

A Novel Digital Patient-Reported Outcome Platform for Head and Neck Oncology Patients—A Pilot Study

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ABSTRACT

INTRODUCTION: The patient's role in toxicity reporting is increasingly acknowledged. There is also a need for developing modern communication methods between the patient and the medical personnel. Furthermore, the increasing number of head and neck cancer (HNC) patients is reflected in the volume of treatment follow-up visits, which remains a challenge for the health care. Electronic patient-reported outcome (ePRO) measures may provide a cost-efficient way to organize follow-up for cancer patients.

MATERIALS AND METHODS: We tested a novel ePRO application called Kaiku[®], which enables real-time, online collection of patient-reported outcomes, such as side effects caused by treatment and quality of life. We conducted a pilot study to assess the suitability of Kaiku[®] for HNC patients at the Department of Oncology, Helsinki University Hospital, Helsinki, Finland. Patients used Kaiku[®] during and one month after radiotherapy to report treatment-related side effects and quality of life. Two physicians and a nurse performed the practical electronic communication part of the study.

RESULTS: Five of the nine patients agreed to participate in the study: three of them had local early-stage larynx cancer (T2N0, T1aN0, and T2N0) and the remaining two patients had early-stage base of tongue cancer (T2N0 and T1N2b). The degree of side effects reported by the patients via Kaiku[®] ranged from mild to life threatening. The number of outcome data points on patients' progress was significantly increased, which resulted in a better follow-up and improved communication between the patient and the care team.

CONCLUSIONS: Kaiku[®] seems to be a suitable tool to monitor side effects and quality of life during and after radiotherapy among HNC patients. Kaiku[®] and similar tools could be useful in organizing a cost-effective follow-up process for HNC patients. We recommend conducting a larger study to further assess the impact of an ePRO solution in routine clinical practice.

- ePRO solutions may aid in the follow-up for cancer patients.
- They seem suitable to monitor, for example, side effects and quality of life.
- These systems ensure fast patient-driven reporting.

KEYWORDS: head and neck cancer, radiotherapy, health-related quality of life, patient-reported outcome, side effects

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Introduction

Head and neck cancers (HNCs) include malignancies of the oral cavity, pharynx, larynx, sinonasal tract, and salivary glands. They form the sixth most common malignancy among men. According to the Finnish Cancer Registry, there are annually approximately 750 new patients diagnosed with an HNC in Finland.¹ The most important risk factors are smoking, heavy drinking, and human papillomavirus. HNC treatment consists of either surgery or radiotherapy alone or a combination of both. Chemotherapy combined with radiotherapy will enhance treatment results in selected cases. The five-year disease-specific survival rates for advanced HNCs vary between 33.8% (hypopharyngeal cancer) and 97.4% (lip cancer), with an overall survival rate of 65.9%.²

Treatment modalities for HNC induce early side effects and long-term consequences. Surgery often changes

the patient's ability to chew, swallow, or talk. Patients who receive radiotherapy may experience skin redness and irritation, pain, dry mouth, difficulty in swallowing and breathing, changes in taste, and nausea. A cause of interruption in the radiotherapy course for HNC is acute mucosal reaction, which can, if not properly treated, lead to significant loss in the probability for local control. In chemoradiotherapy, these reactions are enhanced, and concomitant chemotherapy also predisposes the patient to other side effects such as neutropenia, thrombocytopenia, and renal toxicity. It is crucial to recognize the adverse effects of cancer therapies as promptly as possible to ensure early medical interventions. Technologies that facilitate communication between cancer treatment teams and patients may be helpful in this respect and will probably be integrated in normal hospital communication systems in the near future.



Globally, surgeons and oncologists use different protocols to follow-up their patients during and after treatment. The goal of the follow-up activities is to detect possible cancer recurrence or new primary tumors as early as possible and to manage late morbidities related to the tumor or the treatment. It is controversial whether a frequent, routine follow-up program will aid in early detection of cancer recurrence or in diagnosing new tumors.^{3,4} Nevertheless, more than 40% of HNC survivors are reported to suffer from one or more tumor- or treatment-related morbidities three years after the treatment,⁵ and thus, a regular follow-up may be needed to manage these problems. Furthermore, implementing a self-reporting system, a *questionnaire on patient-reported outcome (PRO) measures*, has been suggested.⁶

The United States Food and Drug Administration defines PRO as any report of the status of a patient's health condition that comes directly from the patient, without interpretation of the patient's response by a clinician or anyone else.⁷ Several benefits have been identified with collecting PROs in routine cancer care: health-related quality of life has been found to be a predictor of cancer survival;^{8,9} collecting PROs improves communication between clinicians and patients^{10–14} as well as patient satisfaction¹⁴ and enables early detection of symptoms,^{10,14,15} and patient-reported symptoms have been found to better reflect the daily health status of a patient than clinician-reported symptoms.¹⁶ There is even weak evidence that routine collection of PROs may improve health outcomes (such as quality of life).¹⁴

Along with the traditional pen-and-paper format, several electronic PRO solutions have been applied to cancer care.^{10,17,18} Electronic PRO solutions offer several benefits over the pen-and-paper versions. First, Internet-based and interactive phone systems allow the patients to report data outside the clinic and allow the collection of immediate data. This information can be used to recognize important symptoms or changes in the patient's health. Second, the data collected using an Internet-based PRO system have also been found to be more complete than that collected from a pen-and-paper questionnaire.¹⁹ Third, computing scores can be automatized, eliminating the source for error and increasing the efficiency. Fourth, new methodologies, such as item response theory and computerized adaptive testing, can be applied in designing PRO instruments. Finally, both pen-and-paper and electronic modes of administration of PROs have been found to be equivalent.²⁰

The purpose of this study was to assess the suitability of Kaiku®, a new Internet-based PRO application, for collecting PROs on early adverse effects of radiotherapy and on health-related quality of life among HNC patients and also to gain insight into how the patient experienced the system: is it easy enough to use?

Materials and Methods

A prospective pilot study was performed on five patients with HNC treated at the Department of Oncology, Helsinki University Hospital, Helsinki, Finland. Approval for the pilot

was obtained from the Operative Research Ethics Committee in the Helsinki and Uusimaa Hospital District (Dnro 296/13/03/02/2013) at our institute. Participation in the pilot study was voluntary. All parts of the study were performed in compliance with the principles of the Declaration of Helsinki.

The investigated innovation is a browser-based application called Kaiku® (later referred to as the system or Kaiku®), which has been developed by NetMedi (<http://www.netmedi.fi>), a private software provider based in Helsinki, Finland.

In this study, Kaiku® was used by the patients, nurse, and medical doctors

- to self-assess patient's side effects arising from the treatment on a scale adapted (translated to Finnish) from CTCAE v. 4.03 (see Fig. 1A for a screenshot),²¹
- to monitor the quality of life of the patients using the Finnish versions of the 15D²² and the EORTC QLQ-H&N35 instruments (see Fig. 1B for a screenshot),²³
- to communicate in a free-text format.

Nine HNC patients were asked to participate in the study on their first visit to the cancer center. The patients were approached face-to-face or by telephone by the physician. Altogether, five patients consented to participate in the study between November 2013 and October 2014, and four patients declined. The declining patients cited information technology reasons, such as *difficulty in using the Internet*. All five patients were male with a median age of 63 years (range, 50–80 years). Two of them were retired, one patient had a higher socioeconomic status, and the remaining two patients had a lower socioeconomic status. Patient eligibility was not constrained by their possible lack of experience with computers or the Internet. The patients did not receive any training to use the system; the system contained some instructions for use.

Two physicians and one nurse performed the practical communication part in the study. The participating medical staff received one training session that lasted for an hour. During the treatment period, the nurse saw the patients daily. She helped the patients if they encountered any problems in using the system. The patients visited the physician three times: before, during, and after the radiotherapy. Head and neck surgeons are responsible for the five-year follow-up period after radiotherapy at our institution.

After agreeing to participate in the study, the patients received a message to the email address that they had provided with a link to register to Kaiku®. The registration consisted of filling in basic personal information. An individual follow-up plan, based on the treatment, was created for each participating patient. The plan was programmed into Kaiku®, which then automatically administered self-assessment questionnaires on experienced symptoms and health-related quality of life. After the patient had registered to the system, the selected follow-up protocol was automatically activated.



A

Kaiku Home Care progression Conversation Calendar My information Sign out

Report adverse effects

Alopecia 1/5

A disorder characterized by a decrease in density of hair compared to normal for a given individual at a given age and body location.

Instructions for adverse effect reporting

0. I am not suffering from this adverse effect.

1. Hair loss of <50% of normal for that individual that is not obvious from a distance but only on close inspection; a different hair style may be required to cover the hair loss but it does not require a wig or hair piece to camouflage

2. Hair loss of >=50% normal for that individual that is readily apparent to others; a wig or hair piece is necessary if the patient desires to completely camouflage the hair loss; associated with psychosocial impact

Description

You can write a description in here

Time

2015-10-14 09:57

You must give time in format hh:mm, for example 10:57.

Report

Monitored adverse effects

1. Alopecia
2. Dry skin
3. Fatigue
4. Headache
5. Nausea

No other adverse effects

Click here to report that you do not suffer from other adverse effects than those you have already reported (marked with ✓).

B

Kaiku Home Care progression Conversation Calendar My information Sign out

EORTC QLQ - H&N35 (suomeksi)

Arvioikaa, missä määrin Te olette kärsinyt näistä oireista tai vaivoista kuluneella viikolla. Valitkaa numero, joka parhaiten kuvaa oireen laatua.

(Osa 1) (1 / 7)

Oliko teillä suukipua? (Optional)

Ei lainkaan

Vähän

Melko paljon

Hyvin paljon

Oliko teillä leukakipua? (Optional)

Ei lainkaan

Vähän

Melko paljon

Hyvin paljon

Figure 1. Screenshots from Kaiku®: (A) the patient reporting side effects and (B) the patient filling the QLQ-H&N35 quality of life questionnaire.



The side effects for self-assessment were selected individually for each patient, based on the treatment of the patient. For each side effect, the patients were offered a choice of 1–4 grades differing in severity. The side effects and the descriptions of the grades were translated into Finnish by the research group from the CTCAE v. 4.03 English originals, as no validated Finnish translation of the CTCAE exists. The patients were also encouraged to report the absence of the selected side effects (zero grades). The self-assessment was not enforced, but the patients were sent an automatic weekly reminder by email. Email reminders of the quality of life questionnaires were sent to the patients during and a month after radiotherapy. Patients could send messages via Kaiku® to the nurse and the physician freely during the study. The medical staff received email notifications when patients sent a message, reported side effects, or filled in questionnaires in the system. The patients used Kaiku® on their own computers. The patients were also offered the opportunity to use a tablet at the hospital, but none of them chose to do so.

To assess the suitability of Kaiku® for the follow-up of side effects and quality of life among HNC patients, we recorded the number of reported side effects (including zero grades), filled in forms, and sent messages during the pilot period. Furthermore, any clinical actions triggered by contacts made via the system were recorded.

Results

Details of the participating patients and their use of Kaiku® are presented in Table 1. All patients used the system regularly. Four of the five patients reported side effects, and

all patients filled in the quality of life forms. Patient 4 filled in these forms even after the intended follow-up period due to misconfiguration of the follow-up protocol. In total, the five patients reported 514 adverse effect grades (including zero grades), filled in 23 quality of life questionnaires, and sent 38 messages. The reported side effects ranged from mild to severe (Grades I–III CTCAE v. 4.03).

Three of the five patients reported severe side effects (Grade III) and also reported severely affected quality of life according to their self-assessment using the QLQ-H&N35 and 15D instruments. The reported Grade III side effects included anorexia, dry mouth, dysphagia, mucositis, nausea, dry mouth, and skin ulceration. The most often-reported radiotherapy-related morbidity was mucosal pain and consequent difficulties in eating and nutrition. In one patient, neutropenic infection was also treated during the radiotherapy course. The medical interventions during the trial period are presented in Table 1.

The information collected using Kaiku® did not lead to any additional visits during the study period. Patient 1 was prescribed an opioid analgesic based on a message sent via the system.

Discussion

We conducted a prospective pilot study on online self-assessment of the early side effects of long-term radiotherapy and the quality of life in clinical practice among HNC patients, using a PRO collection tool called Kaiku®. The results from our study group of five patients are encouraging: all patients filled in quality of life questionnaires and four of them reported side effects via the system. Patients used the

Table 1. Patient summary.

	PATIENT 1	PATIENT 2	PATIENT 3	PATIENT 4	PATIENT 5
Summary					
Gender and age	M 68	M 50	M 51	M 63	M 80
Tumor site	Larynx	Base of tongue	Larynx	Base of tongue	Larynx
TNM category	T2N0M0	T2N0M0	T1aN0M0	T1N2bM0	T2N0M0
Treatment	RT 70/2 Gy	CRT 68/2 Gy	RT 66/2 Gy	CRT 70/2 Gy	RT 70/2 Gy
Reported adverse effects	None	33 data points — Anorexia, gr. III, Dry mouth, gr. III, Dysgeusia, gr. II, Dysphagia, gr. III, Fatigue, gr. I and II, Headache, gr. I, Laryngeal mucositis, gr. II and III, Nausea, gr. III, Pharyngeal mucositis, gr. II and III, Tracheal mucositis, gr. II	340 data points — Dry mouth, gr. I, Dry skin, gr. I, Dysgeusia, gr. I, Dysphagia, gr. I, Fatigue, gr. I, Laryngeal mucositis, gr. I, Pain, gr. I, Pharyngeal mucositis, gr. I, Skin induration, gr. I, Skin ulceration, gr. I	21 data points — Alopecia, gr. I, Anorexia, gr. I, Dry mouth, gr. III, Dry skin, gr. I, Dysgeusia, gr. I, Dysphagia, gr. II, Fatigue, gr. II, Laryngeal mucositis, gr. I, Nausea, gr. I and III, Pharyngeal mucositis, gr. II, Tracheal mucositis, gr. I	120 data points — Anorexia, gr. I and II, Dry mouth, gr. I and II, Dysgeusia, gr. I, Dysphagia, gr. I and II, Fatigue, gr. II, Laryngeal mucositis, gr. I, Nausea, gr. II, Pharyngeal mucositis, gr. I and II, Skin induration, gr. I, Skin ulceration, gr. II and III, Tracheal mucositis, gr. I
Medical interventions	Opioid analgesic	Opioid analgesic hospitalization iv. antibiotics, hydration	None	Opioid analgesic antimycotic	Opioid analgesic nutritional consulting
Number of filled QOL-forms	4	1	5	9	4
Number of sent messages	0	1	0	34	3

Abbreviations: RT, radiotherapy; CRT, chemoradiotherapy.



system during radiotherapy and one month after the end of the treatment. To further determine the impact of regular self-assessment in clinical practice using an online tool during the treatment and the follow-up, we recommend a larger, longitudinal study to be conducted.

Four patients declined to participate in the study, citing reasons related to information technology (little experience in using a computer or a mobile device, not having a computer or a mobile device available).

The patients participating in this study reported many radiotherapy-related side effects that required medical attention. The high compliance rate for the self-assessment indicates that the patients found the investigated system easy enough to use. Email reminders may have increased patient compliance to the self-assessment. The validated quality of life instruments used in this study corroborated the information from the nonvalidated side effect self-assessment scheme. Our findings concerning the patient compliance rate and the clinical impact of self-assessment are in-line with those obtained using a system similar to Kaiku[®] with patients recovering from a major gynecological cancer surgery.¹⁵ The study by Andikyan et al also found good compliance rates and suggested that online symptom reporting might be helpful in the early identification of disturbing postoperative symptoms.

Efficient monitoring of alarming symptoms is an integral part of organizing a cost-effective HNC follow-up. It is important for detecting cancer recurrence or new primary tumors as early as possible and for managing the late side effects from the treatment. Patient-reported symptoms have been found a sensitive predictor of cancer recurrence.²⁴ Kothari et al also found that patients would have preferred less regular visits to the clinic. Studies by Pagh et al⁶ and Kothari et al²⁴ stress the importance of patient education as a part of the follow-up program. A patient self-reporting system asking the patient for regular reports of possible symptoms and instructing the patient based on the symptoms could prove a cost-effective way to organize individualized follow-up for HNC survivors.

We are aware of several limitations to our study. First, our sample size of nine patients, of whom five consented to participate in the study, does not allow statistical analysis and cannot be taken to represent the patient demographic. Second, suitability of the investigated system was measured only by the patient compliance rate. Future studies should assess also other dimensions that patient self-reporting might affect, such as patient satisfaction, patient management, early detection of symptoms, clinical impact, and administrative burden. Third, the small sample size prevents us from evaluating how existing patient management processes should be changed to accommodate for routine collection of PROs on a larger scale. Fourth, the patients reported side effects on a nonvalidated scale. If the system is to be used on a larger scale in the future, symptoms should be reported on a validated scale to ensure the quality and comparability of the data.

We found the investigated system to be suitable for online self-assessment of the early side effects of radiotherapy and of the quality of life of HNC patients. We base this conclusion on the fact that all patients of the study reported adverse effects and/or quality of life in the system and on the amount of data collected from the patients. Other studies on similar systems have, too, found Internet-based PRO systems as feasible tools for collecting PROs.^{15,17,25} Because this was only a pilot study, no process for giving feedback to the patients based on the self-reported symptoms and health-related quality of life was instituted. Research indicates that for routine collection of PRO to bring about positive changes in patient management, the PRO collection should be integrated into patient management plan.¹⁴

Conclusion

We recommend further investigation on the impact of patient self-assessment in clinical routine in a larger study. Furthermore, the availability of Kaiku[®] and other similar systems should be considered in the broad context of how to arrange follow-up for HNC survivors, as these systems may offer a cost-effective way of monitoring alarming symptoms and late morbidities caused by the tumor or the treatment.

Author Contributions

Conceived and designed the experiments: MKP, JSL, LTS, KS, AAM. Analyzed the data: MKP, JSL. Wrote the first draft of the manuscript: MKP, JSL. Contributed to the writing of the manuscript: MKP, JSL, LTS, KS, AAM. Agree with manuscript results and conclusions: MKP, JSL, LTS, KS, AAM. Jointly developed the structure and arguments for the paper: MKP, JSL, LTS, KS, AAM. Made critical revisions and approved final version: MKP, JSL, LTS, KS, AAM. All authors reviewed and approved of the final manuscript.

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