# Effect of Patient Characteristics on Treatment Decisions Regarding Keratinocyte Carcinoma in Elderly Patients: A Review of the Current Literature

Marjolijn S. HAISMA<sup>1</sup>, Linda BRAS<sup>2</sup>, Mehran Alizadeh AGHDAM<sup>2</sup>, Jorrit B. TERRA<sup>1</sup>, Boudewijn E. C. PLAAT<sup>2</sup>, Emöke RÁCZ<sup>1</sup> and Gyorgy B. HALMOS<sup>2</sup> Departments of <sup>1</sup>Dermatology, and <sup>2</sup>Otorhinolaryngology – Head and Neck Surgery, University of Groningen, University Medical Center

Departments of 'Dermatology, and 'Otorhinolaryngology – Head and Neck Surgery, University of Groningen, University Medical Center Groningen (UMCG), Groningen, The Netherlands

There are straightforward guidelines for treatment of keratinocyte carcinoma (formerly known as non-melanoma skin cancer); however, there are no clear recommendations specifically for elderly patients. The aim of this review was to provide an overview of the current literature about the effect of patient characteristics, specifically life expectancy, frailty and comorbidity, on treatment decisions in elderly patients with keratinocyte carcinoma, by searching PubMed database. It was found that the literature is limited and based mostly on small retrospective studies. Therefore, it is difficult to give firm recommendations about how to treat elderly people who have keratinocyte carcinoma. A "one-sizefits-all" approach to this population is not sufficient: life expectancy and frailty need to be considered in the decision-making process regarding treatment for elderly people with keratinocyte carcinoma. Among the comorbidity scores, Adult-Comorbidity-Evaluation-27-index seems to have the best prognostic value. Prospective studies are needed to generate more individualized recommendations for this increasing and often vulnerable group.

*Key words:* keratinocyte carcinoma; elderly people; treatment; patient characteristics.

Accepted May 26, 2020; Epub ahead of print Jun 3, 2020

Acta Derm Venereol 2020; 100: adv00189.

*Corr:* Marjolijn S. Haisma, Department of Dermatology, University Medical Center Groningen, Hanzeplein 1, NL-9700 RB Groningen, The Netherlands. E-mail: m.s.haisma@umcg.nl

Uv radiation cumulatively damages the skin, and therefore non-melanoma skin cancer, currently termed "keratinocyte carcinoma" (KC), affects a significant number of patients with advanced age (1). In the Netherlands, for example, approximately half of the patients with basal cell carcinoma (BCC) were 70 years old or older and almost 3/4 of patients with squamous cell carcinoma (SCC) were 70 years or above (2). Confirming the theory of cumulative damage to the skin by UV radiation, KC occurs mostly in the sun-exposed head and neck region (2). This fact, together with the substantial increase in the elderly population, results in an excessive

### SIGNIFICANCE

This study collected data about the effect of patient characteristics (life expectancy, frailty and comorbidity) on treatment decisions in elderly people with keratinocyte carcinoma, by searching PubMed database. Literature about how patient characteristics affect treatment decision is sparse and is mostly based on small retrospective studies. Therefore, it is difficult to give firm recommendations. A "one-size-fits-all" approach to this population is not sufficient: life expectancy, frailty and comorbidities must be taken into account in the decision-making about treatment, and registered using a validated scoring system, especially before major treatment modalities.

number of elderly patients with KC, especially in the head and neck area (KCHN).

There are straightforward clinical guidelines for the treatment of both BCC and SCC, and in some cases individualized treatment can be applied, as alternatives are given in case the first choice treatment is not applicable (3, 4). However, no clear recommendations are given for the increasing population of elderly people, who may benefit from a different approach than their younger counterparts.

The aim of the present review is to provide clinical recommendations on how to assess the most relevant patients' characteristics, specifically in elderly patients with KC, after reviewing the literature on life expectancy, frailty and comorbidity. The effect of age on treatment outcomes and alternative treatment schedules for elderly patients are discussed in another review article (5).

# **METHODS**

A literature search was performed using PubMed database in March 2020. The following issues were systematically reviewed from the literature: life expectancy; frailty; and comorbidity.

A search term was created for each individual topic, as described in **Table I**. Full-text English manuscripts about KC and patient characteristics, especially in elderly people, were eligible for inclusion and have been retrieved, reviewed and checked for references by at least 2 authors.

#### Table I. Literature search method performed in PubMed

Торіс	Last search date	Search term	Results
Life expectancy	8 March 2020	("Skin Neoplasms"[Mesh] OR skin cancer*[tiab] OR keratinocyte carcinoma*[tiab]) AND ("Carcinoma, Basal Cell"[Mesh] OR "Carcinoma, Squamous Cell"[Mesh] OR nonmelanoma*[tiab] OR non-melanoma*[tiab] OR basal cell carcinoma*[tiab] OR squamous cell carcinoma*[tiab] OR keratinocyte carcinoma*[tiab] OR Planocellular Carcinoma*[tiab]) AND ("Aged"[Mesh] OR elder*[tiab] OR older patient*[tiab] OR older person*[tiab] OR older people[tiab] OR older adult*[tiab] OR older cancer patient*[tiab] OR old patient*[tiab] OR old person*[tiab] OR old people[tiab] OR geriatr*[tiab] OR old age*[tiab] OR octagenarian*[tiab] OR onagenarian*[tiab]) AND ("Life Expectancy"[Mesh] OR "Quality-Adjusted Life Years"[Mesh] OR (life[tiab] AND expecta*[tiab]) OR life year*[tiab] OR qaly[tiab] OR life table*[tiab] OR LLE[tiab])	This search identified 53 articles, and after cross-referencing, a total of 6 articles were found relevant (Table II)
Frailty	8 March 2020	("Skin Neoplasms"[Mesh] OR skin cancer*[tiab] OR cutaneous head and neck malignancies*[tiab] OR keratinocyte carcinoma*[tiab]) AND ("Carcinoma, Basal Cell"[Mesh] OR "Carcinoma, Squamous Cell"[Mesh] OR nonmelanoma*[tiab] OR non-melanoma*[tiab] OR basal cell carcinoma*[tiab] OR squamous cell carcinoma*[tiab] OR keratinocyte carcinoma*[tiab] OR cutaneous head and neck malignancies*[tiab] OR head and neck cancer*[tiab] OR planocellular Carcinoma*[tiab]) AND ("Aged"[Mesh] OR elder*[tiab] OR older patient*[tiab] OR older person*[tiab] OR older people[tiab] OR older adult*[tiab] OR older cancer patient*[tiab] OR old patient*[tiab] OR old person*[tiab] OR older patient*[tiab] OR old age*[tiab] OR octagenarian*[tiab] OR nonagenarian*[tiab]) AND ("Frailty"[Mesh] OR "Frail Elderly"[Mesh] OR "Geriatric-8[stiab] OR g8[tiab] OR g-8[tiab]) OR vulnerab*[tiab] OR geriatric assessment*[tiab] OR geriatric-8[tiab] OR g8[tiab] OR g-8[tiab])	This search resulted in 37 hits and 3 relevant studies (Table III)
Comorbidity	8 March 2020	("Skin Neoplasms"[Mesh] OR skin cancer*[tiab] OR keratinocyte carcinoma*[tiab]) AND ("Carcinoma, Basal Cell"[Mesh] OR "Carcinoma, Squamous Cell"[Mesh] OR nonmelanoma*[tiab] OR non-melanoma*[tiab] OR basal cell carcinoma*[tiab] OR squamous cell carcinoma*[tiab] OR keratinocyte carcinoma*[tiab] OR Planocellular Carcinoma*[tiab]) AND ("Aged"[Mesh] OR elder*[tiab] OR older patient*[tiab] OR older person*[tiab] OR older people[tiab] OR older adult*[tiab] OR older cancer patient*[tiab] OR old patient*[tiab] OR old person*[tiab] OR old people[tiab] OR older cancer patient*[tiab] OR old patient*[tiab] OR old person*[tiab] OR old people[tiab] OR on onagenarian*[tiab] OR old age*[tiab] OR octagenarian*[tiab] OR nonagenarian*[tiab]) AND ("Comorbidity"[Mesh] OR comorbid*[tiab] OR co-morbid*[tiab] OR co-exist*[tiab] OR multi- morbid*[tiab])	This search identified 208 articles. After cross-referencing, a total of 11 relevant articles were included (Table IV)

# RESULTS

# Life expectancy

This section reviews literature regarding all relevant articles about the influence of limited life expectancy (LLE) on treatment decisions in elderly people with KC (the results are summarized in **Table II**).

The most obvious difference between young and elderly patients with KC is their life expectancy. KC, especially BCC, but also SCC in early stage, is in most cases not life-threatening; therefore, a wait-and-see policy can be considered in vulnerable elderly patients with a short life expectancy. Esserman et al. (6) proposed the term "indolent lesion of epithelial origin" (IDLE), drawing attention to the danger of the overdiagnosis and overtreatment of cancer. KC is one of the targeted IDLEs, a candidate for change in terminology and to bring wait-and-see policy to the foreground, instead of surgery. These suggestions harmonize with the large prospective study by Linos et al. (7). Based on more than 1,500 cases of KC, this study showed that choice of surgery was not influenced by the patients' prognosis, even after adjusting for tumour and patient characteristics. They suggest that clinicians consider less invasive treatment in patients with KC and LLE because of the low recurrence rates and high mortality rates unrelated to KC. On the other hand, these tumours can cause longerterm significant morbidity, such as pain and cosmetic or functional impairment, when left untreated, which may necessitate (major) treatment in a more advanced stage. In some cases, it is extremely difficult to make a proper prediction as to whether these patients live long enough to benefit from the treatment. This dilemma is often referred to as "time to benefit".

www.medicaljournals.se/acta

Another more recent study by Linos et al. (8), which included 9,653 KC in patients aged  $\geq$ 65 years, showed that type of treatment was not influenced by the patient's life expectancy.

As emphasized in the review of Lubeek et al. (9), not only medical aspects, but also personal preferences of the patient and their family should be involved in the decision-making process, weighing potential benefits and risks of treatment in patients with a LLE. However, the definition of LLE is not straightforward and data on the prediction of life expectancy in KC patients based on comorbidity is inconsistent.

Charles et al. (10) found, in a retrospective study on nonagenarians undergoing Mohs micrographic surgery (MMS) for KC, that patients without comorbidities (measured by the Charlson Comorbidity Index; CCI) survived longer. On the contrary, another study which included patients of 90 years and older, did not find any association between CCI and survival and confirmed a substantial survival time of these patients without morbidity or mortality after surgery (11). Subsequently, a prospective study in patients with KC who were 80 years and older, found CCI to be a predictor of increased overall mortality (12). According to a recent study, the comorbidity indexes Adult Comorbidity Evaluation-27 (ACE-27) and age-adjusted CCI can predict LLE in the very elderly ( $\geq$ 85 years) (13). The different outcomes of these studies can be explained by the differences in the inclusion criteria (i.e. age, type of surgery), as highlighted by the study of MacFarlane & Goldberg (14).

Based on the above-mentioned studies, we can conclude that type of treatment does not seem to be influenced by LLE; however, it should be involved in the decision-making process.

'nΛ
-
<u>ම</u>
0
H
Þ
-
9
56
οIJ
an
õ
입 0
ğ
ğ
tolog
atolog
atolog
atolog
matolog
matolog
rmatolog
matolog
lermatolog
lermatolog
lermatolog
lermatolog
i dermatolog
n dermatolog
i dermatolog
es in dermatolog
n dermatolog
es in dermatolog
es in dermatolog
inces in dermatolog
inces in dermatolog
inces in dermatolog
es in dermatolog
vances in dermatolog
vances in dermatolog

L	
	σ
	cta
	9
<	1

Study	Type	Participants/age	и	Treatment	Outcome	Limitations
Linos et al. (7) 2013	Prospective cohort study	Patients with KC, median age 69.0 years (IQR, 55.0–78.0 years)	1,360 patients with 1,739 KC	No treatment, destruction 2 types of surgery; - Elliptical excision - MMS	<ul> <li>Most patients were treated surgically</li> <li>Choice of surgery was not influenced by the patients'</li> <li>Descriptional design if expectancy</li> <li>A significant part of patients</li> <li>Higher incidences of complications were observed in the LLE lived longer than 5 years down of patients with LLE</li> </ul>	<ul> <li>Observational design patient preference was not measured</li> <li>A significant part of patients with an estimated LLE lived longer than 5 years</li> </ul>
Linos et al. (8) 2016	Cross-sectional study	Patients with KC, aged ≥65 years, mean age 79 years	2,702 patients, 9653 KC	MMS, simple excision or electrodessication and curettage	<ul> <li>Most tumours were treated surgically</li> <li>Type of treatment was not different between patients with normal life expectancy and LLE</li> </ul>	<ul> <li>KC treated with topical therapies, radiotherapy and untreated KC were not included</li> <li>Information about patient preferences was not available</li> </ul>
Charles et al. (10) 2002	Retrospective study	Nonagenarians (90-99 years) 99 patients with KC	99 patients	SMM	<ul> <li>Patients no comorbidities had a longer survival than The variability in survival among patients within a patients with multiple commonly (measured with CCI). patients CI was broad. Therefore, predictions - Women survived longer than men.</li> <li>Women survived longer than men.</li> <li>No patient died within 30 days after surgery.</li> </ul>	The variability in survival among patients within a particular CCI was broad. Therefore, predictions of life expectancy for individual patients are not very reliable.
Delaney et al. (11) 2013	Retrospective study	Patients with KC aged ≥90 years, mean age 92.3 years	214 patients	SMM	<ul> <li>No significant difference in survival in patients with different CCI scores.</li> <li>Defect size, tumour characteristics, number of surgical stages and closure type did not affect survival rates.</li> </ul>	Data about follow-up and causes of death were not available.
Pascual et al. (12) 2013	Prospective study	Patients with KC aged ≥80 years	130 patients	Surgery	Age, comorbidity (measured by the CCI), closure with a graft and the Barthel Index* before surgery were associated with increased mortality	An univariate analysis was performed, no multivariate analyses were performed
Rogers et al. (13) 2018	Retrospective study	Patients with KC aged ≥85 years, mean age 88.1 years	488 patients	MMS vs no MMS	<ul> <li>ACE-27 and ACCI scores can predict LLE</li> <li>Higher comorbidity scores were associated with decreased survival</li> </ul>	Retrospective study design

Therefore, we recommend assessing life expectancy in elderly people, especially before major treatment is performed. Predicting life expectancy is complex; however, comorbidity (measured by ACE-27 or age-adjusted CCI) is an important factor in the very elderly and should therefore be considered. In case of LLE, minimal invasive treatment can be recommended. Nevertheless, the personal preferences of the patient and their family should always be considered in the decision-making process.

# Frailty

This section reviews literature regarding all relevant articles about the influence of frailty on treatment decisions in elderly with KC (results summarized in Table III).

In recent decades, the concept of "frailty" has been widely investigated, reflecting a major impact on the physical state of a vulnerable patient by a minor stressor (15). A comprehensive geriatric assessment (CGA) is the current gold standard in detecting frailty by thoroughly screening for possible impairments in multiple domains of life in elderly patients. Functional, nutritional, cognitive and psychological state, social support and physical performance needs to be analysed (16). A CGA is time consuming and therefore not commonly used in clinical practice, especially for patients with KC. Several shorter screening instruments have been developed and tested in various patient cohorts, but their predictive value seems disappointing (17, 18).

The study by Bras et al. (19) primarily analysed the relation between frailty (measured by the Groningen Frailty Indicator, GFI) and postoperative complications, including, beside skin malignancies, also mucosal and salivary gland malignancies of the head and neck. No separate analysis was performed on patients with skin cancer. The total GFI score was not predictive for complications; however, its dimension "health problems" was related to complications. Other predictors of complications were advanced tumour stage and prolonged surgery. The study also analysed the subjective experiences of the recovery by the patients and the surgeons. Interestingly, frail patients experienced more often difficult recovery, but the surgeon often underestimated this. Based on this study, it is not possible to evaluate the role of frailty screening in elderly patients with KC.

A recent study by De Vries et al. (20) prospectively analysed the value of geriatric assessment for predicting postoperative complications in patients undergoing surgery for cutaneous head and neck malignancies. This study identified the Geriatric 8 (G8) frailty screener as the strongest independent predictor of postoperative complications. However, almost three-quarter of the patients were scored as frail according to this test, questioning the value of this frailty screener in daily practice.

In another recent study of patients diagnosed with KC undergoing excision and reconstructive surgery, frailty was scored using the FRAIL scale, which includes 5

#### Table III. Overview of literature on frailty

Study	Туре	Participants/age	n	Treatment	Frailty tool	Outcome	Limitations
Bras et al. (19) 2015	Retrospective study	Patients aged ≥65 years with head and neck cancer	90	Surgery	GFI	<ul> <li>Frailty did not predict postoperative complications</li> <li>The GFI section 'health problems' was a significant predictor for postoperative complications</li> <li>Frail patients experienced more often difficult postoperative recovery</li> </ul>	- Both mucosal and cutaneous head and neck cancer were included - Retrospective character, with no information about the decision-making of both the patient and surgeon
De Vries et al. (20) 2019	Prospective study	Patients with cutaneous head and neck malignancies Mean age 78.9 years	151	Surgery	G8, GFI	<ul> <li>Frailty measured by the G8 was the strongest predictor of postoperative complications</li> <li>The GFI had no significant influence on postoperative complications</li> </ul>	Study performed in a tertiary care hospital, which included a high amount of complex patients and tumours
Valdatta et al. (21) 2019	Retrospective study	Patients with massive KC, aged ≥65 years, mean age 81 years	587	Plastic/ reconstructive surgery	FRAIL scale	<ul> <li>The FRAIL scale was predictive of mortality or surgical complications</li> <li>FRAIL scores 4 and 5 were the best predictors of mortality or moderate/ severe complications</li> <li>FRAIL score 5 was the best predictor of mortality or severe complications</li> </ul>	Overall deaths of the old study population may confound deaths specifically related to surgery

GFI: Groningen Frailty Index; G8: Geriatric 8.

items: fatigue, resistance, ambulation, illnesses and loss of weight. In this study, FRAIL was a significant predictor of surgical complications and mortality. Using different cut-off values for complication grade, FRAIL scores were associated with adverse surgical outcomes (21).

From our literature search, it can be concluded that frailty is under-reported in studies on KC and in current clinical guidelines.

The lack of literature and limited integration of frailtyrelated items in current guidelines is also emphasized in 2 reviews about skin cancer in elderly people, stating that frailty is under-reported in studies on skin cancer (22) and in clinical practice guidelines (23). The integration of frailty-related items into clinical practice guidelines may stimulate a more personalized approach (tailored treatment) of the frail older patients with KC (23, 24).

Frailty tests seem to have a clinical value in predicting postoperative complications and mortality; however, data is conflicting and depending on the applied screening tool. G8 and "FRAIL scale" seems to have such a predictive value.

Therefore, assessment of frailty in elderly people is recommended before major treatment, and this may help in the prediction of treatment outcome. Furthermore, it may also play a role in the pretreatment optimization (prehabilitation) of patients; however, there is no data on this issue in dermato-oncology. More prospective studies are needed to evaluate the role of different frailty screeners and CGA items in dermato-oncology patients.

### Comorbidity

This section presents literature regarding all relevant articles about the influence of comorbidity on treatment decisions in elderly patients with KC, among which a systematic review about comorbidity indices used in patients with KC (25) (results summarized in Table IV).

It is known that both the number and severity of comorbidities are increasing with age. This finding has

already been verified in patients with KC (26). Inflammatory bowel disease (IBD), rheumatoid arthritis (RA), extra-cutaneous malignancies, solid organ transplantation, alcohol consumption and various skin disorders were significantly more often observed in patients with BCC compared with patients without BCC. Smoking and obesity do not seem to be risk factors for BCC (27). Furthermore, older people ( $\geq 60$  years) with diabetes mellitus (DM) had increased incidence rates of KC compared with patients without DM (28).

The systematic review by Connolly et al. (25) aimed to identify comorbidity instruments used in the KC population and prefers comorbidity instead of age in treatment decision-making. The most commonly used comorbidity score is the CCI, followed by ACE-27 and American Society of Anesthesiologists risk classification system (ASA score). This review concludes that there are only small and heterogeneous studies available. ACE-27 seems to be superior to the other scoring systems, as it analyses the most conditions and at the same time allows for comorbidity grading. However, larger studies are needed to judge its real value.

There is a correlation between comorbidity and postoperative complications; however, it is not obvious whether comorbidity scores could be used as predictive instruments to forecast treatment-related adverse events. One of these studies, by Chossat et al. (29), investigated the morbidity and mortality associated with (plastic) surgical treatment of BCC in patients aged >75 years. They found, among others, that patients with one or more comorbidity, long-term use of anticoagulant treatment and age >85 years were more likely to have major complications after surgery. In another, previously discussed, study, comorbidity score (CCI) was used as one of the factors that defined LLE and higher incidences of complications were observed in the group of patients with LLE (7). In a prospective study including 633 patients treated for KC, comorbidity (measured by CCI) was found to be a predictor for post-treatment quality of life

Study	Туре	Participants/age	и	Treatment	Comorbidity score system	Outcome	Limitations
Connoly et Systerr al. (25) 2017 review	Systematic review	Patients with KC	22 studies	n/a	CCI, ASA, ACE-27	<ul> <li>The most commonly used comorbidity score was the CCI, followed by the ACE-27 and the ASA score</li> <li>The ACE-27 seems to be superior to the other scoring systems, as it analyses the most conditions and allows for comorbidity grading</li> </ul>	The included studies were small and heterogeneous
Dhiwakar et al. (26) 2007	Retrospective study	Patients with KC of the head and neck ≥80 years	152 patients (208 NMSC) Compared to 311 patients (430 NMSC) aged <80 vears	Surgery	CCI, ASA	<ul> <li>CCI and ASA scores were higher in elderly patients</li> <li>Lesion size at presentation was larger in elderly people (required also larger defect)</li> <li>Disease-free survival and wound complication rate were comparable in the younger and elderly patients</li> </ul>	<ul> <li>Non-surgical options were not included</li> <li>Retrospective character</li> </ul>
Reinau et al. (27) 2014	Retrospective case control study	Patients with BCC, mean age 69.5 years		n/a	п/а	Inflammatory bowel disease, mheumatoid arthirtits, extra- cutaneous malignancies, solid organ transplantation, alcohol consumption and various skin disorders were significantly more often observed in patients with BCC compared with controls	n/a
Tseng et al. (28) 2016	Retrospective cohort study	Patients with DM, compared with non-DM mean age 57.41 years	41,898 patients with DM and non-DM	n/a	DM and non-DM	<ul> <li>The risk of developing skin cancer was significantly higher in older patients with DM, compared with non-DM.</li> <li>Males and having chronic obstructive pulmonary disease were also significant risk factors for KC in older adults with DM</li> </ul>	Several information facts were not available, such as body mass index, details of smoking, alcohol consumption, exposure to ultraviolet etc.
Chossat et Retro al. (29) 2018 study	Retrospective study	Patients with BCC >75 years mean age 81.75 years	158 patients	Surgically (reconstructive and cosmetic plastic surgery)	n/a	Statistical significant risk factors for major postoperative complications were: After the second of	The retrospective character of the study
Chen et al. (30) 2007	Prospective cohort study	Patients with KC	633 patients	ED&C, excision, or MMS	CCI	Less comorbidity (measured by CCI) and better mental health predicted better QOL outcomes	Only patients who responded to the pretreatment questionnaire were included
Basu et al. (31) 2019 ::	Retrospective study	Patients with KC	927 biopsied KC	No treatment, Cryotherapy, ED&C MMS, excision, topical therapy	n/a	<ul> <li>Patients with 24 comorbidities and elderly patients (285 years) had significant higher chances of no treatment</li> <li>No treatment was most likely in patients with impairment in activities of daily living, neurocognitive impairment and hemiplegia</li> </ul>	<ul> <li>The single centre retrospective design</li> <li>Exclusion of non-biopsied cancers</li> <li>Potential selection bias; i.e.</li> <li>ninfluences by distance from the hospital and insurance status</li> </ul>
Bouhassira et al. (32) 2016	Retrospective study	Patients aged >75 years 241 patients with BCC, SCC and melanoma, mean age 84.7 years	241 patients	Surgery	n/a	<ul> <li>Complication rate was 20%</li> <li>No relation between the number of comorbidities and complication was found</li> <li>Anale gender, histological type (SCC, melanoma) and positive surgical margins were independent predictors for complication after surgery</li> </ul>	Lack of statistical power of the study
Arguello- Guerra et al. : (33) 2018	Retrospective study	Patients undergoing surgery for skin cancer	655 patients	Surgery	n/a	<ul> <li>Complication rate was 4.2%</li> <li>Dermatological surgery was found to be safe in patients with multiple comorbidities, without discontinuing antithrombotic therapy or antibiotic prophylaxis</li> </ul>	<ul> <li>The retrospective single centre study design</li> <li>The number of cigarettes consumption before surgery and the size of tumour and surgical defect were not available</li> </ul>
Lubeek et al.   (34) 2017	Retrospective study	Patients with KC, median age 71 years	401 patients	Conventional excision, PDT, imiquimod, MMS, radiotherapy, other	CCI	Guideline-adherence/management was not influenced by comorbidity or high age	The single centre retrospective design; population and management differences can occur between different hospitals and countries, non-reporting bias might occurred
Linos et al. (8) 2016	Cross-sectional study	Patients with KC, aged ≥65 years, mean age 79 years	2,702 patients, 9653 KC	MMS, simple excision or CCI electrodessication and curettage	CCI	Comorbidity status, advanced age, functional status and life expectancy did not influence the choice of treatment	<ul> <li>KC treated with topical therapies, radiotherapy and untreated KC were not included</li> <li>Information about patient</li> <li>Dreferences was not available</li> </ul>

ActaDV

ActaDV Acta Dermato-Venereologica

Advances in dermatology and venereology

(QoL) (measured by Skindex 16). However, tumour factors and age were not prognostic for QoL change (30). Harmonizing with these findings, a recent retrospective study including 927 KC found that patients having  $\geq$ 4 comorbidities were significantly more likely to receive no treatment (31).

In contrast, several other studies found that the complication rate after treatment of KC was not different between young and elderly patients with more comorbidities, suggesting that (surgical) treatment is safe in this group, despite the higher comorbidity rate in elderly patients (26, 32, 33).

A different question is whether advanced age or multicomorbidity influence treatment decision. Lubeek et al. (34) found that comorbidity (measured by CCI) and high age ( $\geq$ 80 years) did not have a significant influence on guideline-adherence in both BCC and SCC. Similarly, the study by Linos et al. (8) confirmed that comorbidity status (measured by CCI), together with advanced age, functional status and life expectancy did not influence the choice of treatment in patients with KC. In this study, for example, no significant difference was found in the treatment rate of MMS between patients who died within one year after treatment and patients who lived longer (15% vs 17%, respectively).

In conclusion, CCI is the most commonly used comorbidity score in elderly patients with KC; however, ACE-27 seems to be superior, based on a systematic literature search. Studies are contradictory regarding the influence of comorbidities on complication rate and treatment decision.

We recommend registering comorbidities according to one of the validated comorbidity scores, especially before major treatment. More and larger prospective studies are needed to evaluate the prognostic value of different comorbidity scores.

#### Conclusion

The "one-size-fits-all" approach to the elderly patients with KC is not sufficient; beside tumour characteristics, life expectancy, frailty and comorbidities have to be considered. Therefore, it s recommended that these items are registered before treatment according to one of the validated scoring systems, especially before major treatment modalities.

As seen in the present review, literature data is sparse; therefore, prospective studies including elderly patients with KC are needed to draw firmer clinical recommendations and to reach a consensus, in order to avoid improper treatment of this increasing and potentially vulnerable patient group.

#### REFERENCES

1. Xiang F, Lucas R, Hales S, Neale R. Incidence of nonmelanoma skin cancer in relation to ambient UV radiation in white populations, 1978–2012: empirical relationships. JAMA Dermatol 2014; 150: 1063–1071.

- Louwman W, Lemmens V, van Akkooi A. In :Lemmers V, Siesling S. (editors) Attention for cancercare: the elderly patient. IKNL 2016: 21–31.
- Kim JYS, Kozlow JH, Mittal B, Moyer J, Olenecki T, Rodgers P. Guidelines of care for the management of cutaneous squamous cell carcinoma. J Am Acad Dermatol 2018; 78: 560–578.
- Kim JYS, Kozlow JH, Mittal B, Moyer J, Olencki T, Rodgers P. Guidelines of care for the management of basal cell carcinoma. J Am Acad Dermatol 2018; 78: 540–559.
- Leus AJG, Frie M, Haisma MS, Terra JB, Plaat BEC, Steenbakkers RJHM, et al. Treatment of keratinocyte carcinoma in elderly patients – a review of the current literature. J Eur Acad Dermatol Venereol 2020; [Epub ahead of print].
- Esserman LJ, Thompson IM, Reid B, Nelson P, Ransohoff DF, Welch HG, et al. Addressing overdiagnosis and overtreatment in cancer: a prescription for change. Lancet Oncol 2014; 15: 234–242.
- Linos E, Parvataneni R, Stuart SE, Boscardin WJ, Landefeld CS, Chren MM. Treatment of nonfatal conditions at the end of life: nonmelanoma skin cancer. JAMA Intern Med 2013; 173: 1006–1012.
- Linos E, Chren MM, Stijacic Cenzer I, Covinsky KE. Skin Cancer in US. Elderly adults: does life expectancy play a role in treatment decisions? J Am Geriatr Soc 2016; 64: 1610–1615.
- Lubeek SF, van Vugt LJ, Aben KK, van de Kerkhof PC, Gerritsen MP. The epidemiology and clinicopathological features of basal cell carcinoma in patients 80 years and older: a systematic review. JAMA Dermatol 2017; 153: 71–78.
- Charles AJ, Jr, Otley CC, Pond GR. Prognostic factors for life expectancy in nonagenarians with nonmelanoma skin cancer: implications for selecting surgical candidates. J Am Acad Dermatol 2002; 47: 419–422.
- Delaney A, Shimizu I, Goldberg LH, MacFarlane DF. Life expectancy after Mohs micrographic surgery in patients aged 90 years and older. J Am Acad Dermatol 2013; 68: 296–300.
- Pascual JC, Belinchon I, Ramos JM. Mortality after dermatologic surgery for nonmelanoma skin cancer in patients aged 80 years and older. J Am Acad Dermatol 2013; 69: 1051–1052.
- Rogers EM, Connolly KL, Nehal KS, Dusza SW, Rossi AM, Lee E. Comorbidity scores associated with limited life expectancy in the very elderly with nonmelanoma skin cancer. J Am Acad Dermatol 2018; 78: 1119–1124.
- MacFarlane DF, Goldberg LH. Life expectancy after Mohs micrographic surgery in patients aged 80 years and older. J Am Acad Dermatol 2013; 69: 1052–1053.
- Hamaker ME, Jonker JM, de Rooij SE, Vos AG, Smorenburg CH, van Munster BC. Frailty screening methods for predicting outcome of a comprehensive geriatric assessment in elderly patients with cancer: a systematic review. Lancet Oncol 2012; 13: 437–444.
- Extermann M, Hurria A. Comprehensive geriatric assessment for older patients with cancer. J Clin Oncol 2007; 25: 1824–1831.
- Bongue B, Buisson A, Dupre C, Beland F, Gonthier R, Crawford-Achour E. Predictive performance of four frailty screening tools in community-dwelling elderly. BMC Geriatr 2017; 17: 262.
- Smets IHGJ, Kempen GIJM, Janssen-Heijnen MLG, Deckx L, Buntinx FJVM, van den Akker M. Four screening instruments for frailty in older patients with and without cancer: a diagnostic study. BMC Geriatr 2014; 14: 26.
- Bras L, Peters TT, Wedman J, Plaat BE, Witjes MJ, van Leeuwen BL, et al. Predictive value of the Groningen Frailty Indicator for treatment outcomes in elderly patients after head and neck, or skin cancer surgery in a retrospective cohort. Clin Otolaryngol 2015; 40: 474–482.
- de Vries J, Heirman AN, Bras L, Plaat BEC, Rácz E, van Kester MS, et al. Geriatric assessment of patients treated for cutaneous head and neck malignancies in a tertiary referral center: predictors of postoperative complications. Eur J Surg Oncol 2020; 46: 123–130.
- 21. Valdatta L, Perletti G, Maggiulli F, Tamborini F, Pellegatta I, Cherubino M. FRAIL scale as a predictor of complications

and mortality in older patients undergoing reconstructive surgery for non-melanoma skin cancer. Oncol Lett 2019; 17: 263–269.

- 22. Garcovich S, Colloca G, Sollena P, Andrea B, Balducci L, Cho WC, et al. Skin cancer epidemics in the elderly as an emerging issue in geriatric oncology. Aging Dis 2017; 8: 643–661.
- 23. Lubeek SFK, Borgonjen RJ, van Vugt LJ, Olde Rikkert MG, van de Kerkhof PCM, Gerritsen MJP. Improving the applicability of guidelines on nonmelanoma skin cancer in frail older adults: a multidisciplinary expert consensus and systematic review of current guidelines. Br J Dermatol 2016; 175: 1003–1010.
- 24. Albert A, Knoll MA, Conti JA, Zbar RIS. Non-melanoma skin cancers in the older patient. Curr Oncol Rep 2019; 21: 79.
- Connolly KL, Jeong JM, Barker CA, Hernandez M, Lee EH. A systematic review of comorbidity indices used in the nonmelanoma skin cancer population. J Am Acad Dermatol 2017; 76: 344–346.
- Dhiwakar M, Khan NA, McClymont LG. Surgery for head and neck skin tumors in the elderly. Head Neck 2007; 29: 851–856.
- Reinau D, Surber C, Jick SS, Meier CR. Epidemiology of basal cell carcinoma in the United Kingdom: incidence, lifestyle factors, and comorbidities. Br J Cancer 2014; 111: 203–206.
- Tseng HW, Shiue YL, Tsai KW, Huang WC, Tang PL, Lam HC. Risk of skin cancer in patients with diabetes mellitus: a nationwide retrospective cohort study in Taiwan. Medicine (Baltimore) 2016; 95: 4070.

- Chossat A, Marco O, Chaouat M, Mimoun M, Boccara D. Complications with surgical treatment of basal cell carcinomas in individuals over 75 years of age: a retrospective study of prognostic factors in 158 cases. Ann Chir Plast Esthet 2018; 63: 299–306.
- Chen T, Bertenthal D, Sahay A, Sen S, Chren MM. Predictors of skin-related quality of life after treatment of cutaneous basal cell carcinoma and squamous cell carcinoma. Arch Dermatol 2007; 143: 1386–1392.
- Basu P, Beckles A, Porter ML, Olbricht S. Non-melanoma skin cancers are more likely to be untreated in elderly patients. J Am Acad Dermatol 2020; 82: 505–507.
- Bouhassira J, Bosc R, Greta L, Hersant B, Niddam J, Zehou O, et al. Factors associated with postoperative complications in elderly patients with skin cancer: A retrospective study of 241 patients. J Geriatr Oncol 2016; 7: 10–14.
- 33. Arguello-Guerra L, Vargas-Chandomid E, Diaz-Gonzalez JM, Mendez-Flores S, Ruelas-Villavicencio A, Dominguez-Cherit J. Incidence of complications in dermatological surgery of melanoma and non-melanoma skin cancer in patients with multiple comorbidity and/or antiplatelet-anticoagulants. Five year experience in our Hospital. Cir Cir 2019; 86: 15–23.
- Lubeek SFK, Michielsens CAJ, Borgonjen RJ, Bronkhorst EM, van de Kerkhof PCM, Gerritsen M-JP. Impact of high age and comorbidity on management decisions and adherence to guidelines in patients with keratinocyte skin cancer. Acta Derm Venereol 2017; 97: 825–829.