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The therapeutic dilemma of basal cell carcinoma in older adults: A review of the current literature.

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ABSTRACT

Skin cancer is known to be a significant health care threat due to the massively increasing numbers of diagnoses. In 2019, 4 million basal cell carcinoma (BCC) cases were diagnosed globally, making BCC the most frequent of all cancers worldwide in fair skinned populations. Given the increasing life-expectancy for all countries worldwide (by 2050, the world's population of people aged 60 years and older will have doubled), the incidence of BCC is expected to keep increasing in the future. Management of BCCs is challenging, especially among older adults, as mortality due to BCCs is extremely rare, whereas locally destructive growth can cause significant morbidity in certain cases. Therapeutic management in this population is further hampered because of the presence of comorbidities, frailty, and the heterogeneity of these aspects in older patients, leading to treatment dilemmas. A literature review was conducted to identify relevant patient, tumour, and treatment related factors that should be considered in the decision making for BCC treatment in older adults. This narrative review synthesizes all aspects concerning BCC treatment in older adults and aims to make some specific suggestions considering BCC treatment in older adults that can be used in daily practice.

We found that nodular BCC was found to be the most common subtype in older adults, most frequently located in the head and neck region. In non-facial BCCs, current literature has shown no significant impact on the quality of life (QoL) in older patients. Besides comorbidity scores, functional status should guide clinicians in treatment decisions. Taking all aspects into account when making treatment decisions is of great importance. When treating superficial BCCs on difficult-to-reach lesions in older adults, a clinician-administered treatment should be suggested because of possible impaired mobility in these patients. Based on current literature, we recommend assessing the comorbidities, the functional status, and frailty in older patients with BCC to evaluate life expectancy. In patients with low-risk BCCs and a limited life expectancy (LLE), an active surveillance or watchful waiting strategy can be suggested.

1. Introduction

Globally, an estimated 524 million people in 2010 were aged 65 or older (8% of the world population), and by 2050 this absolute number is expected to triple to 1.5 billion, representing 16% of the global population [1]. Over the last ten years, incidence of keratinocyte carcinoma (KC), the most frequent cancer type worldwide, increased from 5.8 million to 7.7 million patients. 76.6% of all KCs are basal cell carcinomas (BCCs). Approximately 66% of the incidence increase can be attributed to an increased proportion of the population comprising older adults, and the other one third can be attributed to an overall population growth [2]. The higher incidence of skin cancer in older patients can be explained because carcinogenesis due to sun exposure is a cumulative process. However, experimental studies have also shown that aged patients are less likely to repair DNA damage due to ultraviolet (UV) exposure because there is an age-related reduction and morphologic change of cutaneous melanocytes, resulting in an increased UV penetration and a decrease in their cell-mediated cutaneous immunity [3–6].

Fortunately, mortality due to BCC is extremely rare. The occurrence of metastasis is described in literature as 0.0028% to 0.5% [7]. BCCs can,

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however, influence quality of life (QOL) in a distinct way, by slowly growing into the surrounding tissues resulting in functional complications, secondary infection, or pain. It is important to note that BCC treatment mainly aims to improve patients' QoL and to reduce possible morbidity. It is usually not seen as a mortality-reducing intervention, since mortality due to BCC is very rare. Because of this concept, it is important to determine in BCC treatment at what point the 'time to benefit' outweighs the 'time to death' in patients with limited life expectancy (LLE).

The management of BCC is especially challenging in the older population because this patient group is heterogenous with a wide variety in comorbidity incidences, overall functional status, and social support systems. Dermatologists, general practitioners, and geriatricians will be faced with these treatment dilemmas more frequently in the next decades because of aging of the population and increasing overall life expectancy [8,9].

As a clinician, it would be of great interest to be able to determine which older adults with BCC would benefit from treatment and which patients would be better off with a wait-and-see approach. However, data that could support this approach and on BCC treatment outcomes in general are often obtained in younger patients. Older patients may currently be over- or undertreated, not taking into account their specific health needs, the biological heterogeneity of the tumour, or the clinical justification for the treatment. Indeed, several studies have shown that most KC (69%) were treated surgically regardless of patients' life expectancy [10]. In addition, >100,000 patients are treated for BCC every year in the US in their final year of life [11], and clinical practice guidelines rarely consider age and comorbidities [12]. The decision not to treat KC or to offer active surveillance or watchful waiting remains rare. However, certain patients could benefit from a watchful waiting approach, as we also stated in a recent perspective [13].

In this narrative review, we will discuss clinical characteristics of the older patient with BCC based on the available evidence. The overall goal of this review is to evaluate tumour, patient, and treatment related factors that play a role in the balanced choice of BCC management in older adults in a context of shared-decision making. This manuscript aims to provide health care workers specific suggestions considering BCC treatment in older adults and aims to evaluate in which specific older patients treatment outweighs the possible side effects.

2. Materials and Methods

A structured narrative review was conducted via an extensive literature search. Relevant studies were retrieved from three electronic databases: PubMed (MEDLINE), Excerpta Medica dataBASE (EMBASE) and Cochrane Library. The search strategy was created by using a combination of Mesh-terms and free-text words such as "basal cell carcinoma", "nonmelanoma skin cancer", "elderly", "older adults", etc. All synonyms retrieved via the MeSH database were used in the literature search to achieve a broad result of all available articles concerning this topic. Study selection was based on the title and the English language abstracts. Similar articles, citing articles, and articles found via reference lists were evaluated. Quality assessment and data extraction was performed by Hoorens I. and Van Coile L. Older patients are in this review defined as patients with the age of 75 years or older unless otherwise specified. Because the aim is to synthesize all relevant aspects to consider in our BCC approach in older adults, we started from an arbitrary age limit and not from other, more narrow characteristics such as frailty or functional status, for example. Data in older persons was described through a structured narrative synthesis and tabulation.

3. Results

3.1. Tumour Related Factors

Clinical and epidemiological studies suggest that BCCs differ between young patients and older patients. The biological and clinical features that are over- or underrepresented in older patients are displayed in Table 1 [7,14,15].

In older patients, nodular BCCs are the most common histological subtype and the superficial BCC subtype was found to be more common in younger patients. Both patient groups showed a significant difference in tumour location, with BCC being more frequently located in the head and neck area in older persons [15,16]. These BCC aspects in older adults are important because different histological subtypes come with different treatment possibilities (and thus complication risks), different recurrence rates, and a different treatment burden for the patient.

Several authors propose that different histological subtypes of BCCs are in fact part of one spectrum of BCC and that these skin tumours represent different phases of tumour growth (superficial, nodular, infiltrating). This hypothesis is supported by the observation of an increasing median age of the patients suffering from superficial to nodular to infiltrating BCC subtypes [17,18]. An interesting pilot study showed the overall BCC growth was small (2.5 mm^2/month). This suggests a relative indolent growth of low-risk BCCs, specifically in older patients [19]. A study in 2021 showed a diameter increase of 4.46 mm/year in BCCs with an infiltrating or micronodular component and an increase of 1.06 mm/year in superficial or nodular BCCs [20].

3.2. Patient Related Factors

Biological age, comorbidities, functional status, mental health, nutritional status, polypharmacy, home environment, and family support are important to take into account in treatment decisions [21,22]. These aspects are generally captured within a comprehensive geriatric assessment. Also, the impact on a patient's QoL should always be considered when treating older adults.

Comorbidities have been shown to be an important factor to consider in treatment decisions in nonmelanoma skin cancer (NMSC) [23]. As we know, comorbidities are frequently present in older patients [24]. In a recent study, two comorbidity scores were shown to be predictive for LLE in patients aged 85 years or older. These two scores were the Adult Comorbidity Evaluation-27 (ACE-27) and the age-adjusted Charlson Comorbidity Index (aCCI) [25]. Connolly et al. found that ACE-27 is potentially superior to other comorbidity scores because it captures more conditions and allows for comorbidity grading, which is not possible with the Charlson Comorbidity index (CCI) [23]. In a study by Linos et al., LLE was defined as patients older than 85 at the time of diagnosis or patients with a CCI of 3 or more. Almost half of the patients with a LLE status died within five years, with no KC related death cases, and 20% of the treated patients reported a therapy related complication within two years after treatment [10].

Table 1
Characteristics of basal cell carcinoma according to age.

	Younger patients (<75 years)	Older patients (≥75 years)	
Stratification by sex (male: female ratio) [8]		1.1:1 to 4.1:1	
Histological subtype [15]			
Nodular	39.5%	51.7%	
Superficial	43.0%	27.0%	$P <$ 0.05
Infiltrative/morpheaform	17.5%	21.3%	
Location [15]			
Head and neck	36.0%	57.3%	$P <$ 0.01
Trunk	59.3%	31.5%	P < 0.01
Limbs	4.7%	11.2%	

The functional status of patients is assessed based on the ability of successfully fulfilling daily activities such as self-care and mobility. Functional status has shown to be predictive for survival in older adults and it is a measure independent of comorbidities [26]. The Karnofsky Performance Status (KPS) Scale and the Katz Activities of Daily Living (Katz ADL) index are validated indices to evaluate functional status [27]. In older adults with KC, lower functional status scores of KPS $\leq$ 40 and Katz ADL $\leq$ 4 are associated with 37% and 53% survival at two years, respectively. This in contrast with 75% in the high KPS score group and 79% in the highest scoring Katz ADL group [27]. Renzi et al. was the first to demonstrate that functional status of patients with skin cancer influenced the treatment selection in their cohort of 203 patients aged over 75 years [28].

A 2021 study investigating predictors for surgical treatment burden, outcomes, and overall survival in older adults (> 70 years) found an overall low treatment burden in this patient population. Higher treatment burden was seen in patients with lower functional status (more ADL dependency), female patients, more complications, larger tumour diameter, and polypharmacy [29]. Chronological age was not found to be significantly associated with a higher treatment burden in this patient population [29].

Assessing the effect on the QoL in older patients when making treatment decisions is crucial. KC can have an influence on the health-related QoL (HrQoL) of patients through physical effects of the tumour, but also by the diagnosis itself and the subsequent treatment [22]. Older patients are at greater risk for experiencing inadvertent harms as a result of the diagnosis or the treatment of BCCs. These harms can be treatment side effects, but they also include anxiety and fear of metastasis or recurrence induced by the diagnosis of the tumour [30]. In KC, exact assessment of the HrQoL remains difficult and is a topic that is not frequently studied.

It seems that patients younger than 65 years old show a larger HrQoL improvement after their treatment compared with older patients [31,32]. A study from Siegel et al. showed an average Skindex-29-score decrease of 2.00 for every increase of ten years in age and an average Skin Cancer Index score increase with 2.20 for every increase of ten years of age [33]. Other studies, however, contradict the above findings, and found that age was not a significant predictor for QoL after treatment [32,34]. It is important to note that both studies used different QoL-scores, making results difficult to compare. Another important factor is the need for an evaluation of the HrQoL associated with BCC treatment using disease-specific questionnaires such as the Basal and Squamous Cell Carcinoma Quality of Life (BaSQoL) questionnaire [35].

3.3. Treatment Related Factors

An important question for physicians to keep in mind is whether treatment-related morbidity outweighs the expected benefit from treating the tumour. Older persons are at greater risk for complications due to compromised wound healing, comorbidities, malnutrition, and drug treatment for other medical conditions (polypharmacy) [21,24,36–38].

3.3.1. SURGERY – Standard Excision and Mohs Micrographic Surgery

In BCC, a surgical excision of the lesion is most frequently, if possible and technically achievable, the treatment of choice. Holtmann et al. studied histopathological and patient-related characteristics of BCCs of the head and neck influencing therapeutic management. An older age (mean age of 75.22 years) led to significantly more clinical stays and longer hospitalizations [39].

A specific surgical method that is frequently used for high-risk BCCs on a centrofacial location is a Mohs micrographic surgery (MMS). With this technique, the tumour is excised with narrow margins and is evaluated with complete three-dimensional histological examination, which ensures maximal preservation of the surrounding uninvolved tissue. This technique is, however, a more time-consuming technique and comes with a high logistical demand and treatment cost. Concerning MMS, results in older patients are contradictory [40,41]. Questions are being raised about whether a MMS is still to be considered in older persons. Some authors suggest not, since it is a long procedure that comes with possible side-effects in older adults, with average time to complete MMS being three hours, compared with one hour for a standard excision (SE) [42]. However, another study detected no difference in patient satisfaction scores or complication rates between patients aged <80 years and patients aged >80 years who received MMS, illustrating patients tolerated the procedure of a MMS well with high levels of patient satisfaction [43]. A study examining postoperative pain scores after MMS found no significant association between pain scores and age [44]. Another study investigating postoperative pain after MMS even found higher pain scores were associated with younger age [45]. Functional status is, however, important to consider, since a recent study showed an overall high functional status in patients undergoing MMS [46]. A large prospective multicentre cohort study of 2018 aimed at comparing the characteristics of patients and tumours in patients younger and older than 80 years who underwent MMS. The study included 2575 patients. The results showed that older patients have more frequent tumours with deeper tissue invasion, and thus a higher number of MMS rounds was needed [47]. This last finding was already illustrated by the study of Hoorens et al. in 2016. Clinicians should be aware of this finding because it can require more time in the operating room [48]. However, postoperative complications and five-year recurrence rates were similar in both age groups [47]. In a recent study of our group, which is not yet published, in older adults receiving MMS, we found a median survival of only 3.60 years in patients with multiple comorbidities, assessed with the aCCI. Because of the low median survival in this particular patient group we would question the need for a MMS in these patients because of the intensive and expensive character of this treatment. Other treatment options could be a better choice in older patients with a high comorbidity score.

Cure rates with a SE in primary low-risk BCCs is approximately 95 to 98% [21]. Data directly comparing complication rates of local SEs in older patients with those in younger patients is not available. A retrospective study of Chossat et al. investigating the complication risk in patients over 75 years of age who were treated surgically for at least one BCC identified the following risk factors: being over 85 years of age, long-term use of anticoagulant treatment, presence of at least one comorbidity, hospitalization, and general anesthesia. Clinicians should keep these risk factors in mind when searching the optimal treatment of choice for their BCC patients [49].

A study in 2021 showed no difference between patients' experienced treatment burden after MMS and SE [29].

3.3.2. Electrodessication and Curettage

Another treatment option for BCCs is electrodessication and curettage (ED&C). This is a technical procedure in which the BCC is removed by curettage with an electrodessication of the surgical plane afterwards. Cure rates for ED&C for low-risk BCC range up to 95%. Lubeek et al. studied the possibility of also treating high-risk BCCs with ED&C. In this retrospective study, patient and tumour characteristics were compared between non-recurrent and recurrent BCC cases. Results showed no influence of increasing age on the recurrence risk of the BCC [50]. Regarding QoL, a study by Chren et al. investigating patients with an average age of 65 years who were treated with MMS, SE, or ED&C showed improved QoL after MMS and SE, but not after ED&C [51].

3.3.3. Topical Treatments

In low-risk BCCs, topical treatments can be a good alternative for the surgical treatment. There are two main possible therapies: treatment with imiquimod 5% (application scheme: one application a day, five days a week, for six weeks) and treatment with 5-fluoro-uracil (5-FU) (application scheme: two applications a day, for four weeks). These schemes led to 85% five-year disease free rate and an 80% clearance rate

in superficial BCCs, respectively [21]. In a case study with four older patients who declined surgical treatment and who were offered a topical treatment with imiquimod instead, results were promising with no recurrence after 1 or 1.5 years of follow-up with the exception of one case who had multiple wide lesions [52]. All patients experienced local side effects such as erythema, erosion, ulceration, crust formation, burning sensation, or itch, but these side-effects did not lead to cessation of the treatment with imiquimod [52].

Treatment with photodynamic therapy (PDT) is another treatment option in which a photosensitizing substance is applied on the skin lesion followed by illumination of the lesion to kill the superficial skin cells. PDT of superficial BCCs and nodular BCCs leads to clearance rates ranging from 70% to 90% after one or two PDT treatments with gentle curettage as preparation in nodular BCCs [21]. A disadvantage of this treatment is the frequent occurrence of pain as side-effect. In the literature, it is still debated whether the response to PDT could be different among older patients. Nissen et al. investigated whether there is an age-related effect on the formation of protoporphyrin IX, which is known to be essential for the effect of topical PDT. Results were compared between a younger patient group (18–54 years) and an older patient group (65–85 years). In the younger group, a significantly higher amount of protoporphyrin IX formation was found and treatment efficacy of BCCs three months after PDT was significantly higher in the younger patient group. This suggests of potential reduced efficacy of PDT in older adults [53]. Another study evaluated the observed recurrence after treatment with PDT. Patients aged 60 years or older were found to have significantly higher recurrence rates compared with younger patients [54]. Another important matter is the potential side-effect of an acute post-procedure hypertension, most common in older patients and especially in older patients with hypertension in their medical history [38,55].

In one subgroup of the randomized controlled trial of Roozeboom et al., the results were slightly different. In older patients with superficial BCCs on the lower extremities, methyl aminolevulinate (MAL) PDT had a higher probability of treatment success compared with imiquimod [56]. The authors point out that MAL-PDT may be preferable in older patients with superficial BCCs on the lower extremities compared with other topical treatments. A potential explanation could be that cream application by the patients themselves is less feasible on the lower extremities in older patients [56]. Corresponding to this finding, Bahner et al. remarked in their review that topical 5-FU is a self-administered treatment which should only be used on easy-to-reach lesions. In older adults, impaired mobility could play an important role in treatment selection. Clinician-administered treatments are potentially a better option in older patients with impaired mobility [57].

3.3.4. Superficial Ablative Procedures

Cryotherapy is a treatment option in which liquid nitrogen is applied on the lesion and induces cell death. This technique could be used as treatment in superficial BCCs. Especially in patients who desire a noninvasive treatment option, cryotherapy could be offered because of low rates of post-procedure infection and bleeding and minimal to no post-treatment care or follow-up. However, healing after cryotherapy takes more time than ED&C and sutured wounds and more pronounced scarring can be seen [21]. A study from 2016 investigated cryotherapy of BCCs in older patients. This study illustrated the fact that a single session of cryotherapy can completely eradicate BCCs on the lower extremities in older persons. Over the follow-up period of 28 months, no wound infections or tumour recurrences were documented. The median healing time was 63 days and scarring levels were satisfactory. However, we need to address the rather small cohort in this study of eight patients [58].

Radiation therapy (RT) is suggested in frail patients who have poor wound healing or take multiple anticoagulant medications or in patients who cannot provide proper wound care [21]. However, disadvantages of this therapy are radiation-induced skin side effects as well as the fact patients need to come to the clinic frequently. The latter may be an issue among older adults who potentially are less mobile. However, RT should have a position in the treatment of large, esthetically disturbing BCCs in older patients in whom extensive surgeries are not possible or not desirable. In the literature, it is mentioned that some clinicians prefer to reserve RT for patients in their late 70s or $>$ 80 years old [21].

Ferro et al. investigated the outcome of RT for six consecutive days in patients aged between 70 and 90 years old who suffered from an early stage of KC. Almost all patients (97%) showed a complete response. The two-year local control rate was 93.2%. Acute and late skin toxicity was only of grade 1 in this study. The authors conclude that RT in a short-course gives a high local control of the disease [59]. Another study of RT specific in older patients (aged over 80 years) with KC investigated two hypofractionated schedules (bi-weekly fractions of RT) and found a high (92.4%) complete response and an improvement of symptoms in all patients. This treatment was found to be safe and effective in this population [60]. Several different studies assessed the effectiveness of RT in hypofractionated schemes (weekly RT) in older patients, concluding that this therapy is a well-tolerated treatment in older patients with similar response rates to conventional radiation schemes [61,62]. Pampena et al. retrospectively compared patients with KC who had received RT in a weekly regimen with patients with KC who had received a daily schedule. Mean age of the patients in the weekly regimen (81.3 years) was significantly higher than the mean age of the group with daily treatment (73.3 years). This study found no significant differences concerning mortality, recurrence rate, and cosmetic outcome between the two treatment regimens. A weekly, hypofractionated regimen could be a good treatment option in frail older patients in order to reduce the number of hospital visits [61].

3.3.5. Hedgehog Pathway Inhibition

Data concerning the administration of a hedgehog inhibitor (HHI) such as vismodegib in frail older patients remains very rare. Older patients with advanced BCC are considered to be at greater risk to experience adverse effects due to their therapy with vismodegib [38]. In literature, a small retrospective study has shown similar clinical efficacy in older patients compared with younger patients. Also, the safety profile was similar in older patients compared with younger patients, although patients aged 65 or older experienced more grade 3–5 adverse events. Despite numerical differences in the incidence of adverse events, no consistent trends could be observed. The authors conclude that the safety profile of vismodegib is comparable between older patients and younger patients. However, it remains important to note that there was only a small group of older patients included in the pivotal trials [38,63].

A recent exploratory retrospective study of eight older patients who had multiple comorbidities and received treatment with vismodegib showed good results concerning the tolerability and the safety profile of this medication in these frail older adults. Six of these patients had heart disease. Over the course of treatment, common side effects were detected in some patients (alopecia, dysgeusia, muscular spasms, and nausea). No aggravation of the existing heart disease was detected. The authors suggested that treatment with HHI can be useful in patients with locally advanced BCC, even if they have multiple comorbidities [64]. However, to date several clinical characteristics have been reported as potential predictive markers for a good response to HHIs. One of these characteristics was a young age [38]. Based on these findings, we can state that the tolerability and the safety profile may be similar between older and younger patients; however, if the tumour response to this medication is less positive in older patients, clinicians should re-evaluate if benefits outweigh the well-known side-effects, as well as the high cost that is linked with this treatment.

Head to head trials with vismodegib and sonidegib, the two HHI currently available on the market, comparing the efficacy and safety profile are to date not available. A post hoc analysis between both medications has suggested that the overall incidence of adverse events could be lower with sonidegib compared to vismodegib. This post-hoc

analysis did not compare age-specific incidences of adverse events between both treatments. Specific studies with sonidegib in older patients are currently non-existent [65].

3.3.6. *Watchful Waiting/Active Surveillance*

BCCs are typically indolent growing tumours and generally have a nonfatal course. In older patients with LLE, a potential strategy could be to forego treatment [21]. Of course, this approach is more suitable in patients with low-risk BCCs who are unable or unwilling to undergo treatment or in patients that potentially will not benefit from their treatment. Caution is necessary in tumours located on the head and neck area because of the higher potential of becoming symptomatic or disfiguring tumours; however, even among these tumours it remains possible to postpone treatment in favor of the patients' condition or personal preference because of their generally low growth velocity. Patients should be informed about the histological subtype of their tumour, because clinical follow-up is, for example, more difficult in infiltrating BCCs compared with superficial BCCs [66]. Clinicians need to have a broad communication with their patient to discuss the goals of potential treatment and the patient's expectations [30]. Watchful waiting has been put forward as an alternative to treatment in patients with asymptomatic low-risk BCCs and LLE [12].

In an observational study by van Winden et al., patients who chose not to treat their mostly biopsy-proven BCC were followed every three to six months. Reasons patients did not choose treatment in this study were patient-related factors influencing their choice (e.g., frailty, LLE), tumour-related factors (e.g., lack of symptoms, slow growth), expected treatment burden, and practical considerations (e.g., planning, transportation). Patients who chose to treat one of their BCCs after initially choosing for active surveillance had the following reasons: concern for potential tumour burden, resolved practical consideration, reevaluation of patient-related factors, and expected tumour burden in case of tumour growth [20].

Recently, an interesting study by Han et al. concerning patients' views on active surveillance in BCCs was published. The authors wanted to shed light on possible concerns patients would have regarding active surveillance for BCC. The most common concerns were tumour growth (41%) and metastasis (38%). Interestingly, concerns about not treating their BCC and following an active surveillance strategy instead decreased significantly after watching an educational video on BCCs. This study found almost half of the included patients would feel comfortable participating in a BCC-monitoring study [67].

4. Discussion

This narrative review aimed to shed light on the current treatment landscape of BCCs in older patients based on the most recent data available in the literature. It gives clinicians specific suggestions concerning BCC treatment in older adults based on different aspects that need to be taken into account in this population. This review tries to address the question of whether treatment and/or follow-up is warranted in every older adult with BCC. Fig. 1 summarizes all tumour, patient, and treatment related factors impacting clinical decision making in older patients. Only characteristics with available data in the literature concerning older adults with BCC were discussed in the results section. As illustrated by Fig. 1, the approach for BCC in older adults is influenced by a range of different factors. A central role for shared decision making together with the patient and their family is necessary to keep in mind.

Treatment decisions regarding BCC in older (frail) patients should be made with relevant patient-related factors taken into account, especially comorbidities and functional status of the patient. MMS and SE have been shown to results in a similar treatment burden in older adults. Postoperative complications and recurrence rates did not differ between

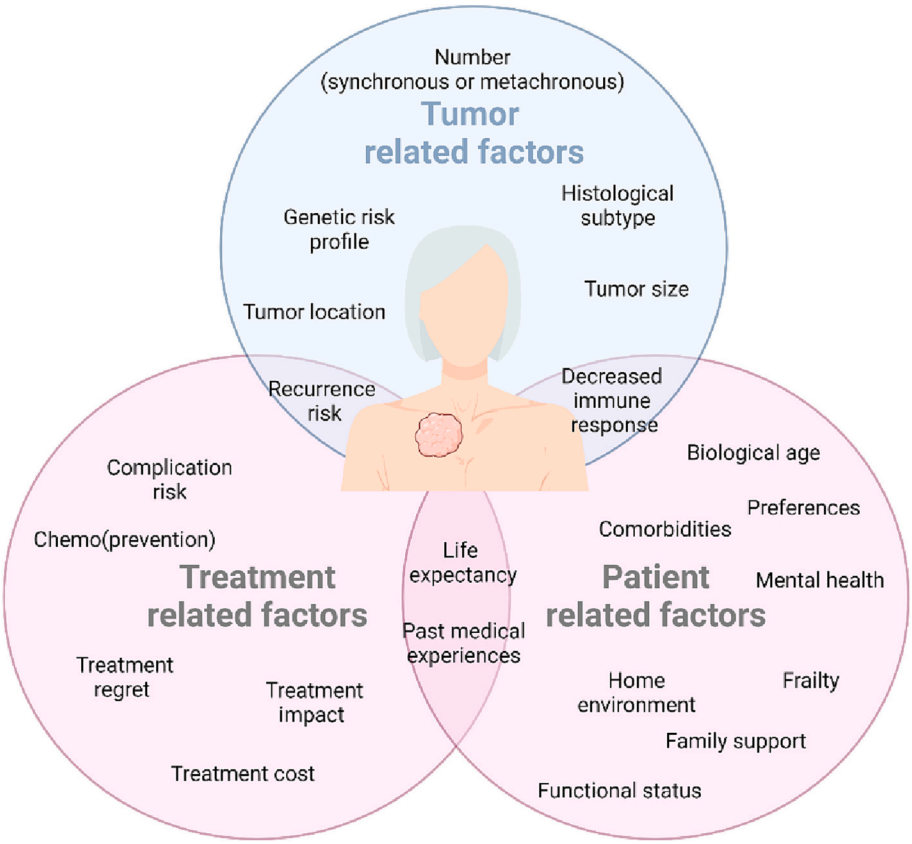

Fig. 1. Overview of all tumour, patient, and treatment related factors impacting clinical decision making in older basal cell carcinoma patients.

younger and older patients.

However, older patients are at higher risk for more and longer hospitalizations [39]. Older patients also tend to have more complex tumours that need more rounds of MMS to obtain a complete resection [47,48]. Other treatment options can be a better choice in older patients with a lower functional status or a high comorbidity score. Information concerning potential lag-time to benefit is important in the consideration of pursuing MMS. RT can be an alternative among older adults if surgery is not considered the optimal choice, with specific attention on hypofractionated schedules.

Topical treatments can be a good alternative for surgery in superficial BCCs in older patients. A case series with imiquimod in older patients has shown promising results. PDT in older adults could have a reduced efficacy due to a reduced formation of protoporphyrin IX. When treating superficial BCCs on difficult-to-reach lesions in older adults, a clinician-administered treatment should be suggested because of possible impaired mobility of these patients. Cryotherapy can potentially play a more prominent role in superficial BCCs in older patients, because of its physician-administered character, low rates of complications, relative high efficacy, high accessibility during the consultation, and low cost.

Non-facial BCCs have been shown to not significantly impact QoL in older patients. The limited available data on BCC growth has shown that these tumours have an indolent growth pattern. Based on current literature, we recommend an assessment of comorbidities, functional status, and frailty of these patients to estimate potential reduced life expectancy. This is an important aspect, since BCC treatment is mainly seen as a morbidity-reducing intervention with the aim of enhancing the patients' QoL. It is usually not a mortality-reducing intervention, since mortality as a result of BCC is extremely rare.

In patients diagnosed with low risk disease and a limited life expectancy, an active surveillance or watchful waiting strategy should be discussed with the patient during shared decision making. Unlike active surveillance, watchful waiting carries a palliative, non-aggressive intent, and does not involve routine monitoring. With watchful waiting, patients who develop symptomatic progression from BCCs are offered (noninvasive) treatments to palliate these symptoms without the intent to cure disease.

More data is needed concerning the natural evolution of this type of skin cancer in order to estimate whether a chosen treatment will positively affect the patients' QoL within a predetermined timeframe. The ultimate goal should be to develop a personalized approach and a new innovative, cost-effective care pathway for the treatment of BCC in an aging population.

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Author Contributions

Isabelle Hoorens and Laura Van Coile conducted the literature review, data extraction and drafted the manuscript. All authors were involved in defining the structure of this manuscript. All authors revised the final version of the article before submission.

Declaration of Competing Interest

None declared.

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