Basal cell carcinoma is the most common form of skin cancer with a slow growing rate and extremely rare metastasis, but with an important susceptibility of local recurrences. In recent years its incidence has increased significantly, putting an important strain on global health systems. This higher rate of new cases may be explained by excessive UV exposure, in the form of outdoor or indoor tanning (especially at a young age), air pollutants, chemical carcinogens, and immunosuppression. BCCs arises frequently on sun exposed areas, most commonly on the head and neck, followed by the trunk and extremities. There is no standardized approach to BCC treatment. Physicians can offer patients a few surgical and non-surgical treatment options depending on the size, location, number of lesions and clinical form of BCC, that take up an important amount of medical and financial resources. Prevention strategies are the key for lowering BCC incidence in the long term, whether it is de novo tumor development or tumor recurrence, and restricting the overuse of health system resources. These strategies should include limitation of UV exposure, correct sunscreen use, restriction of tanning bed use and regular skin cancer screenings.
Introduction

Basal cell carcinoma (BCC) is the most common form of skin cancer, with a growing incidence in recent years. There is evidence that the number of patients that present with multiple BCC (mBCC) is also on the rise. The exact incidence of BCC is difficult to estimate, and for mBCC even more so, due to the lack of a national skin cancer registry. Patients developing another BCC after the first one are a common occurrence. One possible explanation for this growing incidence is higher UV exposure, in the form of outdoor sun exposure or the use of tanning beds. A 5-year prospective study reported that 36% of patients that had one treated BCC developed a second one. The rising incidence that 36% of patients that had one treated BCC is difficult to estimate, and for mBCC even more so, due to the lack of a national skin cancer registry. Patients developing another BCC after the first one are a common occurrence. One possible explanation for this growing incidence is higher UV exposure, in the form of outdoor sun exposure or the use of tanning beds. A 5-year prospective study reported that 36% of patients that had one treated BCC developed a second one. The rising incidence that 36% of patients that had one treated BCC.

1. Epidemiology

Basal cell carcinoma incidence rates are rising worldwide, carrying an increasingly important public health burden because of the large number of patients presenting with single or multiple BCCs, high cost of treatment and follow-up. The major difficulty in assessing the true incidence of BCC comes from poor registration practices or, in most countries, lack thereof. The causes of this sustained rise are the effects of increasing UV exposure, ozone depletion, population aging, growing popularity of tanning beds, but also increased surveillance. Genetic defects causing basal cell carcinoma syndromes will not be discussed here. Increased longevity probably plays a major part in the growing incidence of BCC owing to cumulative sun exposure and photodamage over time.

BCCs usually occur in populations over 50 years of age, usually men, but studies show increasing rates among people younger than 40 years, with patients likely being women. Contrasting with most countries, Denmark has an extensive registration of non-melanoma skin cancers (NMSC) in two nation-wide population registries: the Danish Cancer Registry and the Danish Cancer Registry of Pathology, facilitating the analysis of NMSC over time. Using data from these two registries, one study has shown that women showed a higher average incidence for BCC compared to men. Another observation was that the average annual increase in BCC among people aged between 20-40 years was significantly higher compared to older people for (both) men and especially for women. The explanation could reside in the fact that younger people pay more attention to public awareness campaigns, women being more likely to seek medical attention because they are more mindful of their physical appearance. One US-based study evaluated BCC incidence trends over a span of 20 years and found that age-adjusted BCC incidence rates increased from 519 cases per 100,000 person-years to 1,019 cases per 100,000 person-years for women and increased from 606 cases per 100,000 person-years to 1,488 cases per 100,000 person-years for men.

While it is rarely life-threatening, it causes important functional and cosmetic morbidity, since most lesions are located on the head and neck. However, many patients present with multiple lesions located on the trunk and extremities. One study predicted that by 2020 incidence rates for primaries on the arms will increase 3.5-fold and 2.3-fold on the trunk in women. A recent prospective population-based study in a population over 55 years of age showed that one third of BCC patients developed multiple BCC lesions over an average period of follow-up of 10 years, of whom 18.1% developed two and 12.9% three or more BCCs.

2. Risk factors

Although the precise etiology of BCC remains unclear, it encompasses a plethora of risk factors. Exposure to ultraviolet radiation has long been considered as the most important risk factor for BCC development, responsible for most of the skin damage, especially UVB radiation with a wavelength between 290-320 nm. Recent studies have shown that intermittent or “recreational” sun exposure as a child or teenager plays a major role in the occurrence of adulthood BCCs. Sunburns, especially in non-tanners, are the result of intermittent high-dose UV exposure and have a positive correlation with BCCs in terms of number and intensity. In this regard, several researchers have suggested that BCC and melanoma might share some risk factors. Also, there is evidence that the increasing number of truncal lesions and in particular superficial tumors in young patients are the result of intense intermittent sun exposure and skin damage, rather than the accumulation of long-term UV exposure. However, increasing incidence with age most likely reflects cumulative sun exposure and photodamage over time. A study from 2013 found a strong and consistent association between BCC risk and cumulative UVB exposure in both men and women, with a relative risk for cumulative UVB exposure being...
much higher in women than in men. This in turn shows that, over time, women may be more susceptible to cumulative UV radiation than men. The last few decades have witnessed a change in sun exposure habits: families tend to work most of the year and go on vacation over the weekend, thus not permitting the skin to develop and preserve photo-protective systems.

Furthermore, tanning beds have become an integrative part of western culture, mainly targeting the young population. One 2002 study reported that ever-use of tanning beds increased BCC risk by 50% and young age at first use was associated with a higher risk. Tanning beds can produce 10-15 times as much radiation as sun exposure during noon hours, resulting in a reaction similar to sunburn. There is extensive evidence that there is a dose-response relation between tanning bed use and the risk of developing a BCC at a young age, especially in individuals who used tanning beds in highschool or college or between ages 25 and 35. Classically, light hair color (especially red and blond), fair skin and freckling are regarded as independent risk factors for BCC development, with brown eyes being a protective factor. However one study showed that there is no significant difference for the risk of BCC development among women with low pigment score and those with high pigmentation that use indoor tanning, similarly affecting all phototypes.

One measure adopted in a growing number of countries is age restriction from tanning salons. Brazil has banned indoor tanning for cosmetic purposes and, as of the beginning of 2015, Australia has banned indoor tanning in five out of six states, according to the Centers for Disease Control and Prevention. European countries have taken action as well, adopting an 18-year old age restriction for tanning bed use:

3. Clinical features

BCCs arises on sun exposed areas, most commonly on the head and neck (in 80% of cases),
followed by the trunk and extremities\(^3\). Less common sites include the axillae, groin, breasts, palms and soles, which lends to a more difficult positive diagnosis. Some authors observed a change in the anatomical tumor distribution, with only 60% of BCCs occurring on the head and neck, and a growing number developing on the trunk in younger patients, probably explained by excessive UV exposure, whether it is indoors or outdoors\(^10\). Regarding clinical subtypes, between 56% to 78.9% are nodular tumors, followed by the superficial subtype found in between 9% and 17.5% of cases, and the morpheaform subtype in 0.5-16.6% of cases\(^28,29\). Uncommon variants such as basosquamous, keratotic, micronodular, granular-cell, adamantinoid and clear-cell BCCs are found in fewer cases\(^3\). Metastases rarely occur, and are correlated with tumor size and depth and, to a lesser extent with tumor subtype\(^30\).

The importance of classifying tumors by subtype and location resides in the fact that some variants tend to be more aggressive (micronodular, infiltrative, basosquamous, morpheaform types), while in most cases tumors take a less aggressive clinical course (nodular and superficial types)\(^31\). Clear assessment of tumor characteristics dictates treatment choice. Moreover, early diagnosis results in lowering patient morbidity and treatment costs. Another important issue in BCC patients is that a noteworthy percentage return with multiple new lesions a few years after treatment of the first one. One study reported that almost half of patients studied over a 10-year period returned with multiple BCCs\(^12\), similar to another 2005 study that observed that 43% of patients developed a second BCC within a 4 and half year time frame\(^32\). Patients with multiple lesions tend to have been diagnosed with a first BCC before the age of 65, have red hair, and a higher educational level\(^13\). The consequence of this high number of patients with mBCCs is a substantial strain on health care systems consuming a great amount of resources on treatment.

### 4. Treatment options

There is no standardized approach to BCC treatment, since there are few randomized trials, prospective or comparative studies available. Therefore, physicians can offer patients a few options depending on the size, location, number of lesions and clinical form of BCC. Treatment should focus on local control, maximal conservation of function and cosmesis\(^3\). Another important goal is prevention of recurrence, because recurrent tumors are more difficult to treat\(^7\). Treatment options can be surgical and non-surgical. Surgical options are electrodesiccation and curettage, cryosurgery, surgical excision and Mohs micrographic surgery (MMS). Non-surgical treatments include topical therapies (5-Fluorouracil, Imiquimod), photodynamic therapy (PDT), intralesional therapy (interferons, 5-Fluorouracil or bleomycin) and radiation therapy. Radiotherapy is recommended for lesions in difficult to treat locations and for patients that cannot be subjected to surgical excision\(^6\).

The rise of BCC incidence as well as greater exposure to risk factors translate in many different aspects with direct impact on treatment. From treatment costs that burden health systems, to quality of life related issues, all must be taken into account when choosing the appropriate form of treatment. There is insufficient literature considering exact treatment costs per procedure. According to one study\(^34\) BCC is one of the more expensive cancers to treat. Another study shows that surgical excision is similar in cost to MMS\(^35\), however MMS is not readily available in all physician-office settings. Therefore, resorting to traditional surgical excision is widely accepted as an adequate option, with good results and a low recurrence rate. M-M Chren et al. noted that there was no significant difference regarding quality of life for patients receiving either classical surgical excision or MMS\(^41\), but both therapies had better outcomes than electrodessication and cautery. Some authors suggest that curettage and cryotherapy may be
be an option for minimally invasive BCC. In the majority of cases alternatives as curettage and electrocautery, PDT, laser, topical imiquimod and cryosurgery should not be regarded as first line due to recurrence risk which in turn results in additional healthcare costs.

The main goal of treatment is not only prevention of tumor recurrence but also increasing/raising quality of life in the form of years of potential life and productivity conservation. Given that most BCCs develop on the head and neck, areas with high psycho-social impact, treatment choice in this particular areas should have as end points total tumor removal, adequate cosmesis and function conservation. Moreover, physicians must take into account the social, familial and individual impact that a skin tumor diagnosis and treatment generate.

Data regarding such issues are scarce. In 2009 Baker et al. studied the impact of NMSC overall and observed that NMSC patients were concerned about the public’s lack of understanding and recognition of skin cancer and about possible scarring and disfigurement. Another study on data recorded from discussion groups with patients regarding BCC knowledge and treatment processes, found that patients were unsatisfied with the amount of information offered by their physician about their treatment options, side-effects and possible pain and scarring. Therefore the psychosocial impact of NMSC must not be underestimated or minimized and more effort should be put into informing patients and raising public awareness.

5. Prevention

Prevention strategies are the key for lowering BCC incidence in the long term, whether it is de novo tumor development or tumor recurrence. Primary prevention focuses on modifiable risk factors like excessive UV exposure. Active campaigns promoting sunscreen use should be initiated, all the more so as studies have shown that the use of broad spectrum sunscreens offers a good protection against UV-related tumors. Importantly, it was shown that sun-protective behaviours increased after sun-protective behaviours increased after sun-protective behaviours increased after sun-protective behaviours increased after sun-protective behaviours increased after.

In summary, the growing incidence of basal cell carcinoma, although curable when early diagnosis is made, represents an important financial burden on health care systems. In order to plan public health strategies against aggressive intermittent sun exposure, especially in children and young adults, in addition to regular sunscreen use, it is important to understand basal cell carcinoma risk factors and incidence. Awareness campaigns may represent an important weapon in public education that could lead to lowering skin cancer incidence in general, as well as overuse of health-related resources.
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7. Mary-Margaret Chren, Eleni Linos, Jeanette S. Torres, Sarah E. Stuart, Rupa Parvataneni and W. John Rocsardin. Tumor Recurrence 5 Years after Treatment of Cutaneous Basal Cell Carcinoma and Squamous Cell Carcinoma.