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CLINICAL REPORT

Patient Preferences for Treatment of Basal Cell Carcinoma: Importance of Cure and Cosmetic Outcome

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Treatment options for localized resectable basal cell carcinoma (BCC) include micrographically controlled surgery, simple excision, curettage, laser ablation, cryosurgery, imiquimod, 5-fluorouracil, photodynamic therapy and radiotherapy. The aim of this study was to assess the preferences of patients with BCC for outcome (cure and recurrence rate, cosmetic outcome, risk of temporary and permanent complications) and process attributes (type of therapy, treatment location, anaesthesia, method of wound closure, duration of wound healing, out-of-pocket costs) of these treatments with conjoint analysis. Participants ($n = 124$) attached greatest importance to recurrence rate (relative importance score (RIS) 17.28), followed by cosmetic outcome (RIS 16.90) and cure rate (RIS 15.02). Participants with BCC on the head or neck were particularly interested in cosmetic outcome. Those with a recurrence were willing to trade risk of recurrence, treatment location and duration of wound healing for a better cosmetic result. In summary, participants particularly valued cure and cosmetic outcome, although preferences varied with individual and tumour-associated characteristics. ***Key words: basal cell carcinoma; patient preferences; conjoint analysis; discrete choice; excision; cosmetic outcome.***

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Basal cell carcinomas (BCC) are the most common skin cancers in Caucasians worldwide (1, 2), with a yearly incidence of approximately 100 per 100,000 inhabitants in Northern Europe and the USA (3, 4). A substantial increase in incidence, and an age shift with a tendency towards younger age of onset, have been noted in recent years worldwide (5–7). The main risk factors for development of BCC are sun exposure, fair skin, immunosuppression, carcinogens, such as arsenic, chronic irritation and certain genodermatoses (8–10). Metastasis or life-threatening courses are extremely rare (11), but BCC can infiltrate and destroy deeper tissues and lead to functional impairment and cosmetic disfiguration (12, 13). The gold standard for treatment of BCC in challenging localizations, such as the head/neck region, is micrographically controlled excision (14). This method allows sparing healthy tissue and provides low risk of recurrence, but may involve surgical complications (15). Treatment alternatives include simple excision, curettage, carbon dioxide laser ablation, cryosurgery, topical treatment with imiquimod or 5-fluorouracil, photodynamic therapy, radiotherapy (12, 16) and vismodegib for unresectable or metastasizing BCC (17). Dependent on the localization, size and histological subtype of the BCC as well as on the age and health of the patient, several treatment options may be feasible. However, they imply fundamental differences in outcome (e.g. chance of cure, risk of recurrence, risk and nature of complications and cosmetic result) and in the treatment process (e.g. treatment location, duration and costs) (18–21). These aspects should be discussed during shared decision-making in order to identify the most suitable approach for each patient and to optimize both clinical outcome and patient satisfaction.

Information on patient preferences for treatment of BCC and on their appreciation of particular outcome and process attributes remains limited (22–24). A method for preference elicitation that originally stems from market research, but which has recently been increasingly used in the medical field, is conjoint analysis (CA) (25–29). This method provides the advantage of realistically reflecting clinical decision-making. In CA, also known as discrete choice experiments, participants are asked to choose between treatment options, which are decomposed into and described by their attributes. CA exercises force trade-offs in a choice context and allow quantification and comparison of attributes related to treatment outcome and process (30–32). CA has been used previously to compare preferences of healthy individuals (22, 24) for different surgical approaches of BCC or for surgery vs. photodynamic therapy and to compare preferences of patients with BCC for surgery vs. imiquimod cream (23). According to these studies, participants preferred Mohs surgery over standard excision and photodynamic therapy or imiquimod cream over surgery.

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The aim of our study was to elicit patient preferences for all treatment modalities currently available for localized resectable BCC (micrographically controlled excision, simple excision, curettage, carbon dioxide laser ablation, cryosurgery, topical treatment with imiquimod or 5-fluorouracil, photodynamic therapy and radiotherapy) with CA and to determine the impact of sociodemographic, socioeconomic and disease-related characteristics on these preferences.

METHODS

Study participants

Individuals attending outpatient clinics at the Department of Dermatology of the University Medical Center Mannheim, Germany between 24 May 2012, and 8 May 2013 with clinically suspected and/or histologically confirmed BCC were invited to participate. In the patient information it was explained that BCC are semi-malignant skin tumours, which invade and destroy the surrounding tissue, but usually do not metastasize. Patients were informed that BCC are often treated by surgery, but that alternatively, non-surgical approaches may be feasible, depending on the size, localization and histological subtype of the tumour. The different types of therapies and techniques of wound closure were described as outlined in Tables SI[1] and SII[1]. If the final histological diagnosis was different from BCC, participants were retrospectively excluded, i.e. only data from participants with histologically confirmed BCC were analysed. The study was approved by the ethics committee of the Medical Faculty Mannheim and performed according to the principles of the Declaration of Helsinki.

Data collection

After providing written informed consent, participants received a printed survey to be completed before clinical consultation. Assistance was available in case of questions or problems with the survey.

The first part of the survey contained information on sociodemographic (age, sex and marital status (living alone or with a partner)) and socioeconomic characteristics (net monthly household income (< 1,500 €, 1,500–3,000 €, > 3,000 €), working status (working or not working) and professional qualification (no vocational degree, completed vocational education or (technical) college degree) as well as information on disease-related characteristics, i.e. number of current BCC (1 or > 1), localization of the tumour (head/neck, body, or both head/neck and body), and history of previous skin cancers (yes or no; if yes: 1 or > 1 skin cancers).

In the second part, participants' preferences for treatment of BCC were assessed using CA (26). For generation of key attributes and attribute levels used in the discrete choice experiments, all treatment options currently available for localized resectable BCC were considered. Key attributes consisted of 5 outcome attributes (cure rate, recurrence rate, cosmetic outcome, risk of temporary complications, risk of persistent complications) and 6 process attributes (type of therapy, treatment location, anaesthesia, method of wound closure, duration of wound healing, out-of-pocket costs). Four realistic attribute levels, derived from actual treatment options, were assigned to each attribute based on literature review and expert opinion (Table SI[1]) (12, 18, 21, 33–35).

To reduce complexity and avoid information overload, attributes were separated into 2 groups. The cost attribute was made part of both groups to guarantee internal consistency and allow later comparability of both groups. Cure rate and recurrence rate were presented in different groups.

The final survey was compiled in a reduced design. From 4,096 (4^6) possible scenarios, 12 pairs of choice sets were selected randomly for each group of attributes using commercially available CA software (www.sawtoothsoftware.com). Respondents were asked to repeatedly choose the preferred treatment scenario from among pairs of options (for examples of scenarios of group 1 and group 2 attributes, see Table SII[1]). Each participant was provided with the same version of questionnaire.

Statistical analysis

Part-worth utilities were calculated for each attribute level and scaled to sum to zero within each attribute using logit regression. The range between the lowest and the highest part-worth utility was measured for each attribute. To allow comparability of the different attributes, relative importance scores (RIS) were calculated as a percentage by dividing each attribute's range by the sum of all attribute ranges and multiplying by 100. RIS were assessed separately for each attribute and each participant and later averaged across the sample.

Subgroup analyses were performed according to sociodemographic characteristics (age (< 60, 60–69, 70–79, ≥ 80 years), sex, marital status (living alone or with a partner)), socioeconomic features (professional qualification (no vocational degree, completed vocational education or (technical) college degree), net monthly household income (< 1500 €, 1,500–3,000 €, > 3,000 €), working status (employed or unemployed/retired) and disease-related characteristics (primary BCC or recurrence, number of current tumours (1 or >1), tumour localization (head/neck, body, both head/neck and body)). Differences in RIS between subgroups were tested for significance with analysis of variance (ANOVA) and Fisher's least significant difference (LSD) *post-hoc* tests. When the assumption of homogeneity of variance was violated the Brown-Forsythe F-ratio was reported. Significance was assumed at $p \leq 0.05$.

Multivariate logistic regression analysis

For each attribute a multivariate regression model calculated standardized regression coefficients (ß) for age, sex, education, tumour localization, recurrence, marital status, working status and income by using the function RIS= $ß_0$+$ß_1$ age+$ß_2$ sex+$ß_3$ education+ $ß_4$ localization+$ß_5$ recurrence+$ß_6$ marital status+$ß_7$ working status+$ß_8$ income. The ß indicates how the values of the RIS change when one independent variable is varied while the others are held constant.

RESULTS

A total of 207 patients with clinically suspected and/or histologically confirmed BCC were invited to participate; 18 refused, mostly due to lack of time, and 189 provided written informed consent. Forty-two participants had to be retrospectively excluded because the clinically suspected diagnosis of BCC was not histologically confirmed and 23 because of inability to complete the survey. Data for 124 participants were included in the final analysis (mean age 69.2 years, 56.5%

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males, 70.2% living with a partner, 19.4% employed; Table SIII[1]). 26.6% had more than one tumour, 14.5% experienced a recurrence, and 42.7% had a history of previous skin cancer. Of the BCC, 87.1% were located in the head/neck region.

Preferences averaged across the study sample

Averaged across all participants, the attribute regarded as most important was recurrence rate (RIS 17.28), followed by cosmetic outcome (RIS 16.19) and cure rate (RIS 15.02), whereas temporary (RIS 3.83) and persistent complications (RIS 3.38) were perceived as least relevant. Among process attributes participants attached greatest value to out-of-pocket costs (RIS 9.61), followed by duration of wound healing (RIS 8.42), type of anaesthesia (RIS 7.34), treatment location (RIS 6.64), kind of wound closure (RIS 6.30) and type of therapy (RIS 6.00) (Fig. 1).

Impact of sociodemographic, socioeconomic, and disease-related factors

The impact of sociodemographic, socioeconomic, and disease-related factors on preferences was assessed in bivariate analyses (Figs S1–S3[1]) and multivariate regression models (Tables I and II). Regarding sociodemographic factors, regression analyses indicated duration of wound healing to gain importance with increasing age (ß = 0.245, $p = 0.049$, Table II). No significant differences were found with respect to sex and marital status (Fig. S1[1], Tables I and II).

Subgroup analyses according to socioeconomic characteristics (professional qualification, working status and income) revealed that the importance attached to duration of wound healing varied with professional qualification ($p = 0.043$). Specifically, participants without a vocational degree cared less about duration of wound healing than those with a (technical) college degree (RIS 7.33 vs. 10.64, $p = 0.008$, Fig. S2A[1]) or a completed vocational education (ß= –0.241, $p = 0.043$ in regression models; Table II). Furthermore, a trend of income group differences regarding costs emerged ($p = 0.077$). *Post-hoc* tests revealed participants with a monthly net household income between 1,500 and 3,000 € to be significantly more concerned about out-of-pocket costs than those with higher income according to descriptive analyses (RIS 11.48 vs. 5.36, $p = 0.018$, Fig. S2C[1]). However, this finding was not significant in multivariate models (Table II). Working status did not significantly influence preferences (Fig. S2B[1]).

Regarding disease-related factors, participants with BCC in the head/neck region attached greater importance of cosmetic outcome than those with tumours both in the head/neck region and on the rest of the body (RIS 17.13 vs. 10.75, $p = 0.028$, Fig. S3A[1]; ß = –0.225, $p = 0.036$, Table I). Participants with recurrent tumours worried less about the risk of recurrence than those with a primary BCC (RIS 12.13 vs. 18.15, $p = 0.028$, Fig. S3B[1]; ß = –0.221; $p = 0.038$) but more about cosmetic outcome (RIS 19.44 vs. 15.64, $p = 0.044$; not significant in regression models). However, they put less emphasis on treatment location (RIS 5.16 vs. 6.89, $p = 0.029$, Fig. S3B[1]; ß = –0.318; $p = 0.003$, Table II) and duration of wound healing (RIS 6.52 vs. 8.74, $p = 0.036$). Subgroup analyses comparing the preferences of participants with 1 or > 1 BCC revealed no significant differences (Fig. S3C[1]).

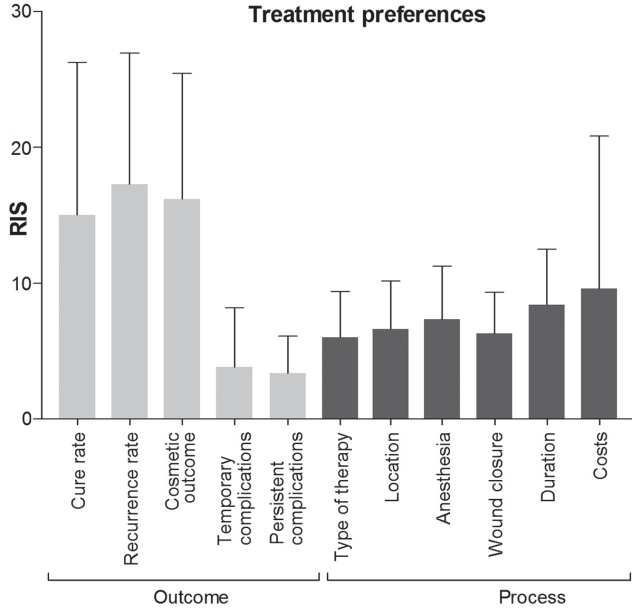

Fig. 1. Relative importance scores (RIS) averaged across the study cohort. The attribute regarded as most important was recurrence rate, followed by cosmetic outcome and cure rate. Bars: means with standard deviations.

DISCUSSION

This study is the first to examine patient preferences for outcome and process attributes of all treatment alternatives available for localized resectable BCC with CA. We show that participants attach greatest importance to low risk of recurrence, high chances of cure and favourable cosmetic outcome. Compared with these attributes, the treatment process appears to be less important, indicating that participants are willing to accept different surgical and non-surgical approaches, types of anaesthesia, methods of wound healing and treatment locations, including inpatient stays in a hospital, in order to optimize chances of cure and favourable appearance. Interestingly, participants worried only a little about complications, although specific examples were given in the CA scenarios.

Treatment preferences for BCC have been examined with CA in 3 studies (22–24). Weston & FitzGerald (24) performed a discrete choice experiment along with a willingness-to-pay analysis in healthy Australians

Table I. *Multivariate linear regression models investigating the impact of sociodemographic, socioeconomic and disease-related characteristics on relative important scores (RIS) of outcome attributes*

	Cure rate		Recurrence rate		Cosmetic outcome		Temporary complications		Persistent complications	
	β	*p*	β	*p*	β	*p*	β	*p*	β	*p*
Age	0.210	0.114	0.044	0.735	–0.011	0.934	–0.133	0.303	–0.099	0.450
Male sex[a]	–0.205	0.116	0.058	0.647	0.069	0.582	–0.090	0.479	0.061	0.637
Living alone[b]	–0.026	0.839	0.044	0.725	–0.065	0.601	–0.164	0.193	–0.064	0.619
Education[c]										
College degree	0.017	0.878	0.037	0.735	–0.163	0.133	0.050	0.647	0.100	0.370
No vocational degree	–0.145	0.253	–0.167	0.176	0.162	0.184	–0.066	0.592	–0.185	0.142
Working[d]	0.026	0.844	–0.085	0.505	0.161	0.206	–0.247	0.056	0.042	0.744
Income[e]										
1,500–3,000 €	–0.025	0.856	–0.141	0.290	–0.002	0.989	–0.160	0.230	–0.196	0.147
>3,000 €	0.062	0.667	–0.166	0.238	0.082	0.553	0.001	0.997	–0.214	0.135
Tumour localization[f]										
Body	0.083	0.456	0.108	0.320	–0.088	0.413	–0.034	0.752	–0.113	0.306
Both head/neck and body	0.039	0.725	0.045	0.677	**–0.225**	**0.036**	–0.049	0.647	–0.045	0.677
Recurrence[g]	–0.033	0.758	**–0.221**	**0.038**	0.089	0.394	0.175	0.099	–0.076	0.479

Reference group: [a]female, [b]participants living with a partner, [c]completed vocational education, [d]not working (i.e. unemployed, retired or homemaker), [e]income <1,500 €, [f]head/neck, [g]primary BCC. RIS was defined as the dependent variable. Age, sex, marital status, education, working status, income, tumour localization and recurrence were included as independent variables. β is the standardized regression coefficient. For the metric variable age, a positive β value indicates that the attribute gains importance with increasing age. For categorical variables (all others), a positive β value signifies that an attribute is more relevant for the respective category than for the reference group. Significant findings are highlighted in **bold**.

($n = 60$) to compare preferences for methyl aminolevulinate photodynamic therapy (MAL-PDT) and simple excision. According to their data, the most important determinant of treatment choice was risk of scarring, compatible with our finding that participants attached great value to cosmetic outcome. The lesion response rate, indicated as 93% for simple excision and 84% for MAL-PDT, had no significant impact, contrasting with the high preferences for cure noted in our cohort. In our experiments the chances of cure were specified with a broader range, i.e. with 98–100% for micrographically controlled excision (15, 36) and <85% for topical therapy and PDT (19, 37, 38), which may partly explain the differences. Moreover, it is possible that interest in cure is greater in patients who are affected by BCC than in the healthy individuals surveyed by Weston & FitzGerald (24), for whom BCC constitutes a theoretical risk.

The second study group, by Tinelli and colleagues, performed discrete choice experiments to examine preferences for imiquimod vs. surgery in participants of the SINS (surgery vs. imiquimod in nodular and superficial basal cell carcinoma) trial from the UK (9, 23). Respondents worried more about cosmetic outcome and side effects than about chance of clearance and cost (23). However, they experienced superficial or nodular

Table II. *Multivariate regression models assessing the influence of sociodemographic, socioeconomic and disease-related characteristics on relative important scores (RIS) of process attributes*

	Type of therapy		Location		Anaesthesia		Wound closure		Duration		Costs	
	β	*p*	β	*p*	β	*p*	β	*p*	β	*p*	β	*p*
Age	0.052	0.702	–0.005	0.971	–0.119	0.372	–0.005	0.968	**0.245**	**0.049**	–0.205	0.103
Male sex[a]	–0.160	0.227	0.032	0.798	0.002	0.986	0.114	0.390	–0.101	0.403	0.210	0.089
Living alone[b]	–0.013	0.921	0.019	0.881	0.026	0.839	0.027	0.836	–0.205	0.089	0.161	0.189
Education[c]												
College degree	0.038	0.739	–0.021	0.845	–0.028	0.800	0.139	0.224	0.167	0.110	–0.061	0.562
No vocational degree	–0.041	0.749	–0.078	0.522	0.088	0.488	0.048	0.708	**–0.241**	**0.043**	0.197	0.101
Working[d]	–0.028	0.834	0.005	0.969	–0.106	0.421	–0.072	0.589	0.166	0.174	0.019	0.879
Income[e]												
1,500–3,000 €	0.011	0.935	–0.099	0.454	0.117	0.389	0.033	0.811	–0.012	0.924	0.212	0.101
>3,000 €	0.081	0.577	0.030	0.828	–0.065	0.652	–0.051	0.724	–0.027	0.841	–0.065	0.632
Tumour localization[f]												
Body	–0.059	0.601	0.022	0.841	–0.128	0.249	0.014	0.902	0.000	0.999	–0.049	0.640
Both head/neck and body	–0.084	0.455	0.017	0.873	–0.013	0.904	0.042	0.711	–0.058	0.573	0.032	0.758
Recurrence[g]	–0.034	0.757	**–0.318**	**0.003**	0.071	0.512	–0.028	0.796	–0.088	0.378	0.138	0.176

Reference group: [a]female, [b]participants living with a partner, [c]completed vocational education, [d]not working (i.e. unemployed, retired or homemaker), [e]income <1,500 €, [f]head/neck, [g]primary BCC. RIS was defined as the dependent variable. Age, sex, marital status, education, working status, income, tumour localization and recurrence were included as independent variables. β is the standardized regression coefficient. For the metric variable age, a positive β value indicates that the attribute gains importance with increasing age. For categorical variables (all others), a positive β value signifies that an attribute is more relevant for the respective category than for the reference group. Significant findings are highlighted in **bold**.

BCC in low risk areas and not tumours on the central face. By contrast, most of our participants had a BCC in the head/neck region and/or a large tumour.

Both the study by Weston & Fitzgerald and the trial by Tinelli et al. identified adverse events, in particular, infections (24) or pain (23), as strong drivers in decision-making, conflicting with our results. We did not address pain. However, we believe that given the mostly complicated localization and large size of their BCC our participants were prepared to trade a certain risk of complications for increased chances of cure and favourable cosmetic outcome.

Essers et al. (22) conducted CA, comparing the attributes of Mohs surgery vs. simple excision in healthy Dutch individuals. As expected participants preferred surgical treatment with lower probability of recurrence, shorter surgery time, shorter travelling time, shorter waiting time, no risk of re-excision and lower cost. The strongest driver for choosing a specific scenario was reduction in recurrence rate, well in accordance with our findings.

Sociodemographic characteristics did not significantly impact preferences in our sample, in line with data from Weston & FitzGerald (24), except for the finding that older participants considered duration of wound healing more relevant than younger ones. Performing dressing changes at home, or visiting physicians for this purpose, may be more troublesome for older patients, making them more interested in rapid wound healing.

Among the process attributes presented in our study, out-of-pocket costs were considered most important, particularly by participants with intermediate household income. By contrast, according to the study by Tinelli et al. (23) costs had the least impact on choice. These divergent attitudes towards out-of-pocket costs might be ascribable to differences in the healthcare systems and reimbursement policies. In Germany all treatment costs for BCC, except costs for PDT and expenses for certain kinds of wound dressings, are covered by statutory health insurance. Therefore, patients from Germany may be less willing to pay out-of-pocket costs than patients from other countries.

Participants with BCC in the head/neck region valued cosmetic outcome more than participants with tumours both in the head/neck area and on other parts of the body. It is self-explanatory that the appearance of the face is more important than the appearance of other body regions that can be covered by clothes. In addition, preferences of patients with several BCC in different body regions may shift due to other concerns.

Our finding that participants with recurrent BCC were willing to trade a higher risk of recurrence in favour of a better cosmetic outcome is, at first glance, surprising. However, it is highly conceivable that patients with recurrent BCC are less afraid of relapse than those with a primary BCC because they have already had the experience that their BCC was not life-threatening and did not metastasize. Compatible with our findings, Tinelli and colleagues (23) reported that participants who had experienced treatment of BCC attached greatest importance to cosmetic outcome, whereas inexperienced participants were more afraid of side effects.

A major limitation of our study is the monocentric setting. Our cohort predominantly contains patients with BCC in challenging localizations and/or with large tumours. Therefore, it is representative of a collective from a university medical centre, but not from a dermatological practice. Most of the participants were referred for surgery, which implies selection bias towards preferences for the attributes of surgery, e.g. high interest in cure. Some participants, in particular elderly ones, had difficulties in understanding the CA exercises despite assistance and therefore had to be excluded. However, data from participants included the final analysis are reliable, as participants making random choices could have been identified through fixed choices with a single clearly superior scenario.

In conclusion, patients with BCC from a tertiary care centre particularly appreciate cure and cosmetic outcome, although preferences vary depending on individual and tumour-associated characteristics. Considering that BCC is not immediately life-threatening and mostly takes a relatively benign course, patients' concerns (40), preferences and patient-reported outcomes (41–43) for treatment of this tumour need to be integrated into shared decision-making in order to optimize treatment satisfaction, compliance and ultimately outcome.

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