced sequelae compared to the literature/self-reported side effects independent of the differences in criteria and definitions. The questions in the questionnaire are more specific than in other studies (2;9-13). The NOC Network has shown where the problems are, and this may be one of the reasons for a higher rate of side effects.

Our results are in accordance with the conclusion from another Danish study that addresses the need for patient reported side effects, which are not sufficiently detected by the objective side effects measurement tools as well as common quality of life instruments (8).

Bias and limitations

This study contains a few general problems. The number and detail of questions increase the risk or possibility of getting positive response by chance, but on the other hand also enhances the possibility of generating new knowledge. A response rate like ours

yields the risk of both overestimations because those with most complications may feel more obliged to respond and may therefore contribute with a relatively higher part of the results. In complete contrast, they may also feel too ill to be able to respond at all; thereby adding to an underestimation.

The study is based on a limited cohort with specific interests, i.e. patient network aiming to improve patient perspective/conditions, thus focusing more on problems in patients than the case would be outside the network. Furthermore, the issue of co-morbidity that could be at least part of or the reason of side effects was not registered. One other limitation is the sample size, and another the representational value of a patient network. Thirdly is the gender issue, i.e. overrepresentation of women in contrast to gender specific incidence rate. Fourthly there is an overrepresentation of socio-economically advantaged patients in the NOC Network. The disease is socially imbalanced as it in many cases is caused by a high intake of alcohol and tobacco. Fifthly, the treatment is standardised after Danish Head and Neck Cancer Group (DAHANCA) guidelines(14), but rehabilitation initiatives are diverse and therefore the possibility of local issues in relation to rehabilitation in Denmark may limit the generalisability of the findings.

On the other hand it's probably like any general patient network, advocating the need for patient involvement. Consumer involvement is desirable and already proactive patients will seek information outside the local care setting, wanting to make an educated assessment of own treatment. In the future further consumer involvement seems likely and desirable. A patient driven evaluation of patient information material, which could lead to further cooperation in the developing process, is beneficial to all involved

Conclusion

Independent of gender, age and treatment/intervention, almost all patients experienced pronounced sequelae after radiation treatment for cancer in head and neck.



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Contributors

Conception and design: SHP, NJ, HK, BF, HT

Acquisition of data: NJ, HK, BF

Analysis and interpretation of data: SHP, BP, HT

Drafting the article: SHP, HT

Revising the article critically for important intellectual content: NJ, HK, BF, BP

Approving the article: SHP, NJ, HK, BF, BP, HT

Competing interests: None declared.

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Appendix: Questionnaire

At present, are you experiencing any of the following

- Dryness of the mouth, insufficient saliva, sensitive mucous membranes in your mouth, sore mucous membranes in your mouth, thick or viscous mucus in your throat, thick or viscous saliva in your mouth, pain in your tongue.
- Pain in your jaw joint (right in front of your ears), pain in your lower jaw.
- Swelling of the neck, stiffness in the muscles at the front of the neck, stiffness in the neck muscles, pain in the throat when swallowing.
- Problems with speaking clearly, that you become hoarse, that you have trouble with speaking loud, that you have difficulties making yourself understood when speaking.
- Problems with swallowing, choking on your food, getting food in your nose.
- A loss of appetite, not feeling full, food getting stuck in your food pipe, problems with swallowing pills, that you don't want to eat with people you don't know very well.
- Problems eating acidic food, problems drinking acidic beverages (juice, wine), problems eating spicy food (curry etc.), problems eating rye bread, problems eating white bread, which is not, toasted, problems drinking fizzy drinks.
- Problems eating raw vegetables, problems eating hard raw fruit like apples, problems eating soft raw food like melon and banana, problems eating beef which isn't minced, problems eating other kinds of meat which isn't minced, problems drinking thin liquids like water, that your food tastes different from before the radiation, that your sense of taste is diminished.

At present, what kind of food are you eating?

- I eat through a tube, I drink protein shakes, I am on a liquid diet, I eat blended or mashed food, I prefer soft food, I avoid certain foods, as they are difficult for me to eat.

Within the last year, have you experienced any of the following.

- Pain in your teeth, oral thrush, sores in the corner of your mouth.
- Pains in the mouth and throat which have been hard to treat, feeling unusually tired, that it takes longer for sores to heal in the radiated area, infection of the skin in the radiated area – with high fever, more gastric acid than usual (a burning in the stomach and heartburn), bad memory that you don't believe is due to ageing.

Have you after a year has passed since the radiation noticed any of the following.

- A change in the mobility of the tongue, a change in the size and shape of the tongue, a change in the surface of the tongue. Since the completion of the radiation, have you experienced any of the following.
- More cavities than usual, teeth that crumble, teeth that break, parodontosis, reduced ability to open your mouth wide, a change in your voice.

Additional questions.

- Have you or your physician applied for subsidies for precautionary dental work?
- Have you been granted a subsidy for dental work extending 1500 DKK a year?
- Have you since the radiation been treated for low metabolism?
- Was your hearing impaired due to the radiation?
- Do you suffer from tinnitus since the radiation?
- At the present, are you seeking any treatment for pain in the mouth-throat area?
- Did you receive radiation on both sides?
- Since the completion of the radiation, have you had any problems keeping you weight up?
- Since the completion of the radiation, have you had any problems keeping you weight down?
- Since the radiation have you experienced that some of the jaw bone has decomposed (osteoradionecrosis)?
- Where in the throat and/or mouth did you have cancer?
- When was your last radiation treatment?
- At which hospital were you treated?
- Gender, age and additional comments?