Review Article

An Update on Quality of Life in Malignant Melanoma and Nonmelanoma Skin Cancers

Tubanur Çetinarslan, Mustafa Kürşat Evrenos[1], Aylin Türel Ermertcan[2]

Kırıkkale Yüksek İhtisas Hospital, Dermatology Clinic, Kırıkkale, Manisa Celal Bayar University, Departments of [1]Plastic and Reconstructive Surgery and [2]Dermatology, Manisa, Turkey

Abstract

Skin cancer is the most common type of cancer. Nonmelanoma skin cancers (NMSCs) are more common than malignant melanoma. It is expected that the incidence of skin cancer will increase in the future. Although the mortality rate is low, cancer wording can be frightening for patients. Because skin cancers are most commonly located in the head and neck, unwanted cosmetic consequences can occur as a result of treatments. Therefore, the quality of life (QOL) of patients could be affected negatively. Today, there are various scales that assess the QOL of patients. These can be grouped as general, disease-specific, and cancer-specific questionnaires. Studies have been carried out and are still in progress to develop scales of QOL specific to skin cancers. In this paper, the questionnaires used in malignant melanoma and/or NMSCs and studies on this subject are reviewed.

Keywords: Nonmelanoma skin cancer, quality of life, skin cancer

Introduction

Skin cancer is the most common type of cancer in human and grouped under two main headings: nonmelanoma skin cancers (NMSCs) and malignant melanoma (MM).[1] The incidence has increased dramatically over the past 20 years, especially among women and people aged 30–39 years, as a result of excessive exposure to ultraviolet radiation.[2,3] Unfortunately, NMSCs occur in the most conspicuous location of the body, with approximately 80% occurring in the cervicofacial region; the nose alone accounts for roughly 25% of all cutaneous malignancies and is followed closely by the external ear and surrounding skin.[4] It has been suggested that patients have a 52% risk of developing a second NMSC within 5 years after the diagnosis of squamous cell cancer (SCC), with the highest risk during the first year after diagnosis.[5,6] Morbidity assumes greater importance than mortality in many patients with cutaneous malignancies, making quality of life (QOL) a more relevant endpoint in the assessment of the disease process.[7] Although skin cancer itself is the most important factor affecting the QOL, the QOL of patients can be impaired due to the unexpected results and side effects of treatment methods. While a variety of effective treatment options exist for managing these cancers, such as excision, electrodesiccation and curettage, Mohs micrographic surgery, and topical chemotherapies, patients' QOL can be affected by these treatments as well as by potentially cosmetically unsatisfying results.[8] Minor as well as major degrees of facial disfigurement can result in high levels of anxiety, depression, and social isolation, the severity of which often bears little relationship to the magnitude of the defect itself.[9]

Patient-reported outcomes are increasingly being used to capture patients' perception of a disease, its treatment, and impact on daily living.[10] Several scales have been developed to evaluate the QOL and studies are still underway to develop new scales specific to disease. In dermatology, QOL can be assessed utilizing generic QOL questionnaires, dermatology-specific questionnaires, disease-specific questionnaires, or cancer-specific questionnaires.[11]

Submission: 19-02-2021 **Revision:** 20-03-2021
Acceptance: 05-04-2021 **Web Publication:** 25-06-2021

Access this article online

Quick Response Code:

Website: www.tjdonline.org

DOI: 10.4103/tjd.tjd_16_21

Address for correspondence: Dr. Tubanur Çetinarslan, Uncubozkoy Mah., 5501 Sok, No: 29/5, Manisa, Turkey.
E-mail: t_sarmis@windowslive.com

How to cite this article: Çetinarslan T, Evrenos MK, Ermertcan AT. An update on quality of life in malignant melanoma and nonmelanoma skin cancers. Turk J Dermatol 2021;15:17-27.

In this article, QOL questionnaires used in patients with MM or NMSC are discussed and studies about the QOL in patients with MM or NMSC published in PubMed between 2003 and 2019 are reviewed and summarized.

Quality of Life Instruments Used for Evaluation of Skin Cancers

The questionnaires which dermatology-specific, skin cancer-specific or cancer-specific to assess the QOL in skin cancers have been shown in Table 1.

Dermatology-specific questionnaires

Dermatology-specific or disease-specific instruments include aspects of the health-related QOL (HRQoL) that may not be captured by a generic instrument. Disease-specific instruments are more responsive to disease activity and treatment outcome and are therefore often used to reflect the patient perspective in clinical trials and observational research.[12]

The Dermatology Life Quality Index

The Dermatology Life Quality Index (DLQI), the first dermatology-specific HRQoL questionnaire, was published in 1994.[13] DLQI is a self-administered tool, developed to assess the disease-specific effects of skin conditions on patients' QOL. It consists of 10 items. The items of the DLQI include symptoms and feelings, daily activities, leisure, work or school, personal relationships, and the side effects of treatment.[14] Each item is scored 0–3, yielding a maximum score of 30. Higher scores indicate lower levels of HRQoL. The questions refer to the past week.[14,15]

Skindex

In 1996, Chren *et al*. developed a 61-item self-administered survey instrument called Skindex. Skindex has eight scales, each of which addresses a construct, or an abstract component, in a comprehensive conceptual framework: cognitive effects, social effects, depression, fear, embarrassment, anger, physical discomfort, and physical limitations.[16] The questionnaire measures QoL in the previous 4 weeks, on the assumption that this is a"reasonable timeframe to expect equilibrium after a change in treatment".[17] There are four versions of the Skindex including the original 61-item and the reduced versions: Skindex-29, Skindex-17, and Skindex-16.[17,18]

The Skindex-16 is a one-page version measuring how patients are bothered by their skin condition. This includes skin symptoms (i.e., itching, burning), feelings (i.e., frustration, embarrassment, depression), and effects on function (i.e., interactions with others, daily activities, ability to work). The instrument was not developed to measure surgical issues (i.e., scarring) and treatment satisfaction. It may not be regarded as a suitable scale for assessing QOL in skin cancer patients.[1]

Table 1: Quality of life instruments used for evaluation of skin cancers

Dermatology specific questionnaires	Skin cancer-specific questionnaires	Cancer-specific questionnaires
DLQI	SCQOLIT	FACT-G
Skindex-16	FACT-M	EORTC-QLQ-C30
Skindex-17	SCI	
Skindex-29	EORTC-QLQ-M	
	EORTC-QLQ- MEL38	

DLQI: Dermatology Life Quality Index, SCQOLIT: Skin Cancer Quality of Life Impact Tool, FACT-G: Functional Assessment of Cancer Therapy- General Version, FACT-M: Functional Assessment of Cancer Therapy-Melanoma, EORTC-QLQ-C: European Organization for Research and Treatment of Cancer Quality of Life Questionnaire, EORTC-QLQ-MEL: European Organization for Research and Treatment of Cancer Quality of liFe Questionnaire-Melanoma Modüle, SCI: Skin Cancer Index

Cancer-specific questionnaires

Functional Assessment of Cancer Therapy – General version (FACT-G) and the European Organization for Research and Treatment of Cancer QOL Questionnaire (EORTC QLQ-C30) are two of the most widely used cancer-specific QoL measures. Both instruments have undergone rigorous validation and have been translated and field-tested in approximately 24 different languages, making them suitable for use in multinational clinical trials of cancer therapy and to allow cross-cultural comparisons of people who come from diverse backgrounds.[19]

Functional Assessment of Cancer Therapy– General version

The FACT-G was developed by Cella and colleagues in the United States. The FACT-G meets or exceeds all requirements for use in oncology clinical trials, including ease of administration, brevity, reliability, validity, and responsiveness to clinical change. The five-phase validation process of FACT-G involved 854 patients with cancer and 15 oncology specialists.[20]

The FACT-G has undergone several modifications over the past 20 years, and the version that is in use at is present Version IV, which comprises 27 items.[19] The FACT-G is comprised of four subscales: Physical well-being (7-items, score range 0–28), social/family well-being (7-items, score range 0–28), emotional well-being (6-items, score range 0–24), and functional well-being (7-items, score range 0–28). Users of the FACT-G are able to generate an overall score and four subscale scores with ranges and distributions that are sample-specific. All questions in the FACT-G use a 5-point rating scale (0 = not at all; 1 = a little bit; 2 = somewhat; 3 = quite a bit; and 4 = very much). Provided more than 50% of the items comprising a subscale are answered, a subscale score is computed as the prorated sum of the item responses for that subscale.[21]

European Organization for Research and Treatment of Cancer Quality of Life Questionnaire-C30

The EORTC QLQ-C30 contains subscales for global health status, physical, emotional, role, cognitive and social function, with higher scores indicating better functioning.

Symptom subscales include pain, nausea/vomiting, fatigue, dyspnea, appetite loss, insomnia, diarrhea, and constipation (higher scores indicate greater symptom severity). Extensive evidence is available supporting the reliability, validity, and responsiveness of the EORTC QLQ-C30 in different cancer populations.[22]

EORTC-QLQ-30 is a measure which was originally devised by Aaronson and colleagues in the Netherlands. The questionnaire was administered before treatment and once during treatment to 305 patients with nonresectable lung cancer from centers in 13 countries. Their results support the EORTC QLQ-C30 as a reliable and valid measure of the QOL of cancer patients in multicultural clinical research settings.[22] Müller *et al*. validated EORTC-QLQ-C30 in their study in 172 patients with NMSC.[23]

Skin cancer-specific questionnaires

Among the scales used in skin cancer, Skin Cancer Index (SCI) is used in NMSCs. There are two scales used specifically for melanoma. The first one is EORTC-QLQ-M a disease-spesifik QoL measure devoleped from EORTC-QLQ-30. The second

Table 2. Skin Cancer Index (SCI)[24]

Skin Cancer Index (SCI)					
During the past month how much have you.	**Very much**	**Quite a bit**	**Modaretaly**	**A little bit**	**Not at all**
1. Worried that your skin cancer will spread to another part of your body?	( )	( )	( )	( )	( )
2. Felt anxious about your skin cancer?	( )	( )	( )	( )	( )
3. Worried that family members may also develop skin cancer?	( )	( )	( )	( )	( )
4. Worried about the cause of skin cancer?	( )	( )	( )	( )	( )
5. Felt frustrated about your skin cancer?	( )	( )	( )	( )	( )
6. Worried that your tumor become a more serious type of skin cancer?	( )	( )	( )	( )	( )
7. Worried about new skin cancers occuring?	( )	( )	( )	( )	( )
8. Felt uncomfortable when meeting new people?	( )	( )	( )	( )	( )
9. Felt concerned that your skin cancer may worry friends or family?	( )	( )	( )	( )	( )
10. Worried about the length of time before you can go out in the public?	( )	( )	( )	( )	( )
11. Felt bothered by people's questions related to your skin cancer?	( )	( )	( )	( )	( )
12. Felt embrassed by your skin cancer?	( )	( )	( )	( )	( )
13. Worried about how large the scar will be?	( )	( )	( )	( )	( )
14. Thought about how skin cancer affects your attractiveness?	( )	( )	( )	( )	( )
15. Thought about how noticable the scar will be to others?	( )	( )	( )	( )	( )

Table 3. SCQOLIT Questionnaire[28]

Skin Cancer Quality of Life Assessment Tool (SCQOLIT)				
The purpose of this questionnaire is to measure how much having skin cancer has affected your quality of life OVER THE LAST WEEK. Please tick one box for each question and answer all questions.				
	Very much so	**Modaretaly so**	**Somewhat**	**Not at all**
Over the last week, how much have you been concerned that your skin cancer might come back?	( )	( )	( )	( )
Over the last week, how much have you felt that you need more information on how to recognize skin cancer or prevent it?	( )	( )	( )	( )
Over the last week, how much have you worried about covering up your skin and keeping out of the sun?	( )	( )	( )	( )
Over the last week, how much have you felt a need for reassurance from your doctor or nurse, in respect to your skin cancer or its treatment?	( )	( )	( )	( )
Over the last week, how much have you felt emotional, anxious, depressed, guilty or stressed, in respect to your skin cancer or its treatment?	( )	( )	( )	( )
Over the last week, how much have you bothered about disfigurement or scarring, in respect to your skin cancer or its treatment?	( )	( )	( )	( )
Over the last week, how much have you felt shock or disbelief about having been diagnosed with skin cancer?	( )	( )	( )	( )
Over the last week, how much skin discomfort or inconvenience have you experienced, in respect to your skin cancer or its treatment?	( )	( )	( )	( )
Over the last week, how much have you had concerns about dying from your skin cancer?	( )	( )	( )	( )
Over the last week, to what extent have you felt the need for emotional support from your family or friends, in respect to your skin cancer or its treatment?	( )	( )	( )	( )

melanoma-specific scale is FACT-melanoma (FACT-M). Skin Cancer QOL Impact Tool (SCQOLIT) is developed for use in patients with either non-metastatic MM or non-metastatic NMSC skin cancer.

The Skin Cancer Index

In 2005, Rhee *et al*. developed Facial SCI as a new disease-specific QOL instrument for patients with NMSC of the head and neck.[7] SCI is a 15-item disease-specific QOL instrument [Table 2].[24] It is a sensitive and responsive QoL instrument for patients with NMSC. The SCI consists of three subscales: Emotion (i.e., anxiety, worry, frustration), social (i.e., meeting new people, time away from public), and appearance. There is also an appearance subscale with questions addressing scar visibility, size, and effects on attractiveness. Distinct demographic and clinical variables that impact QoL have been demonstrated using this multidimensional, disease-specific instrument.[24,25]

Unlike the SCI, there are no distinct subscales in the DLQI, although the individual items do address some similar concerns as in the SCI. However, the DLQI items appear to be more tailored for chronic, benign skin conditions such as psoriasis or eczema because they emphasize physical complaints of itchiness and irritation and do not capture issues related to scarring, disfigurement, and worry about recurrence or new lesions.[25] Compared with other dermatological QOL tools, the SCI captures issues specific to facial skin cancers such as scarring, disfigurement and concerns about possible recurrence [Table 2].[26]

Rhee *et al*. validated SCI in their study with 211 patients presenting with cervicofacial NMSC. In this study, they found that the emotional and appearance subscales had lower standardized scores and therefore, demonstrated greater negative effect on QoL with cervicofacial NMSC.[24]

Skin Cancer Quality of Life Impact Tool

Burdon *et al*. developed a questionnaire specifically for use in patients with either non-metastatic MM or nonmetastatic NMSC skin cancer, and named the SCQOLIT [Table 3]. In this study, in 100 patients with nonmetastatic skin cancer [50 with MM and 50 with NMSC] was included. The patients with NMSC, 45% were concerned about the possibility of scarring or disfigurement, particularly on the face.[27] The SCQOLIT consists ten questions. Each question asks to what extent the patient has been concerned about that particular theme, in the last week. Scoring for each question is: (3) Very much so; (2) Moderately so; (1) Somewhat; (0) Not at all. To obtain the total score the responses to all questions are summed, and a maximum total score of 30 is possible.[28] Also Burdon-Jones *et al*. performed SCQOLIT validation study.

Table 4: Functional assessment of cancer therapy-melanoma questionnaire[30]

Melanoma subscale	Not at all	A little bit	Some-what	Quite a bit	Very much
I have pain at my melanoma site or melanoma surgical site	0	1	2	3	4
I have noticed new changes in my skin (lumps, bumps, color)	0	1	2	3	4
I worry about the appearance of surgical scars	0	1	2	3	4
I have been shorth of breath	0	1	2	3	4
I have to limit my physical activity because of my condition	0	1	2	3	4
I have had headaches	0	1	2	3	4
I have had fevers	0	1	2	3	4
I have swelling or cramps in my stomach area	0	1	2	3	4
I have a good appetite	0	1	2	3	4
I have aches and pains in my bones	0	1	2	3	4
I have noticed blood in my stool	0	1	2	3	4
I have to limit my social activity because of my condition	0	1	2	3	4
I feel overwhelmed by my condition	0	1	2	3	4
I isolate myself from others because of my condition	0	1	2	3	4
I have difficulty thinking clearly (remembering, concentrating)	0	1	2	3	4
I feel fatigued	0	1	2	3	4
Melanoma Surgery Scale					
I have swelling at my melanoma site	0	1	2	3	4
I have swelling as a result of surgery	0	1	2	3	4
I am bothered by the amount of swelling	0	1	2	3	4
Movement of my swolling area is painful	0	1	2	3	4
Swelling keeps me from doing the things I want to do	0	1	2	3	4
Swelling keeps me from wearing the clothes or shoes that I want to wear	0	1	2	3	4
I feel numbness at my surgical site	0	1	2	3	4
I have good range of motion in my arm or leg	0	1	2	3	4

FACT-M: Functional assessment of cancer therapy-melanoma

Table 5: Quality of life studies

First of author	Years	Population	Number of patients	Measure of QOL	Time	Treatment modality	Mean age	Study type	Country	Localization	Results
Rhee *et al.*[46]	2003	NMSC	121	FACT-G, SF-36	Before surgery, 1 month after surgery, and 4 months after surgery	Surgery	63	Prospective	USA	Head and neck	Sun-protective behaviors were positively associated with certain QOL subscale scores. General QOL instruments demonstrated minimal impact of NMSC on patients at initial diagnosis. General measures may not be sensitive to the impact of nonmelanoma skin cancer
Rhee *et al.*[44]	2004	NMSC	121	DLQI	Before and after 4 months surgery	Surgery	63	Prospective	USA	Head and neck	General dermatology QOL instruments demonstrated minimal handicap at initial diagnosis and little change after treatment of NMSC
Newton-Bishop *et al.*[60]	2004	Melanoma	426	MOS-SF36	At 1 months, 3 months, 6 months, 1 year, and 2 years after surgery	Surgery	62.2	Prospective	UK	All	Patients with a 3 cm excision margin reported significantly poorer mental and physical functioning compared with those with a 1 cm excision margin. However, within 6 months, the difference in impact on health-related quality of life between the two groups was no longer significant, except for persisting concern about the scar in the 3 cm excision group
Dixon *et al.*[62]	2006	Melanoma	674	EORTC-QLQ-C30	At baseline, 3, 6, 12, 24, 36, 48 and 60 months for a subgroup of patients	Interferon alpha-2a		RCT	UK		As assessed by the EORTC QLQ-C30, statistically significant differences were found in terms of role functioning, emotional functioning, cognitive functioning, social functioning, and global health status. Symptom scores in the IFN group were significantly worse for fatigue, nausea/vomiting, dyspnoea, appetite loss, constipation and diarrhoea
Rhee *et al.*[24]	2006	NMSC	211	SCI		Surgery	63	Validation	USA	CF	SCI is a reliable and valid QOL instrument
Chren *et al.*[48]	2007	NMSC	633	Skindex-16	At baseline, 12, 18, and 24 months after treatment	Mohs, surgery and electrodessication and curettage	66.1	Prospective	USA	All	For NMSC, quality-of-life outcomes were similar after excision and Mohs surgery, and both therapies had better outcomes than ED and C. The skindex-16 scores of NMSC patients were relatively low in all treatment groups
Cormier *et al.*[30]	2008	Melanoma (Stage I-IV)	273	FACT-M	At months 3, 6, 12 and follow up visits		52	Validation	USA	All	The FACT-M questionnaire is a reliable and valid instrument for patients with melanoma that can be used for the assessment of QOL in clinical trials
Berganmar *et al.*[59]	2010	Melanoma	144	EORTC-QLQ-C30	Before randomization, and at 3, 9, and 15 months after inclusion	Surgery	60.4	Prospective	Sweden	Trunk or extremities	No difference was found in emotional distress or health-related QoL between patients randomized to narrow or wide excision

Contd...

Table 5: Contd...

First of author	Years	Population	Number of patients	Measure of QOL	Time	Treatment modality	Mean age	Study type	Country	Localization	Results
Waldmann *et al.*[52]	2011	Melanoma	450	EORTC-QLQ-C30	15 months and 39 months after postdiagnosis	Surgery	63 (male) 56 (women)	Prospective	Germany	All	Clinically relevant changes did not occur between postdiagnosis and 2 years after across all scales of the EORTC QLQ-C30 of patients with stable disease
Loquai *et al.*[61]	2011	Melanoma	30	EORTC-QLQ-C30	At baseline and every 3 months during treatment	PEG-IFN-a-2b	50.8	Retrospective	Germany	All	QOL documented by physicians was significantly higher than QOL from the patients' questionnaires in all QOL dimensions. PEG-IFN-α2b has measurable effects on QOL. Measuring QOL based only on physicians' patient files without explicitly determining patients' assessments leads to a profound underestimation of impairment of QOL
Revicki *et al.*[63]	2012	Melanoma (Stage I-IV)	676	EORTC-QLQ-C30	Baseline to week 12	Ipilimumab	56.2	RCT	USA		Ipilimumab at 3 mg/kg with and without gp 100 vaccine does not have a significant negative impact on HRQL in patients completing the baseline and week 12 follow-up, during the treatment induction phase compared with gp 100 alone
Caddick *et al.*[26]	2012	NMSC and melanoma	53	SCI	Before and after 3 months surgery	Surgery	70% patients aged 66 years above	Prospective	UK	Head and neck	Surgical excision improves social, emotional, and cosmetic well-being in patients with facial skin malignancies
Burdon-Jones and Gibbons[28]	2013	NMSC and Melanoma	120	SCQOLIT	At 7 days, and the other half at 3 months	Surgery	67 (MM), 73 (NMSC)	Validation	Australia		The SCQOLIT is a validated disease-specific QOL questionnaire for use in patients following treatment of nonmetastatic skin cancer. Higher SCQOLIT scores are observed in MM patients than NMSC patients, but diminish with time in the MM group
Vinding *et al.*[45]	2014	NMSC	101	SCQOLIT, DLQI	Before surgery, 3 months after	Surgery	69.4	Responsiveness	Denmark	All	No statistically significant difference was found for the total score testing responsiveness
Tromme *et al.*[58]	2014	Melanoma	395	EQ-5D-5L, VAS, FACT-M	1-24 months after	Surgery	52.6	Prospective	Belgium		The VAS and the FACT-M were found to be less sensitive. The EQ-5D-5L questionnaire seems adequate to provide utilities and DWs in patients with melanoma. Lower HRQoL in female patients with melanoma is probably linked to lower HRQoL in the general population

Contd...

Table 5: Contd...

First of author	Years	Population	Number of patients	Measure of QOL	Time	Treatment modality	Mean age	Study type	Country	Localization	Results
Hawkins *et al*.[8]	2015	NMSC and Melanoma	161	Skindex-16, SCI			44	Prospective	USA	All	There is a modest impact on quality of life in young patients with skin cancer based on the Skindex-16 and SCI. Young skin cancer survivors may benefit from patient counseling, which addresses risk assessment and future risk reduction
Jiang *et al*.[64]	2015	Melanoma	28	FACT-M	At baseline and 2, 6 weeks, and 3 months post-ILI	Isolated limb infusion	69.6	Prospective	USA	Extremities	Using a validated HRQOL measure, quality of life was not impacted by ILI for advanced extremity melanoma
de Troya-Martín *et al*.[50]	2016	NMSC	88	SCI	At time of diagnostic, 7 days after surgery, and 5 months after surgery	Surgery	62.5	Responsiveness	Spain , Australia, USA	CF	Their results confirm the ability of the Spanish version of the SCI to discriminate changes in the HRQL of patients with CFNMSC
Müller *et al*.[23]	2017	NMSC	172	EORTC-QLQ-C30	Beginning or prior to treatment		70	Validation	Germany	All	QLQ-C30 to be a suitable tool for the assessment of QL in patients with NMSC

MOS-SF36: Medical Outcomes Survey-Short Form 36, RCT: Randomize clinical trial, CF: Cervicofacial, FACT-G: Functional Assessment of cancer Therapy- General Version, SF-36: Short Form 36, QOL: Quality of life, NMSC: Nonmelanoma Skin Cancers, DLQI: Dermatology Life Quality Index, , EORTC-QLQ-C30: European Organization for Research and Treatment of Cancer Quality of Life Questionnaire, SCI: Skin Cancer Index, FACT-M: Functional Assessment of Cancer Therapy-Melanoma, HRQL: Health-Related Quality of Life, BCC: Basal cell carcinoma, SCQOLIT: Skin Cancer Quality of Life Impact Tool, MM: Melanoma, VAS: Visual Analogue Scale, CFNMSC: cervicofacial non melanoma skin cancer, IFN: interferon, PEG-IFN-α2b: pegile interferon-a2b

The SCQOLIT was constructed and administered initially to 120 patients with non-metastatic skin cancer, 60 with MM and 60 with (NMSC following treatment, then repeated at seven days, and at 3 months. They found higher SCQOLIT scores in MM patients than NMSC patients, but diminish with time in the MM group. The SCQOLIT is a validated disease-specific QOL questionnaire for use in patients following treatment of non-metastatic skin cancer.[28]

Functional Assessment of Cancer Therapy-Melanoma

The melanoma module for the FACT-G has been developed and validated by Cormier *et al*. as an independent tool and an add-on to the FACT-G; when the FACT-G and the melanoma module are administered together, they constitute the FACT-M. The MM-specific health QoL (FACT-M) was developed for clinical trial purposes involving 273 high risk patients with stages I–IV melanoma, including those with metastatic disease who have lower survival rates than most patients with melanoma in the general population and who receive additional surgical and / or systemic therapy. The FACT-M includes a melanoma module comprised of 24 total items [Table 4]. 24 items encompassing three HRQoL domains: physical, emotional, and social well-being. The melanoma module consists of 16 items related to melanoma and an additional 8 items pertaining to the surgical treatment of melanoma.[29] The FACT-M has been shown to be responsive and sensitive in patients with melanoma at all stages of disease.[30]

European Organization for Research and Treatment of Cancer Quality of Life Questionnaire-MEL38

Winstanley *et al*. developed EORTC QLQ-MEL38 that a new EORTC Melanoma Module in their study. In this study, fifty-six issues were rephrased as questions and piloted with 132 patients. EORTC-QLQ-MEL38 is a measure 38-item questionnaire. It comprises 33 scoring items, two single items and three items associated with clinical trials. Responses to 14 scoring items relate to patient experience "during the past 4 weeks" and the remaining 19 items relate to experience "during the past week."[31]

EORTC-QLQ-M a disease-spesifik QoL measure developed from EORTC-QLQ-30. Winstanley *et al*. tested the cross-cultural reliability and validity of the EORTC QLQ-M. They suggested that many of the important issues could be viewed as "generic"; however, a cross-cultural instrument does not presently exist to gather together all the relevant items that adequately represent a melanoma patients experience.[31]

The another melanoma module of the EORTC-QLQ-C30 is designed for patients only with advanced (stage IV) disease in 1994 by Sigurdardottiret al. This module consists of 13 items and evaluates disease-specific symptoms related to disease treatment and progression.[29,32]

Quality of Life in Nonmelanoma Skin Cancers

Although NMSCs are the most common cancers in humans, it has a low mortality rate (0.1%–0.3%), but its tendency to

affect the face and to recur in the same subject produces a high morbidity rate.[33]

The scarring sequelae secondary to surgery are often unsightly and are sometimes associated with functional disorders, such as ectropion, epiphora, corneal erosion, nasal obstruction, oral incompetence, microstomia, inability to use hearing aids or spectacles and facial paralysis.[4,34] If detected early, even high risk NMSCs can be successfully treated and serve as a wake-up call for behavioral change and enhanced HRQoL.[35] Worries about possible facial disfigurement and potential scarring are important patient-level concerns that may present barriers to early treatment.[36]

Less than 5% of all BCC cases become locally advanced or metastatic.[37] Locally advanced BCC occurs when BCC extends into subcutaneous and soft tissues or other critical structures, and surgery or radiation therapy may be undesirable or contraindicated. BCC that metastasizes to distant sites is rare, accounting for <1% of cases of BCC.[38] Patients with nonadvanced or locally advanced and metastatic BCC experience disease-related symptoms that affect their HRQoL, activities of daily living, emotional well-being, and social and/or leisure activities.[39] Steenrod *et al*. compared symptoms and impact of varying stages of basal cell carcinoma.[40] Similar to Mathias *et al*.,[39] Steenrod found that impacts on emotional well-being and daily activities were common and more frequently reported in patients with more advanced disease.[37,40]

Previously studies have shown a change of sun behavior towards more sunprotective behaviors especially among younger cohorts after surgery for NMSC.[41-44] However, it may be speculated that a reduction in the score of the domain function may be seen with time as people get more used to the behavior one had to adapt after being diagnosed with skin cancer – e.g., protection of skin, using a sunscreen etc., and this simply becomes a lifestyle.[45] Rhee *et al*. performed a cross-sectional study of 121 patients with NMSC of the head and neck using the Medical Outcomes Study Short Form 36-item Health Survey (SF-36) and the Functional Assessment of Cancer Therapy-General (FACT-G). They found sun-protective behaviors were positively associated with certain QOL subscale scores in the population in the study. General QOL instruments demonstrated minimal impact of NMSC on patients at initial diagnosis.[46] For the BCC/SCC population, general dermatology instruments (Skindex, DLQI) with or without generic (e.g., Short Form 36-item Health Survey, United Kingdome Sickness Impact Profile) or cancer-specific (e.g., Functional Assessment of Cancer Therapy-General) instruments have been used but generally show minimal effects on QoL.[35,46,47] Although the results of Finlay and Khan suggest that atopic eczema, pruritus, and psoriasis have a greater impact on HRQoL than BCC, the items were geared more toward these skin conditions rather than skin cancer.[13] As these instruments were not developed for the NMSC population, they may not be sensitive to capture relevant QoL issues.[1]

BCC can be treated with many modalities such as surgical excision, topical immunomodulations, Mohs micrographic surgery, photodynamic therapy, electrodessication and curettage (EDC), and X-ray therapy. Other treatment modalities such as laser, photodynamic therapy, and topical immunomodulators are non-surgical treatment options. In certain situations, nonsurgical treatments may offer some advantages in terms of reduction of scarring and better cosmetic results. Currently, surgical removal, remains the mainstay for the vast majority of patients with NMSC.[25] Chren researched a prospective cohort study of 633 patients with NMSC, evaluating QoL outcomes of EDC, surgical excision and Mohs micrographic surgery (MMS) at baseline, 12, 18 and 24 months. The Skindex-16 scores of NMSC patients were relatively low in all treatment groups.[48] On the contrary, Caddick *et al*. found that surgical excision improves social, emotional, and cosmetic well-being in patients with facial skin malignancies. This is likely to reflect reassurance experienced by the knowledge a lesion has been completely removed.[44]

Vinding *et al*. used SCQOLIT twice-before the operation and 3 months after surgery in 101 patients with NMSC. In their study no statistically significant difference was found for the total score testing responsiveness.[45] Reported outcomes are dependent on the time point of questionnaire completion, therefore differences in the postoperative time interval between NMSC surgery and questionnaire completion may cause disparities in reporting of outcomes.[45,49]

Age, gender, stage, local or metastatic disease and localization are the factors which affect the QOL in NMSCs. Rhee *et al*. demonstrated female sex was predictive of poorer QoL as a main effect for the SCI total score, SCI appearance subscale, and the DLQI. Female sex also predicted greater improvement in QoL over time for the SCI appearance subscale. They suggested that the SCI is a highly sensitive and clinically responsive measure of QoL changes for NMSC patients.[25] de Troya-Martín *et al*. investigated responsiveness of the Spanish Version of the SCI in 88 NMSC patients at time of diagnosis, 7 days after surgery, and 5 months after surgery. They found that HRQoL to be more severely affected among female patients and patients of both sexes aged under 65 years.[50]

Consequently, studies using dermatology-specific QoL and generic health QoL measures have shown only minimal impact of NMSC on patients.[5,51] In contrast, studies using open-ended questions for NMSC[27] have identified a number of significant QoL issues-especially emotional concerns.[5,51]

Quality of Life in Malignant Melanoma

Melanoma affects all age groups and parts of the body, and the treatment pathway varies considerably according to the stage of the disease.[31] Rising incidence rates of MM are of worldwide concern, in particular in the white population.[52]

For many people, there are significant emotional, social, and psychological consequences to having melanoma. A diagnosis

of melanoma may change many aspects of an individual's life from self-identity, self-esteem, body image, and perceived well-being, to family roles and relationships, lifestyle behaviors, sexuality, career opportunities, friendships, and finances. Patients often experience shock, fear, sadness, anger, and sometimes guilt at the time of diagnosis, and some will also have to face progressive illness and approaching death.[53]

In a recent systematic review of literature, studies showed that approximately 30% of all patients diagnosed with MM report levels of psychological distress indicative of the need for clinical intervention. This level of clinical distress is equivalent to that identified in patients with breast and colon cancer.[54-56]

About 80% of patients will survive MM, but will remain at risk of disease progression for many years.[57] MM, therefore, can be considered a chronic disease with a considerable impact on patients' HRQoL, defined by the WHO as "an individual's perception of their position in life in the context of the culture and value system in which they live and in relation to their goals, expectations, standards and concerns."[31]

Tromme *et al*. submitted three quesionnaires (EQ-5D-5 L, VAS and FACT-M) to 395 MM patients. They found that the relatively good HRQoL of patients with stage IV MM in remission, similar to patients with stage 0–II MM in remission.[58] Burdon-Jones *et al*. demonstrated that scores for the MM group (independent of Breslow thickness) were greater than the NMSC group, suggesting an awareness among MM patients of a having had a more potentially serious skin cancer. It is possible that a further reduction in SCQOLIT scores, to clinically significant levels, may be seen over time, as patients became more confident of a favorable outcome following successful treatment of their skin cancer, adapted their behavior to minimize excess sun exposure, and became better informed about skin cancer and recognizing it.[28]

Waldmann *et al*. performed (QoL) study in a total of 450 melanoma patients who filled out the EORTC QLQ-C30, 15 months post diagnosis and follow-up questionnaires two years after. They found that clinically relevant changes did not occur between post diagnosis and 2 years after across all scales of the EORTC QLQ-C30 of patients with stable disease. They suggested the EORTC QLQ-C30, a generic QoL instrument, is not sensitive enough to measure QoL-related issues that are specific to melanoma.[52]

Currently surgery remains the cornerstone of treatment for patients with cutaneous malignancies.[26] In the studies performed, skin-cancer-specific questionnaires were used to examine the effects of excision margin and pathological stage on QOL, in patients with MM. Bergenmar *et al*. investigated the effect of excision margin, a total of 144 patients, using the EORTC QLQ-C30 on QOL in cutaneous melanoma. They found no differences in emotional distress or health-related QoL between patients randomized to narrow or wide excision. Wider excision resulted in no increased emotional distress or reduced HRQoL up to15 months after the operation, despite larger scars that often included skin grafts.[59] In contrast, in a surgical randomized controlled trial of high-risk patients with melanoma, patients with a 3-cm excision margin reported significantly poorer mental and physical functioning compared with those with a 1-cm excision margin. However, within 6 months, the difference in impact on HRQoL between the two groups was no longer significant, except for persisting concern about the scar in the 3-cm excision group.[53,60]

Adjuvant interferon-alpha (IFN-a) is well established as adjuvant therapy in patients with thick primary MM and those with resected regional lymph node metastases. Loquai *et al* demonstrated that the PEG_IFN-a2b (Pegile interferon-alfa 2b) treatment adversely affected patients' QoL in most dimensions of the EORTC QLQ-C30. They found that the function domains were impaired consistently, while within the symptom domains fatigue and appetite loss were more affected than the others.[61] Also Dixon *et al*. randomised 674 MM patients to interferon alpha-2a (3 megaunits three times per week for 2 years or until recurrence) or placebo. As assessed by the EORTC QLQ-C30, statistically significant difference was found in terms of role functioning, emotional functioning, cognitive functioning and global health status.[62]

Revicki *et al*. investigated EORT-QLQ-C30 in 676 previously treated advanced unresectable stage III or IV MM patients. They randomized patients in this trial 3:1:1 to receive either ipilimumab (3 mg/kg q3w x 4 doses) + gp100 (peptide vaccine; 1 mg q3w x 4 doses; ipilimumab plus gpl00); gp100 vaccine + placebo (gp100 alone); or ipilimumab+ placebo (ipilimumab alone). They suggested that ipilimumab at 3 mg/kg with and without gp100 vaccine does not have a significant negative impact on HRQoL in patients completing the baseline and week 12 follow-up, during the treatment induction phase compared with gp100 alone.[63]

Jiang *et al*. investigated quality of life using FACT-M in 28 advanced extremity MM patients treated with ILI (isolated limb infusion). They found using a validated HRQOL measure, quality of life was not impacted by ILI for advanced extremity MM.[64] Quality of life studies in NMSC and MM have been shown in Table 5.

Conclusion

Skin malignancies are the most common cancers in humans. Patient-reported outcomes are increasingly being used to capture patients' perception of a disease, its treatment and impact on daily living.

The DLQI is general dermatology measure and further evaluations suggest that the items do not reflect what is important to patients with skin cancer. The Skindex provides more promising properties for patients with NMSCs but most evaluations have included a general dermatological population of patients with small subsamples of patients with NMSCs. The Skindex and DLQI may not be sensitive enough to capture relevant outcomes specific to skin cancer. The SCQOLIT is

applicable to both NMSC and MM, but is not specific to NMSC, nor does it elicit detailed cosmetic concerns. The SCI has been specifically formulated and validated in patients with NMSC and it demonstrates the most usefulness in patients with NMSC.

It is often difficult to capture disease-specific issues even with the administration of a combination of instruments. For example, in patients with melanoma, issues such as lymphedema and post-surgical scarring would not likely be assessed with most available QOL instruments. The FACT-M was developed to address melanoma-specific issues related to QOL for patients with all stages of melanoma. The FACT-M has more promising characteristics for patients with MMs, especially those with advanced disease and the EORTC-M may also be an attractive option. Consequently, the use of disease-specific scales is likely to be more effective in understanding the effect of the disease on the QOL of the patient. Skin cancer specific measures should be preferred over general dermatology scales in evaluating the QOL in skin cancer patients.

Future studies will lead to the development of more specific questionnaires for melanoma and NMSCs. In this way the impact of skin cancers on the QOL will be better understood and the surgical, topical or systemic treatment effect on QOL of skin cancer patients will compare more easy. Furthermore, we performed cultural adaptation, validation, and reliability study of the SCI which was developed for evaluation of non-metastatic NMSC. We hope to publish the results of this study soon.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

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