

Health-related quality of life, satisfaction with care and cosmetic results in relation to treatment among patients with keratinocyte cancer in the head and neck area: results from the PROFILES-registry

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ABSTRACT

Background

Little is known about the impact of keratinocyte cancer (KC) and its treatment on health-related quality of life (HRQoL). The aims of the present study were to [1] evaluate HRQoL among patients with KC in a population-based setting and compare this with an age- and sex-matched norm population, and [2] compare HRQoL, satisfaction with care and cosmetic results for patients who underwent conventional excision, Mohs' micrographic surgery, or radiotherapy.

Methods

A random sample of 347 patients diagnosed with cutaneous basal cell (BCC) or squamous cell carcinoma (SCC) in the head and neck area between January 1, 2010 and December 31, 2014 were selected from the Netherlands Cancer Registry (NCR) and were invited to complete a questionnaire on HRQoL, satisfaction with care, and cosmetic results. Data were collected within Patient-Reported Outcomes Following Initial Treatment and Long-term Evaluation of Survivorship (PROFILES). Outcomes were compared to an age- and sex-matched normative population.

Results

Two hundred fifteen patients with KC returned a completed questionnaire (62% response). Patients with KC reported better global quality of life (79.6 versus 73.3; $p < 0.01$) and less pain ($p < 0.01$) compared to the norm population. No statistically significant differences in HRQoL, satisfaction with care, and cosmetic results were found between patients with KC who underwent conventional excision, Mohs' micrographic surgery, or radiotherapy.

Conclusion

The impact of KC and its treatment seems relatively low and more positive than negative as patients reported better HRQoL compared to an age- and sex-matched norm population probably due to adaptation. No statistically significant differences between treatment types were found concerning HRQoL, patients satisfaction and cosmetic results. This information could be used by healthcare professionals involved in KC care to improve patients' knowledge about different aspects of disease as patient's preference is an important factor for treatment choice.

INTRODUCTION

Keratinocyte cancer (KC) is the most common cancer in the Western world [1, 2]. Basal cell carcinomas (BCCs) and squamous cell carcinomas (SCCs) account for respectively 80% and 20% of cases of KC [2-4]. These cancers are called KC because they share lineage with keratinocytes and histologically resemble epidermal keratinocytes [3]. Keratinocytes are vulnerable to damage from sun exposure and therefore KCs usually develop on sun-exposed areas, especially the head and neck [5-8]. BCCs are slow-growing cancers that are nearly always asymptomatic, while SCCs may grow faster and may induce tenderness or pain, but are also mostly asymptomatic [3]. However, SCCs are more aggressive cancers with tendency to metastasis, especially the larger ones located on lips and ears [9].

KC is typically treated with surgical excision. However, less invasive options exist, such as radiotherapy, cryotherapy or topical therapy [3, 4, 10]. Choice of treatment depends on various factors, both clinical and personal. Important clinical factors are aggressiveness of the cancer, size and localization of the lesion, and especially for BCC, histological subtype [4, 11]. In addition, elderly patients and those with comorbid conditions are less suitable for surgical excision and are more likely to receive a less invasive treatment option. Furthermore, cosmetic aspects and patients' preferences may also have impact on the choice of treatment, since treatment of KC can cause substantial facial cosmetic and functional disturbances [11]. Previous research showed that most prevalent concerns of patients with KC include worries about tumor recurrence, as well as the potential size and conspicuousness of the scar [12].

Patient-reported outcomes and health-related quality of life (HRQoL) are increasingly important outcomes in daily patient care [8, 13, 14]. HRQoL refers to an individual's physical, psychological and social well-being, which may be affected by disease and treatment [15]. Since patients with KC are likely to develop multiple cancers during lifetime, KC and its treatment may be associated with impaired health-related quality of life (HRQoL) [16]. Despite the high incidence rates of KC and the importance of incorporating patient values into evidence-based medicine, little is known about the impact of specific treatment options for KC on HRQoL [13, 17]. In addition, the attention for perspectives of patients with KC is increasing over the past two decades, since previous research focused mainly on patients with melanoma [14, 18]. Satisfaction with care is also a part of the patient-reported outcomes and more applicable to diseases with multiple treatment options, such as KC [19]. As patients with KC strongly expressed the need for a shared decision making process [20, 21], in which they are actively engaged and value detailed information regarding their disease and treatment options, healthcare professionals that are working with

patients with KC need to understand their psychosocial concerns and needs in order to offer appropriate care services [22].

The aims of the present study were to [1] evaluate HRQoL among patients with KC in a population-based setting and compare this with an age- and sex-matched normative population, and [2] compare HRQoL, satisfaction with care and cosmetic results between patients who underwent conventional excision, Mohs' micrographic surgery, or radiotherapy.

METHODS

Setting and population

A cross-sectional cohort study was performed among patients with KC registered within the Netherlands Cancer Registry (NCR). Data from the NCR Eindhoven area were used to select a random sample of patients who were diagnosed with KC. The NCR Eindhoven area comprises an area with 2.4 million inhabitants (almost 15% of the Dutch population) in the South-Eastern part of the Netherlands. Patients diagnosed with at least one BCC or SCC in the head and neck area between January 1, 2010 and December 31, 2014 were eligible for participation. Patients with unverifiable addresses, with cognitive impairment, who died prior to the start of the study or were terminally ill and those with *in situ* lesions or who were already included in another study were excluded.

The NCR Eindhoven area is one of the few cancer registries that records data on BCC. The available data in the Netherlands Cancer Registry (NCR) does not include data on treatment – only histological diagnosis of first BCC [23]. If there is no histological information concerning BCC (neither biopsy nor excision), patients are not registered in the NCR. This may especially be the case for patients who received radiotherapy, as not all carcinomas are histologically confirmed. We have opted for an oversampling of patients who received radiotherapy as primary treatment to enable a better comparison between treatment groups. Thus, we invited all eligible patients who received radiotherapy from two radiotherapy institutions.

Study measures

The Dutch-validated version of the European Organization for Research and Treatment of Cancer Quality of Life Questionnaire (EORTC-QLQ-C30) was used to assess generic HRQoL [24]. Answer categories range from one (not at all) to four (very much). After linear transformation, all scales and single items measures range in score from 0 to 100. A higher

score on functioning scores implies better health-related quality of life, whereas higher symptom scores refer to more symptoms [24].

The 16-item Basal and Squamous Cell Carcinoma Quality of Life (BaSQoL) questionnaire was used to capture impact of KC on HRQoL [14]. It assesses the relevant dimensions of HRQoL in patients with BCC and those with SCC. The individual items are scored from 0 to 3, where 0 represents no impact and 3 very high impact. The mean score per subscale was calculated. A minimum of 50% of the questions within the subscale has to be answered in order to calculate the subscale score. No total score was calculated.

The Dutch version of the European Organization for Research and Treatment of Cancer In-Patient Satisfaction with care Questionnaire (EORTC IN-PATSAT32) was used to assess patient satisfaction [25]. Items were assigned a score from one (poor) to five (excellent). After linear transformation, all scales and single items measures range in score from 0 to 100. Higher scale scores represent better satisfaction with care. Since the EORTC IN-PATSAT32 was designed for in-patients, items about nurses and information provision at hospitalization and discharge were excluded from our questionnaire.

One single item was used to assess the cosmetic results of the treatment. This item was assigned a score from 1 to 10. A higher score reflects a higher level of satisfaction with the cosmetic result.

Comorbidity was categorized according to the adapted Self-administered Comorbidity Questionnaire (SCQ) [26]. Patients were asked to identify comorbid conditions present in the past 12 months. Positive responses were summed to obtain a total score (range 0-13).

Sociodemographic characteristics and clinical information were available from the NCR that routinely collects data on patients' age and sex, date of diagnosis, cancer type, and treatment. As for BCCs only the first histologically confirmed carcinoma is registered, from the eligible BCC patients additional data on treatment, tumor size and morphology was manually collected by reviewing the patient records. Information on marital status, educational level, and employment status were assessed in the questionnaire.

Data collection

Data were collected within Patient-Reported Outcomes Following Initial Treatment and Long-term Evaluation of Survivorship (PROFILES). PROFILES is a registry for the study of the physical and psychosocial impact of cancer and its treatment from a dynamic, growing population-based cohort of both short- and long-term cancer survivors [27]. PROFILES is linked directly to clinical data from the NCR. In 2016, a survey was conducted among 345

individuals with BCC or SCC in the head and neck area. Eligible patients were informed about the study via a from their (former) dermatologist or radiotherapist. Patients were asked to complete and return the enclosed paper-and-pencil questionnaire. Patients were assured that refusing to participate in the study had no consequences for their follow-up care. If the questionnaire was not completed within 4 weeks, a reminder letter and a questionnaire was sent. More information about PROFILES and the data collection has been published previously [27]. (figure 1) All respondents have given written informed consent. This study was approved by the Medical Research Ethics Committees United (M15-0341).

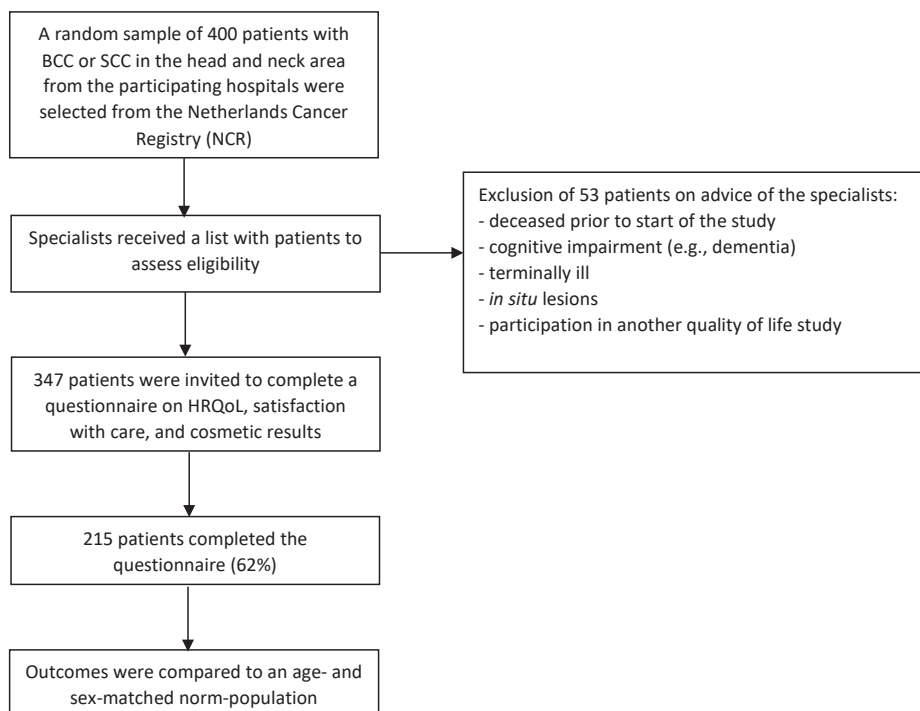


Figure 1. Flowchart of data collection process

Normative population

The normative population was selected from a reference cohort of 2,040 individuals from the general Dutch population (CentER panel). This cohort is representative for the Dutch population [28]. The set of questionnaires completed by this normative population in November 2011 included the EORTC QLQ-C30, SCQ, and data on sociodemographics. From this normative population, an age- and sex-matched selection was made to compare HRQoL with patients with KC. For matching, ten strata were formed using sex and age

(five categories). Within each stratum a maximum number of persons from the reference were randomly matched according to the strata frequency distribution of the patients. This resulted in 277 matched cancer-free individuals for the 215 KC patients.

Statistical analyses

Differences in sociodemographic and clinical characteristics between patients with KC and an age- and sex-matched normative population were assessed with a Chi-square for categorical variables and t-tests for continuous variables. Differences in sociodemographic and clinical characteristics between patients with KC according to treatment regime were also assessed with a Chi-square and t-tests, where appropriate.

Mean EORTC QLQ-C30 scores from the patients with KC were compared with the mean scores of an age- and sex-matched normative population using independent sample t-tests. To compare HRQoL scores between patients with one versus multiple skin cancer, we used analyses of covariance (ANCOVA) adjusting for age. To compare mean scores between patients with KC who underwent conventional excision, Mohs' micrographic surgery, or radiotherapy on QLQ-C30 scales, symptoms, BaSQoL scales, IN-PATSAT32 scales, general satisfaction with care, and cosmetic results, we used analyses of covariance (ANCOVA) adjusting for age. Age was calculated at the time of administering the questionnaire.

All statistical analyses were performed using SAS (version 9.4 for Windows; SAS Institute Inc., Cary, NC). *P* values of <0.05 were considered statistically significant. Clinically relevant differences were determined using the evidence-based guidelines for interpretation of the EORTC QLQ-C30 between groups [29].

RESULTS

Patient characteristics

Two hundred fifteen patients with KC returned a completed questionnaire (62% response). Respondents were younger compared to non-respondents ($p < 0.001$) and had a more recent diagnosis of KC ($p = 0.004$; Table 1). No differences between responding and non-responding patients were found according to type of cancer or localization.

The mean age at completion of the questionnaire was 71.3 years with a mean time since diagnosis of 3.3 years. Most patients were diagnosed with BCC (81%) and almost half of all patients reported they have had more than one skin cancer. Medium educational level was most common (60%). Comorbid conditions were reported by 75% of patients. In the normative population, mean age at questionnaire completion was 69.3 years with

Table 1. Sociodemographic and clinical characteristics of responding and non-responding patients with keratinocyte cancer (KC), and an age- and sex-matched normative population

	Respondents N=215 N (%)	Non-respondents N=130 N (%)	Norm population N=255 N (%)
Sex			
Male	116 (54)	66 (51)	137 (54)
Female	99 (46)	64 (49)	118 (46)
Age at time of survey: mean (SD)	71.3 (11.9)	76.6 (14.1)*	69.3 (12.8)
<50	14 (7)	6 (5)	16 (6)
50-59	24 (11)	13 (10)	27 (11)
60-69	38 (18)	13 (10)	45 (18)
70-79	89 (41)	31 (24)	105 (41)
80+	50 (23)	67 (52)	62 (24)
Years since diagnosis: mean (SD)	3.3 (1.4)	3.7 (1.5)*	
Educational level [#]			
Low	34 (17)		95 (37)*
Medium	120 (60)		62 (24)*
High	47 (23)		98 (38)*
Partner			
Yes	66 (31)		83 (33)
No	149 (69)		172 (67)
Self-reported comorbidities: mean (SD)	1.5 (1.5)		1.4 (1.3)
Most frequent comorbid conditions			
Hypertension	64 (32)		92 (36)
Arthritis	65 (32)		81 (32)

* Significantly different from respondents ($p < 0.05$); [#] Educational levels were low = none/primary school; medium = lower general secondary education/vocational training; or high = pre-university education/ high level vocational training/university.

a comorbidity percentage of 70%. In our sample, 49% of patients with KC underwent conventional excision, 26% radiotherapy and Mohs' micrographic surgery was received by 9% of patients with KC. The remaining patients received a variety of treatments, such as photodynamic therapy, cryotherapy or topical chemotherapy. This group, however, is too small to be further outlined. Patients who received radiotherapy were significantly older (75.9 years) than patients with KC who underwent conventional excision or Mohs' micrographic surgery (68.2 and 67.4 years, respectively; $p < 0.001$). In addition, patients who received radiotherapy had more often cancer located on the nose (60%) compared to patients treated with conventional excision or Mohs' micrographic surgery (25 and 32%, respectively; $p < 0.001$) (Table 2).

Table 2. Sociodemographic and clinical characteristics of questionnaire respondents who were treated with radiotherapy (n=55), conventional excision (n=106), and Mohs micrographic surgery (n=19).

	Conventional excision N=106 N(%)	Mohs' micrographic surgery N=19 N(%)	Radiotherapy N=55 N(%)	p-value
Sex				0.34
Male	54 (51)	8 (42)	33 (60)	
Female	52 (49)	11 (58)	22 (40)	
Age at time of survey: mean (SD)	68.2 (11.9)	67.4 (13.2)	75.9 (9.7)	
<50	9 (8)	4 (21)	0 (0)	≤0.001
50-59	17 (16)	1 (5)	4 (7)	
60-69	24 (23)	4 (21)	6 (11)	
70-79	39 (37)	6 (32)	28 (51)	
80+	17 (16)	4 (21)	17 (31)	
Education level ¹				0.37
Low	14 (14)	1 (5)	10 (20)	
Medium	59 (60)	11 (58)	32 (63)	
High	26 (26)	7 (37)	9 (18)	
Partner (yes)	77 (73)	17 (89)	36 (65)	0.13
Type of cancer				0.30
BCC	86 (81)	18 (95)	48 (87)	
SCC	15 (14)	1 (5)	7 (12)	
Unknown	5 (5)	0 (0)	(0)	
Number of skin cancers				0.04
One skin cancer	44 (42)	9 (50)	33 (63)	
More than one skin cancer	60 (58)	9 (50)	19 (37)	
Localization				≤0.001
Forehead	16 (15)	1 (5)	4 (7)	
Scalp	23 (22)	1 (5)	3 (5)	
Nose	26 (25)	6 (32)	33 (60)	
Ear	9 (8)	3 (16)	6 (11)	
Lip	3 (3)	3 (16)	2 (4)	
Other parts of head and neck	29 (28)	5 (26)	7 (13)	
Number of comorbidities: mean (SD)	1.2 (1.2)	1.4 (1.7)	1.6 (1.2)	0.22
Most frequent comorbid conditions				
Hypertension	21 (21)	8 (42)	20 (41)	0.02
Arthritis	26 (26)	6 (32)	16 (33)	0.67

¹ Education levels were low = none/primary school; medium = lower general secondary education/ vocational training; or high = pre-university education/ high level vocational training/university.

Comparison between patients with multiple skin cancers and one skin cancer

Patients with multiple skin cancers were less satisfied with the cosmetic results compared to patients with one skin cancer (8.3 versus 7.7, $p < 0.01$) (Figure 2), and were more concerned about their appearance (0.18 versus 0.32, $p = 0.04$). No significant differences were found on HRQoL (as measured with the EORTC QLQ-C30 and BaSQoL) between patients with one or multiple skin cancers (all $p > 0.05$). No differences between patients with infiltrative and non-infiltrative BCC were found in HRQoL scores, general satisfaction with care and cosmetic results (all $p > 0.05$).

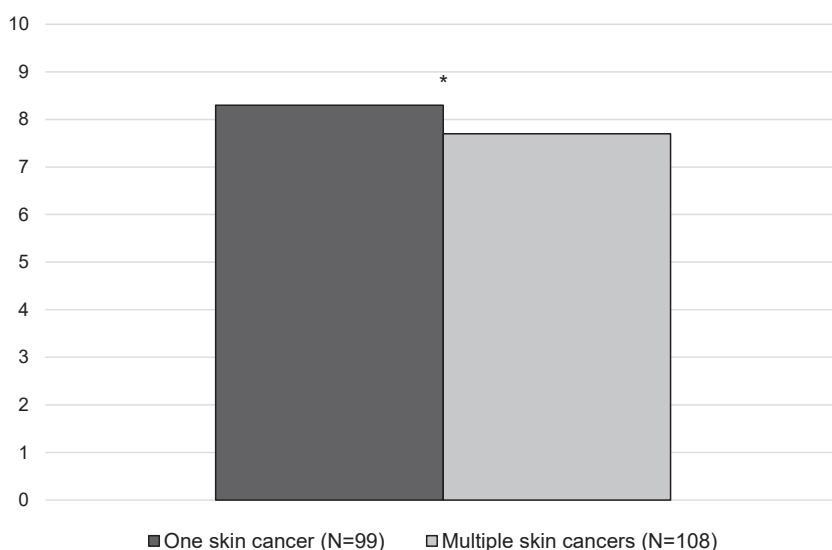


Figure 2. Differences in cosmetic results between patients who have had one skin cancer (N=99) and patients who have had multiple skin cancers (N=108).

* $P < 0.001$

Comparison between patients with KC and an age- and sex-matched normative population

No statistically significant differences were observed between patients with KC and an age- and sex-matched norm population on physical, emotional, cognitive, social, and role functioning (EORTC QLQ-C30) (all $p > 0.05$). However, patients with KC reported statistically significant better scores on global quality of life (79.6 versus 73.3; $p < 0.01$) and they reported less pain ($p < 0.01$) compared to a normative population (Figure 3a and 3b). These represented small clinically important differences. Other symptoms were comparable ($p > 0.05$).

Comparison between treatment groups

No differences in global quality of life, functioning scores (both EORTC QLQ-C30) or BaSQoL mean scores were found between patients treated with conventional excision, Mohs' micrographic surgery and radiotherapy (all $p > 0.05$, Figure 4a and 4b, Table 3).

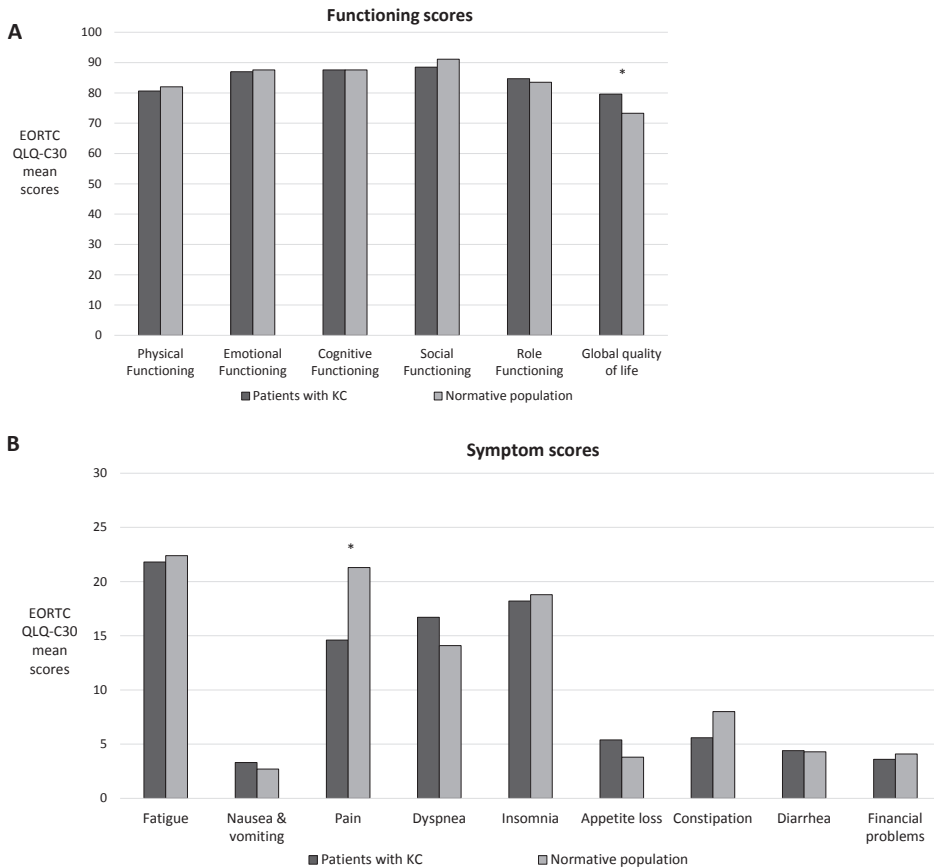


Figure 3a and 3b. Differences on EORTC QLQ-C30 mean functioning and global quality of life (a) and symptom scores (b) between patients with KC (N=215) and an age- and sex-matched normative population (N=255).

* $p < 0.05$ and small clinically important difference; A higher score on functioning scores implies a better health-related quality of life, whereas a higher score on symptom scores refers to more symptoms. EORTC QLQ-C30 = European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire Core 30.

Patients with KC who underwent radiotherapy were more satisfied with the cosmetic results than patients who underwent conventional excision or Mohs' micrographic surgery (8.5 versus 7.8 and 7.9, respectively), but this difference was not statistically significant ($p=0.06$) nor clinically relevant. Patients who underwent radiotherapy reported better scores for hospital comfort/cleanliness (72.1 versus 62.9, $p=0.03$) compared to patients treated with conventional excision. No other statistically significant differences were found

between treatment groups. In all treatment groups, approximately half of the patients rated their general satisfaction with care as “very good” or “excellent”.

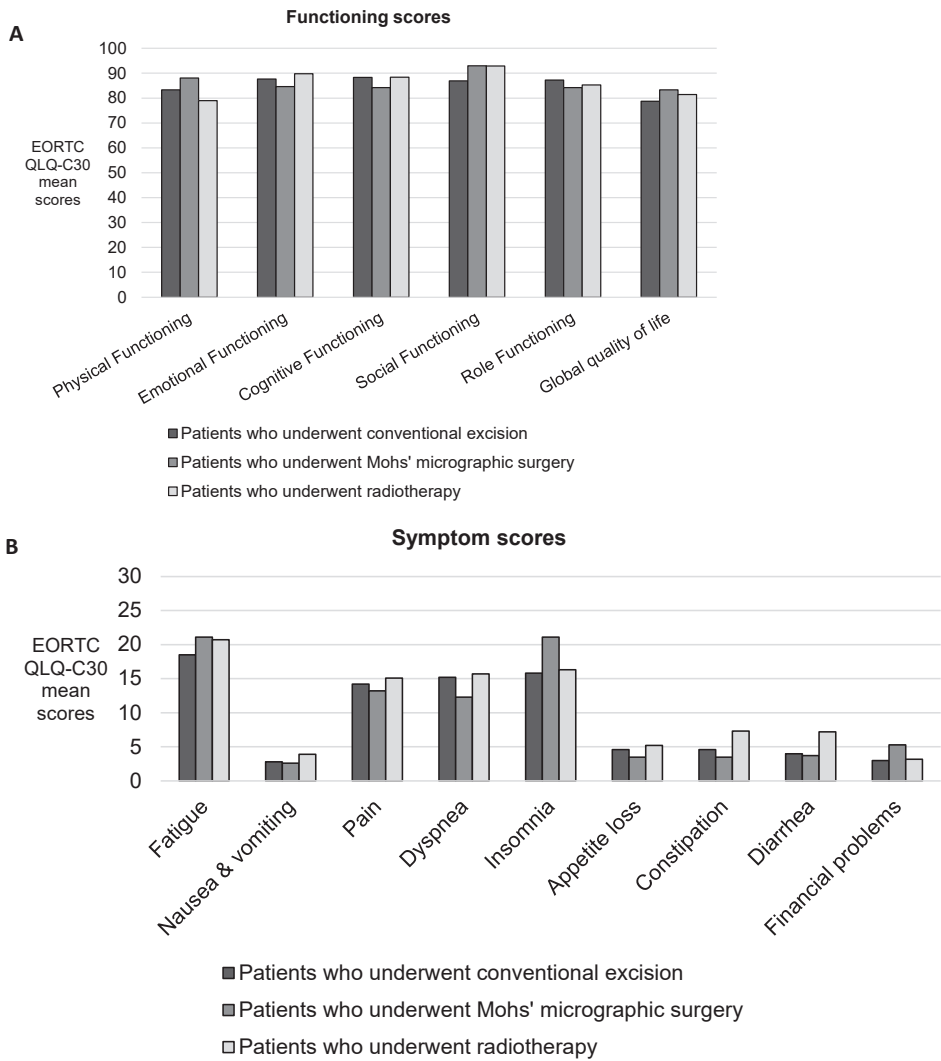


Figure 4a and **4b**. Differences on EORTC QLQ-C30 mean functioning and global quality of life (a) and symptom scores (b) between patients with KC who underwent conventional excision (N=106), Mohs' micrographic surgery (N=19), or radiotherapy (N=55).

A higher score on functioning scores implies a better health-related quality of life, whereas a higher score on symptom scores refers to more symptoms. EORTC QLQ-C30 = European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire Core 30.

Table 3. Differences between patients treated with radiotherapy, conventional excision, and Mohs' micrographic surgery on mean EORTC IN-PATSAT32 scores and cosmetic result, adjusted for age.

	Conventional excision N=106 Mean (SD)	Mohs' micrographic surgery N=19 Mean (SD)	Radiotherapy N=55 Mean (SD)	p-value
BaSQoL (0-3)¹				
Behaviour	0.7 (0.7)	0.5 (0.5)	0.6 (0.7)	0.27
Diagnosis and treatment	0.9 (0.7)	1.0 (1.0)	1.1 (0.7)	0.39
Worries	0.7 (0.6)	0.7 (0.7)	0.9 (0.7)	0.44
Appearance	0.3 (0.5)	0.2 (0.5)	0.3 (0.4)	0.19
Other people	0.7 (0.7)	0.5 (0.6)	0.6 (0.7)	0.28
EORTC IN-PATSAT32 (0-100)²				
Doctors' technical skills	65.4 (19.4)	68.9 (14.4)	66.6 (22.0)	0.77
Doctors' interpersonal skills	58.2 (22.2)	67.1 (20.1)	63.0 (22.9)	0.19
Doctors' information provision	64.5 (21.4)	71.9 (22.1)	69.3 (22.0)	0.24
Doctors' availability	55.5 (24.3)	65.3 (19.0)	59.7 (25.2)	0.23
Other hospital staff interpersonal skills and information provision	66.9 (20.0)	64.5 (20.9)	73.6 (22.9)	0.12
Exchange of information between caregivers	56.1 (21.2)	53.9 (28.0)	58.8 (21.7)	0.66
Waiting time	61.4 (18.2)	54.6 (25.4)	64.9 (22.6)	0.17
Hospital access	60.5 (18.3)	64.5 (21.4)	66.6 (23.2)	0.20
Hospital comfort/cleanness	62.9 (19.2)	68.4 (18.3)	72.1 (23.6)	0.03
General satisfaction	64.4 (19.6)	68.1 (18.8)	68.8 (21.6)	0.43
Cosmetic results (0-10)³				
Cosmetic results	7.9 (1.5)	7.8 (1.5)	8.5 (1.1)	0.06

Results in bold are statistically significant different. ¹ A higher score implies more impact of the disease; ² A higher score implies more satisfaction; ³ A higher score represents more satisfaction with the cosmetic result.

DISCUSSION

In this study, patients with KC reported better global quality of life and less pain compared to an age- and sex-matched norm population. Similar results have previously been observed among patients with other types of cancer [30, 31], and among patients with melanoma [32]. A possible explanation is that patients score better because they adapt the new situation of having a skin cancer diagnosis, assessing their quality of life better than before the diagnosis, the so-called response shift [33].

Although different treatment options may lead to different HRQoL scores, we found similar scores on functioning and global quality of life among patients with KC who underwent conventional excision, Mohs' micrographic surgery or radiotherapy. This is in line with research among patients with KC that showed similar HRQoL after excision and Mohs' micrographic surgery [13]. It was expected that patients who underwent radiotherapy might experience their treatment as more severe, as they need to visit the hospital several days in a row for therapy. Irradiation can also result in complaints about 'burning' of the skin [34, 35]. We found that patients who underwent radiotherapy were more satisfied with the cosmetic results, however this was not statistically relevant. The mean time since diagnosis was more than 3 years, so it might be that complaints about burning of the skin are not relevant anymore after few years, while scars as a result of conventional excision or Mohs' micrographic surgery might remain more visible, especially when patients have had multiple skin cancers. It is likely that adverse aspects of different treatment options are of greater impact on HRQoL when patients are closer to diagnosis [13]. In this study, we included only patients with KC who have been diagnosed at least one year before questionnaire completion. More complaints might be expected when patients are closer to treatment.

Patients who had multiple skin cancers reported lower cosmetic results and more concerns about their appearance compared to patients who had only one skin cancer. Previous research showed that potential disfigurement and scarring is a concern for many patients [11, 12, 36], especially multiple scars from multiple skin cancers.

Approximately half of the patients with KC rated their general satisfaction with care as "very good" or "excellent". High cure rates of both excision and radiotherapy (>90%) might therefore be an explanation for high satisfaction scores [37].

The current study has some limitations, such as the small sample size, which may limit statistical significance of our findings. The sample size is especially small for patients treated with Mohs' micrographic surgery. At the time patients included in this study were treated, the benefits of Mohs' micrographic surgery in the treatment of BCC and SCC had not yet been sufficiently demonstrated [38, 39]. Therefore, Mohs' micrographic surgery was not a standard of treatment for KC yet and as a result of which it was used less frequently. The availability of Mohs' micrographic surgery in the NCR Eindhoven area has increased since 2014. The study should be replicated with a larger sample of KC patients to get more conclusive results. In addition, we did not have detailed information on radiotherapy schedules of KC. Therefore, we are not aware whether the frequency of radiotherapy appointments has impact on HRQoL and satisfaction with care. Furthermore, we did not have detailed information of non-responding patients. Previous research reported that

patients not participating in observational PRO research may systematically have lower HRQoL scores compared to participants [40]. Therefore, observed outcomes might represent the healthier patient with better outcomes.

In conclusion, despite the cross-sectional design of this study, this population-based study give an overview of the HRQoL that patients with KC experience after their disease and treatment. The impact of KC and its treatment seems relatively low and more positive than negative as patients reported better HRQoL compared to an age- and sex-matched norm population probably due to adaptation. No statistically significant differences between treatment types were found concerning HRQoL, patients satisfaction and cosmetic results. This information could be used by healthcare professionals involved in KC care to improve patients' knowledge about different aspects of disease as patient's preference is an important factor for treatment choice.

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