Differences in Disease-specific Quality of Life in Patients with Actinic Keratosis in Australia and Denmark

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Received: September 8, 2015
Accepted: January 18, 2016

ABSTRACT Actinic keratosis (AK) negatively influences patient quality of life as measured by the disease-specific Actinic Keratosis Quality of Life (AKQoL) questionnaire. The quality of life in Australian patients was significantly less affected than in Danish patients. We hypothesize that general factors such as public awareness and cultural connotations of AK, may influence the impact of AK on quality of life (QoL).

KEY WORDS: actinic keratosis, quality of life, Australia, Denmark

INTRODUCTION

Actinic keratosis (AK) is a common disease with a prevalence of around 3% of the population. The prevalence increases with age and is dependent on geography, being higher in countries with higher UV-exposure (1,2). It is often considered a premalignant skin condition which may develop into non-melanoma skin cancer (NMSC) if left untreated, although it is acknowledged that the transformation rate is low (3). The incidence of both AK and NMSC appears to be rising, contributing to the overall burden of these diseases on society (4). AK has a negative effect on dermatology and disease-specific quality of life (QoL) (5,6).

The risk of AK and NMSC is greater in Australia than in other countries such as Denmark, most likely due to differences in ultraviolet (UV) burden and associated exposure. The overall result is reflected in the reported prevalence rates of AK/NMSC, although significant under-reporting of AK is suspected to occur in all countries. The number of people with sun damage and prevalence of AK/NMSC in Australia is one of the highest in the world, with over 434 000 people (1.9% of the 22.7 million inhabitants) being treated for one or more NMSC in Australia annually (7). In comparison, 13 794 patients (2.4% of the 5.6 million inhabitants) were treated for NMSC in Denmark (from the Clinical Database of Non-Melanoma Skin Cancer in Dermatology Practice 2013 - A. Lamberg, Aarhus Univeristy Hospital Denmark). We therefore hypothesized that there is a difference in disease-specific QoL when comparing Australian and Danish patients with AK due to differences in climate, NMSC prevalence, and cultural connotations of AK.

Therefore, our objective was to explore this hypothesis by assessing the disease-specific QoL in patients with AK in Australia and compare it to the disease-specific QoL in patients with AK in Denmark in a pilot study.

To the best of the authors' knowledge no such study has been previously performed.

PATIENTS AND METHODS

The newly developed and validated disease-specific questionnaire Actinic Keratosis Quality of Life (AKQoL) was used to asses QoL (6,8). AKQoL has three domains covering emotion, function, and control and one single global item. It includes 9 questions in total, each question with 4 options, scored 0-3 with a total maximum score of 27; the higher the score the higher the impairment of QoL.

Generic QoL tools such as the EQ5D, or skin-specific QoL tools such as the Dermatology Life Quality Index (DLQI), only poorly reflect morbidity in AK/NMSC and were therefore not included in the study. To the best of our knowledge no other AK-specific QoL instrument exists.

The project was approved by the national Bellberry ethical committee in Australia, and all participants signed an informed consent form. Questionnaire-based studies do not require ethical committee approval in Denmark.

Patients were recruited according to their healthcare-seeking behavior, i.e. at comparable institutions in the two countries. In consequence, no direct comparison regarding the number, location or treatment of AK was made. The English translated and content-validated AKQoL questionnaire was mailed in stamped addressed envelopes to 92 patients with AK attending the Academic Dermatology Practice affiliated with the University of NSW, in Kogarah, Sydney, Australia in April 2013. The patients with AK were identified by the payment code for cryo-treatment of more than 10 AKs, as there is no code for treating less than 10 AKs in Australia.

The same questionnaire was handed out to 105 outpatients with AK during their visit at different Dermatology Practices in Region Zealand in Denmark during the period from November 2005 to February 2006. The patients either filled out the questionnaire at the clinic or returned the filled out questionnaire by post from home.

The Wilcoxon test was used to compare mean AKQoL scores, and the Chi-square test was used to compare the sex-distribution between the two countries. Univariable and multivariable linear regression analyses were undertaken to investigate the difference in the total AKQoL score between the two countries. Age, sex, and the country of origin were chosen as potentially important variables. The analyses were performed in SAS® software (SAS Institute Inc., Cary, NC, USA) version 9.2 and in R, version 2.15.2 (R Development Core Team, 2013).

RESULTS

A total of 29 Australian patients with AK responded yielding a participant rate of 31.5%.

A total of 105 Danish patients with AK responded yielding a participant rate of 100%.

The mean age and sex distribution for the Australian and Danish patients with AK can be found in Table 1.

The mean AKQoL scores for Australian and Danish patients with AK were 6.48 (standard deviation (SD) ±5.28) and 9.51 (SD ±4.96), respectively, yielding a statistically significant mean difference of 3.03 points (95% confidence interval (CI) 0.94 – -5.12, P=0.0047) (Table 2). After adjusting the results for age and sex, the difference between the Danish and Australian

Table 1. Mean age and sex distribution in Australian and Danish patients with AK

	Australian patients with AK n=29	**Danish patients with AK n=105**
Age (mean years (range))	69.29 (48-95)	68.15 (41-86)
Women vs. men (% and number)	34.5% vs. 65.5% (10 vs. 19)	50.5% vs. 49.5% (53 vs. 52)
AKQoL score		
Total (mean ± SD)	6.48 (SD ±5.28)	9.51 (SD ±4.96)
Emotion domain	2.03 (SD ±2.02)	3.31 (SD ±2.14)
Function domain	2.45 (SD ±1.88)	3.83 (SD ±1.82)
Control domain	1.69 (SD ±1.63)	1.82 (SD ±1.82)
Single item 3	0.31 (SD ±0.71)	0.55 (SD ±0.68)

*AK: actinic keratosis; AKQoL: Actinic Keratosis Quality of Life; SD: standard deviation

Table 2. Results of the univariable and multivariable linear regression analyses with the total AKQoL score as the dependent variable

	Univariable analysis		Multivariable analysis	
	Changes in total AKQoL (95% CI)	***P* value**	**Changes in total AKQoL (95% CI)**	***P* value**
Australian AK patients	Reference	**0.0047**	Reference	**0.039**
Danish AK patients	3.03 (+0.94 – 5.12)		2.51 (0.13 – 4.89)	
Women			Reference	**0.013**
Men			-2.35 (-0.51 – -4.19)	
Age (per 1 year increment)			-0.03 (-0.11 – 0.05)	0.50

*AK: actinic keratosis; AKQoL: Actinic Keratosis Quality of Life; CI: confidence interval

patients in the total AKQoL score became slightly smaller; nonetheless, the difference remained statistically significant (2.51, 95% CI 0.13 – 4.89, P=0.039) (Table 2). The Danish population had a significantly higher score in the emotion domain (*P*=0.0019), the function domain (*P*=0.0001), and for the single item (*P*=0.0142) but a non-significantly higher score in the control domain (P=0.2959) (Table 1).

DISCUSSION

The results of this crude survey indicate that patients with AK have impaired QoL in both countries, albeit at different levels when assessed by the AKQoL. AK appears to be associated with a lower disease-specific QoL in Denmark compared with Australia. Several circumstances may influence this. The high prevalence and subsequently increased media coverage of sun damage in Australia may lead to "acclimatization" of the Australian public, i.e. making them care less about sun damage. Alternatively, the increased awareness of skin cancer in Australia may change the perspective of patients, i.e. being relieved to "only" have AKs rather than NMSC. Further cultural connotations and practical management may play a part. The fact that Australian patients had >10 lesions and Danish patients could have far fewer lesions may also have contributed to this possible Australian "desensitization". Similarly, cryotherapy may have been more commonly used in Australian patients, indicating that the group was less cosmetically aware.

To the best of our knowledge no other studies have assessed the difference between QoL in two culturally and geographically different AK populations. In fact very few studies have assessed the impact of AK on patient QoL at all. The definition of the study populations according to their health-seeking-behavior is an obvious weakness of the study. Other weaknesses are the lack of clinical detail. A cross-sectional study using Skindex-29 and 6 keratinocyte carcinoma-specific questionnaires found that higher AK counts and past use of topical 5-fluorouracil (5-FU) were predictors of worse QoL in an American veterans' group (10). In contrast, a longitudinal study from the same group reported that increased AK counts did not influence the QoL (5). The absence of clinical detail may therefore be of lesser importance than expected. The time-lapse between the data-gathering may also be of importance as it may have influenced the perceptions of both patient group as well as treatment opportunities. Finally, the low participation rate among Australian patients may be seen both as a problem but also as suggesting that they consider the problem less important as also reflected by the AKQoL score. Such an interpretation is supported by qualitative studies that have identified significant emotional QoL issues with AK (8,9). The potential influence of physical comorbidities remains unexplored.

Obviously, the exploratory nature of this small study precludes nation-wide generalization of the results, which are nevertheless of interest in view of the increasing attention being given to AK as a skin disease.

The major strength of the study is the use of a validated disease-specific QoL questionnaire. The major limitation of this study is the small number of Australian patients with AK, yielding a low participation rate. It is possible that because the ethics committee in Australia insisted upon a consent form being signed as well as the questionnaire, this extra effort may have been off-putting. Patients sent questionnaires via mail rather than being approached in person are also less likely to have high response rates. However, this may be speculated to reflect the fact that Australian patients with AK are not as concerned with their skin condition as Danish patients. There was a slight non-significant difference in the sex distribution between the Australian and Danish patients with (*P*=0.1266).

CONCLUSION

Danish patients with AK have a lower disease-specific QoL when compared with Australian patients with AK. We hypothesize that climate differences as well as different degrees of public awareness and cultural connotations influenced the impact of AK on QoL.

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