Quality-of-Life Outcomes of Treatments for Cutaneous Basal Cell Carcinoma and Squamous Cell Carcinoma

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Quality of life is an important treatment outcome for conditions that are rarely fatal, such as cutaneous basal cell carcinoma and squamous cell carcinoma (typically called nonmelanoma skin cancer (NMSC)). The purpose of this study was to compare quality-of-life outcomes of treatments for NMSC. We performed a prospective cohort study of 633 consecutive patients with NMSC diagnosed in 1999 and 2000 and followed for 2 years after treatment at a university-based private practice or a Veterans Affairs clinic. The main outcome was tumor-related quality of life 1 to 2 years after therapy, measured with the 16-item version of Skindex, a validated measure. Skindex scores vary from 0 (best) to 100 (worst) in three domains: Symptoms, Emotions, and Function. Treatments were electrodessication and curettage (ED&C) in 21%, surgical excision in 40%, and Mohs surgery in 39%. Five hundred and eight patients (80%) responded after treatment. Patients treated with excision or Mohs surgery improved in all quality-of-life domains, but quality of life did not improve after ED&C. There was no difference in the amount of improvement after excision or Mohs surgery. For example, mean Skindex Symptom scores improved 9.7 (95% CI: 6.9, 12.5) after excision, 10.2 (7.4, 12.9) after Mohs surgery, and 3.4 (−0.9, 7.6) after ED&C. We conclude that, for NMSC, quality-of-life outcomes were similar after excision and Mohs surgery, and both therapies had better outcomes than ED&C.

Journal of Investigative Dermatology (2007) **127,** 1351–1357. doi:10.1038/sj.jid.5700740; published online 15 February 2007

INTRODUCTION

Basal cell carcinoma and squamous cell carcinoma of the skin, typically called nonmelanoma skin cancer (NMSC), are the most common malignancies. The conventional goal of treatment is prevention of tumor recurrence, but quality of life and costs are also important outcomes because NMSC only rarely affects survival.

Existing data about outcomes are insufficient to guide therapy for most NMSCs (Thissen *et al.*, 1999; Bath-Hextall *et al.*, 2004), and there is substantial unexplained variation in performance rates of therapies in different settings (Chren *et al.*, 2004). Each of the common therapies can prevent recurrence for many NMSCs (NCCN, 2005; Rubin *et al.*, 2005). Some data indicate that recurrence rates are lowest after Mohs surgery (Rowe, 1995; Smeets *et al.*, 2004b), but early results of a recent randomized trial for basal cell carcinomas demonstrated no significant difference in tumor recurrence at 30 months after excision or Mohs surgery (Smeets *et al.*, 2004a), findings that have been controversial (Otley, 2005). With respect to costs, electrodessication and curettage (ED&C) is the least expensive therapy (Joseph *et al.*, 2001); in a recent European cost comparison, Mohs surgery was significantly more costly than excision (Essers *et al.*, 2006), results that conflict with other findings (Cook and Zitelli, 1998; Welch *et al.*, 1999). Finally, although NMSC is highly prevalent and generally nonfatal, the specific effects of treatments on quality of life are not known.

The purpose of this work was to measure and compare quality-of-life outcomes of the three most common therapies for basal cell carcinoma and squamous cell carcinoma of the skin. We performed a prospective cohort study of 633 consecutive patients with NMSC diagnosed in 1999 and 2000 and followed for 2 years after treatment at a university-based private practice or a Veterans Affairs (VA) clinic. The main outcome was tumor-related quality of life 1 to 2 years after therapy, measured with the 16-item version of Skindex (Chren *et al.*, 2001). Skindex scores vary from 0 (best) to 100 (worst) in three domains: Symptoms, Emotions, and Function.

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Abbreviations: ED&C, electrodessication and curettage; NMSC, nonmelanoma skin cancer; VA, Veterans Affairs

Received 29 September 2006; revised 27 November 2006; accepted 14 December 2006; published online 15 February 2007

RESULTS

Baseline characteristics

Patients treated with the three therapies were similar in age, but patients treated with Mohs surgery were more likely than those treated with ED&C or excision to be female, with smaller tumors, located in the H-zone of the face. Patients treated with excision were more likely to be poor, to have had squamous cell carcinomas, and to have been treated at the VA. Before therapy, patients whose tumors were ultimately treated with Mohs surgery reported worse Emotional quality-of-life effects of their tumors than patients treated with the other therapies (Table 1).

Change in tumor-related quality of life at 2 years after therapy

Of 633 patients, 508 (80%) responded about tumor-related quality of life at 12, 18, or 24 months after treatment. Those who responded after treatment were similar to nonresponders in multiple characteristics examined, including age, gender, income, baseline tumor-related quality of life, tumor type, tumor diameter, tumor location on the body, type of treatment received, and whether the treatment was performed by an attending physician, resident physician, or nurse practitioner.

Within-treatment group comparisons. Patients treated with excision or Mohs surgery experienced statistically significant ($P<0.05$) improvements in all three quality-of-life domains after therapy (Figure 1, Table 2). For example, after excision and Mohs surgery, mean adjusted Symptoms scores improved by 9.7 and 10.2 points, respectively, and Emotions scores improved by 18.6 and 21.7 points, respectively. Patients treated with ED&C experienced no change in tumor-related quality of life.

Table 1. Characteristics of 633 patients with nonrecurrent NMSCs[1]

	Type of therapy			
Characteristic	**ED&C (*n*=136)**	**Excision (*n*=251)**	**Mohs (*n*=246)**	***P***
Patient characteristics				
Age in years, mean±SD	65 (16)	68 (14)	65 (15)	0.085
Gender male (%)	79	82	70	0.005
Annual income less than $30,000 (%)	45	61	52	0.011
Health status (SF-12)				
Physical Component Score, mean±SD	46.1 (12.2)	44.8 (11.8)	46.2 (11.1)	0.374
Mental Component Score, mean±SD	49.3 (11.0)	48.3 (11.2)	48.5 (10.7)	0.673
Comorbidity (Charlson index), mean±SD	2.1 (2.7)	2.3 (2.8)	2.2 (3.1)	0.768
History of previous NMSC (%)	60	57	48	0.032
Baseline Skindex subscale scores (±SD)				
Symptoms	19.6 (23.6)	21.7 (23.2)	21.8 (23.5)	0.651
Emotions	33.0 (28.0)	38.9 (30.4)	46.3 (27.0)	<0.0001
Functioning	12.1 (21.7)	15.1 (24.6)	14.0 (21.1)	0.482
Number of NMSCs at enrollment, mean±SD	1.3 (0.7)	1.2 (0.6)	1.4 (0.9)	0.088
Tumor characteristics				
Histological type (%)				
Basal cell carcinoma	82	69	83	0.001
Squamous cell carcinoma	18	31	17	
Tumor diameter, mm, mean±SD	9.3 (5.4)	12.0 (13.4)	8.6 (5.8)	0.0006
Tumor present in the 'H-zone' of the face, %	11	32	71	<0.001
Characteristics of care				
Treating clinician type (%)				
Attending physician	61	47	98	<0.0001
Resident physician	30	52	2	
Nurse practitioner	9	1	0	
Practice site, private practice (%)	60	37	60	<0.001

ED&C, electrodessication and curettage; NMSC, nonmelanoma skin cancer; SD, standard deviation.
[1]Number of missings for each characteristic: age 0, gender 0, income 46, health status 47, comorbidity 0, history of NMSC 0, symptoms 14, emotions 3, functioning 5, number of NMSCS 0, histological type 0, diameter 85, H-zone 1, treating clinician type 29, practice site 0.

Between-treatment group comparisons: entire sample. In pair-wise comparisons of the treatment groups, both excision and Mohs surgery were significantly better than ED&C in improvements in Symptoms, Emotions, and Functioning (Table 3). For example, for the Emotional domain, the difference in mean adjusted change scores for excision and Mohs surgery compared to ED&C was 13.2 and 16.3, respectively ($P \leqslant 0.001$). Smaller but statistically significant pair-wise differences were found between both excision and Mohs surgery compared to ED&C for the Symptoms and Functioning domains. Excision and Mohs surgery did not differ, however, in their effects on any domain of tumor-related quality of life (Table 3). These findings were similar in subgroups of tumors located on the face ($n = 326$), or on other parts of the body (results not shown).

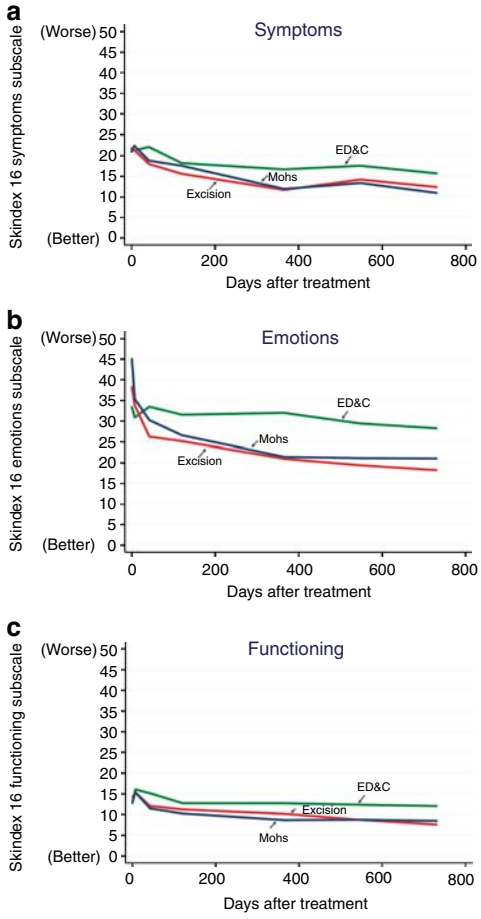

Figure 1. Quality-of-life outcomes of treatment for NMSC. For groups of patients with NMSC treated with ED&C, excision, or Mohs surgery, mean scores of the (**a**) symptoms, (**b**) emotions, and (**c**) functioning subscales of Skindex-16 are plotted over time from before treatment for NMSC, to 2 years after treatment.

Between-treatment group comparisons based on propensity for treatment. Similar results were also found in subgroups of patients matched for propensity for treatment (Table 4). For the Emotional domain, both excision and Mohs surgery resulted in improved scores compared to ED&C; differences in Symptoms and Functioning were not significant. There was no difference comparing excision and Mohs surgery in mean adjusted change scores in any domain of tumor-related quality of life.

DISCUSSION

In patients with NMSC, tumor-related quality of life improved after excision or Mohs surgery but not after ED&C. Moreover, for all domains of tumor-related quality of life, the improvement was similar after excision and Mohs surgery, two common therapies that vary significantly in cost.

Despite the prevalence of NMSC, there is no evidence-based consensus about optimal therapy for the majority of tumors (Thissen *et al.*, 1999; Bath-Hextall *et al.*, 2004). In fact, we have previously reported significant variation in treatments for NMSC in different practice sites (Chren *et al.*, 2004). Mohs surgery was over twice as likely to be performed in a private setting as in a VA clinic, even though all therapies were available at both sites and many clinicians practiced at both sites. This variation was unexplained by patient, tumor, or clinician variables that might likely affect treatment choice. The current study, comparing quality of life in

Table 2. Improvement in Skindex scores after treatments for NMSC: within-treatment group comparisons

	Improvement in Skindex score after therapy, mean (95% confidence interval)					
	Unadjusted			Adjusted[1]		
Treatment group (n)	Symptoms	Emotions	Functioning	Symptoms	Emotions	Functioning
ED&C (105)	3.8 [−0.1,7.7]	3.2 [−1.1, 7.5]	−0.4[2] [−3.8, 3.1]	3.4 [−0.9,7.6]	5.4 [−0.2,11.0]	−1.9[2] [−6.0,2.3]
Excision (204)	8.5**** [5.6,11.5]	16.9**** [13.2,20.6]	4.2** [1.7,6.7]	9.7*** [6.9,12.5]	18.6*** [15.1,22.2]	3.3* [0.7,5.9]
Mohs (195)	9.6**** [6.5,12.7]	23.8**** [20.3,27.3]	5.3*** [2.5,8.1]	10.2*** [7.4,12.9]	21.7*** [18.1,25.3]	5.0*** [2.4,7.6]

ED&C, electrodessication and curettage; NMSC, nonmelanoma skin cancer.
[1]Adjusted for age, gender, income, history of previous NMSC, baseline Skindex subscale score, tumor type, tumor diameter, tumor location in the H-zone of the face, treatment type, whether the treatment was performed by an attending physician, resident physician, or nurse practitioner, and whether the practice setting was the private or the VA site.
[2]Negative score indicates worsening in Skindex score.
*Significantly different change from pretreatment value, $P \leqslant 0.05$.
**Significantly different change from pretreatment value, $P \leqslant 0.01$.
***Significantly different change from pretreatment value, $P \leqslant 0.001$.
****Significantly different change from pretreatment value, $P \leqslant 0.0001$.

Table 3. Differences in Skindex scores after treatments for NMSC: between-treatment group comparisons in entire sample

	Differences between treatment groups in Skindex scores after treatment, mean (95% confidence interval)[1]					
	Unadjusted			Adjusted[2]		
Comparison	Symptoms	Emotions	Functioning	Symptoms	Emotions	Functioning
Excision *vs* ED&C	4.7 [−0.2,9.7]	13.7**** [7.7,19.7]	4.6* [0.3,8.8]	6.3* [1.3,11.3]	13.2*** [6.8,19.7]	5.2* [0.4,10.0]
Mohs *vs* ED&C	5.8* [0.8,10.8]	20.6**** [14.9,26.3]	5.7* [1.1,10.2]	6.8* [1.5,12.1]	16.3*** [9.4,23.3]	6.9** [1.7,12.0]
Mohs *vs* excision	1.1 [−3.2,5.3]	7.0** [1.9,12.1]	1.1 [−2.7,4.8]	0.5 [−3.9,4.9]	3.1 [−2.6,8.8	1.7 [−2.5,5.8]

ED&C, electrodessication and curettage; NMSC, nonmelanoma skin cancer.
[1]Positive difference indicates first treatment had improved score compared with second treatment.
[2]Adjusted for age, gender, income, history of previous NMSC, baseline Skindex subscale score, tumor type, tumor diameter, tumor location in the H-zone of the face, treatment type, whether the treatment was performed by an attending physician, resident physician, or nurse practitioner, and whether the practice setting was the private or the VA site.
*Significantly different mean change scores between treatment groups, $P \leqslant 0.05$.
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***Significantly different mean change scores between treatment groups, $P \leqslant 0.001$.
****Significantly different mean change scores between treatment groups, $P \leqslant 0.0001$.

Table 4. Differences in Skindex scores after treatments for NMSC: between-treatment group comparisons in pairs matched for propensity for treatment

	Differences between treatment groups in Skindex scores after treatment, mean (95% confidence interval)[1]		
Comparison (No. of pairs)	Symptoms	Emotions	Functioning
Excision *vs* ED&C (51 pairs)	−1.6 [−9.8,6.7]	13.2* [3.3,23.1]	3.1 [−3.5,9.8]
Mohs *vs* ED&C (24 pairs)	9.2 [−2.1,20.5]	23.6** [10.1,37.2]	3.7 [−4.6,12.0]
Mohs *vs* excision (81 pairs)	4.0 [−3.1,11.1]	3.4 [−3.8,10.7]	4.2 [−2.3,10.8]

[1]Positive difference indicates first treatment had improved score compared with second treatment; negative difference indicates first treatment had worse score compared with second treatment.
*Significantly different mean change scores between treatment groups, P=0.0230.
**Significantly different mean change scores between treatment groups, P=0.0029.

different treatment groups, contributes important data about outcomes to inform a consensus about care for NMSC.

The inferiority of electrodessication/curettage compared to the other treatments with respect to improving tumor-related quality of life is not surprising. ED&C often leaves scars that are larger than the tumor being treated, and which may themselves affect skin-related quality of life.

The similarity in improvement in tumor-related quality of life after excision and Mohs surgery is important and is consistent across quality-of-life domains. The results are surprising because, conventionally, a major advantage to Mohs surgery is believed to be that it is ''tissue-sparing,'' in that tissue without histological evidence of tumor is preserved. Our finding is consistent, however, with results from a recent randomized trial for basal cell carcinoma in which the two therapies were found to have similar cosmetic outcomes (Smeets *et al.*, 2004a) and similar generic quality-of-life outcomes (Essers *et al.*, 2006).

In addition, our results expand the previous findings about quality of life after NMSC therapy. The previous study had compared the responses of a subset of patients in a randomized trial (110 patients, 27% of the sample) to two generic instruments (Essers *et al.*, 2006). Overall changes in the scores were very small. This finding is not surprising as generic instruments may lack sensitivity to quality-of-life effects of specific conditions (Patrick and Deyo, 1989). Using a skin-specific instrument we demonstrated that, in a substantially larger sample of patients, both excision and Mohs surgery improved tumor-related quality of life in all domains, and that ED&C did not improve quality of life in any domain.

In the US, NMSC is the fifth most costly cancer to treat in the Medicare population (after lung, prostate, colon, and breast) (Housman *et al.*, 2003), and Mohs surgery is commonly used (overall, about 30% of facial basal cell carcinomas are treated with Mohs surgery (Smeets, 2005)). ED&C is the least expensive method of treatment. A recent European cost comparison using microcosting techniques determined that costs for Mohs surgery were significantly higher than those of excision (average costs $898 *vs* $700 (@0.79 Euros/dollar)) (Essers *et al.*, 2006). Given the high prevalence of NMSC and the difference in costs among

treatments, the similarity of quality-of-life outcomes after excision and Mohs has potentially important health policy implications.

This observational study of effectiveness was not a randomized trial, and patients and tumors differed in the three treatment groups. Comparisons were adjusted for baseline differences, however, and the results were similar after analyses using propensity score techniques that permitted comparison of patients with similar measured covariates for the performance of different treatments. On the other hand, unmeasured factors could have affected both choice of therapy and quality-of-life outcomes. For example, we did not measure patients' pretreatment preferences or expectations for different therapies (which may affect patient-reported outcomes) (Peck *et al.*, 2001). It is likely, however, that these aspects of patients' experience affect patient satisfaction with therapy, rather than tumor-related quality of life, which was the outcome measured in this study. Finally, although the sample is typical of most patients with NMSC, the study was conducted in a single city at one academic program, and may not be generalizable to other locations.

Conclusion

For NMSC, quality-of-life outcomes were similar after two common therapies, excision and Mohs surgery, and both therapies had better outcomes than ED&C. Although Mohs surgery is the most expensive therapy, it is thought to be worth the extra costs, in part because it is ''tissue-sparing''. We found that patients did not perceive any difference in the effects of tumor or treatment on their well-being after Mohs surgery compared with excision, even after adjusting for many features of patient, tumor, and care. Although evidence-based care for NMSC will require long-term data about tumor recurrence, these results about quality-of-life outcomes can inform decisions by physicians and patients about these common nonfatal cancers.

MATERIALS AND METHODS

Design, setting, and subjects

This study was approved by the Committee on Human Research of the University of California at San Francisco, according to the Declaration of Helsinki Principles. Tumors were identified by daily review of pathology records at both hospitals. A dermatopathologist was available at both sites. Nonmelanoma skin cancers were defined as those with final histopathological diagnoses of basal cell carcinoma or squamous cell carcinoma. Because recurrent NMSCs are considered more aggressive and at significantly higher risk for poor outcomes than are primary tumors, we eliminated 204 tumors described by the clinician in the medical record as 'recurrent' or 'possibly recurrent'. We also eliminated 61 tumors that were treated with uncommon therapies such as laser or cryotherapy. The total number of patients with nonrecurrent NMSC treated with the three major therapies at the two hospitals during the study period was 1314.

Patients with tumors diagnosed during the study period were enrolled if they had a current mailing address and if, before treatment, they responded to a questionnaire about their tumor-related quality of life. Participants gave their written informed consent. The sample for this study consisted of those 633 patients on which quality-of-life responses were available before treatments. A minority (130 patients, 21%) had more than one tumor diagnosed at enrollment; to measure tumor-related quality of life specific to a single tumor, we asked each patient to respond only about effects related to the tumor that bothered him or her the most. Patients who were enrolled were similar to those not enrolled in age, tumor histological type, tumor diameter, tumor location on the body, and type of treatment received. Enrolled patients were, however, more likely to be male (77 *vs* 69% of those not enrolled, $P=0.002$), to have had a history of previous NMSC (54 *vs* 47%, $P=0.016$), to have been treated at the VA (49 *vs* 31%, $P<0.0001$), and to have had the tumor biopsy performed by a nurse practitioner (19 *vs* 12%, $P=0.001$). No data were collected about tumors that were diagnosed after enrollment.

Data collection and measures

Chart information. Using structured dataforms, trained research staff collected data from clinician notes and pathology records. Data about tumors included clinical descriptions and location on the body, including whether they were located in the 'H' zone of the face, a cosmetically important location on the mid-face in which tumors are believed also to be at particularly high risk for recurrence (Swanson *et al.*, 1983).

Survey instrument. All patients were surveyed by mail before treatment and at 1 week, 6 weeks, and 3, 12, 18, and 24 months after treatment. Patients' reports of sociodemographic characteristics, health status, and comorbidity were measured before treatment; tumor-related quality of life was measured before and at each point after treatment. Annual income was assessed by a patient's response to a single item; response choices were six categories of income, from less than $15,000 to more than $75,000; for comparisons, these data were dichotomized to less than or greater than or equal to $30,000 (the median income of the sample).

Health status was measured with an adapted version of the Medical Outcomes Study SF-12 instrument (Ware *et al.*, 1996). Scores on the SF-12 are reported as a Physical Component Summary Scores and a Mental Component Summary Score; on these scales, higher is healthier and norm-based standardized scores have means of 50 in the general US population. Comorbidity was measured by a version of the Charlson instrument adapted for patient response (Charlson *et al.*, 1987; Katz *et al.*, 1996).

Tumor-related quality of life before therapy and at all points after treatment was measured with the 16-item version of Skindex, a validated measure (Chren *et al.*, 2001). Skindex-16 inquires about potential effects of skin conditions on quality of life; patients choose from seven response choices, anchored by ''Never bothered'' and ''Always bothered''. For example, items inquire about itching, hurting, worry, frustration, and effects on daily activities. Skindex responses are reported as three subscales, addressing three domains: Symptoms, Emotional effects, and effects on social and physical Functioning; scores vary from 0 (least effect on quality of life) to 100 (most effect on quality of life). For this study, patients were asked to respond specifically about quality-of-life effects of their skin cancer and its treatment; we did not specifically inquire about the quality-of-life effects of scar compared to other potential results of the

treatment. To ensure that patients responded over time about quality-of-life effects of the same tumor (even if they had multiple tumors, either at enrollment or subsequently), for each patient with multiple tumors we used a map on which the tumor in question was marked. In addition, the instructions prompted patients to respond about the tumor that was treated ''x'' months ago (at the time of enrollment in the study).

The minimal clinically meaningful change in Skindex scores was determined as follows. In 485 patients from the sample, Skindex-16 scores before and 1 week after treatment were compared with their responses to a global question with seven response choices about overall bother from the skin cancer. A difference in one response choice to the global question was assumed to correspond to the minimal clinically meaningful difference (Guyatt *et al.*, 1993, 2002; Juniper *et al.*, 1994; Sprangers *et al.*, 2002). Based on this analysis, the minimal clinically meaningful difference in all Skindex subscales was 10 points, and changes for improvement or deterioration were similar.

Analytic strategy

Our analytic strategy was, first, to compare baseline clinical features of patients and tumors treated with the three therapies. Differences between treatment groups were evaluated using Fisher's exact test for dichotomous variables, χ^2 test for categorical variables, and analysis of variance for continuous variables.

For each Skindex subscale and each patient, we defined change in tumor-related quality of life after treatment as the average difference between the baseline subscale score, and the subscale scores at 12, 18, or 24 months. The rationale for this strategy was that quality of life likely stabilizes after 12 months after treatment, and using the average of the three time points permitted us to include patients who responded at any of the final follow-up times.

We used multivariable models to evaluate changes in tumor-related quality of life after treatment, adjusted for pretreatment features. To accommodate unequal numbers of follow-up observations from patients, we used mixed effects models, with random effects corresponding to each patient. For each subscale, we modeled the change from baseline subscale score to the subscale score after treatment. In adjusted models, we included the following explanatory variables: age, gender, income, history of previous NMSC, baseline Skindex subscale score, tumor type, tumor diameter, tumor location in the H-zone of the face, treatment type, whether the treatment was performed by an attending physician, resident physician, or nurse practitioner, and whether the practice setting was the private or the VA site.

Because of differences in observed characteristics in the three treatment groups, we also used propensity score methods to adjust for differences between patients that would relate to choice of treatment (Rubin, 1997; D'Agostino, 1998). We calculated propensity scores for patients in each of the three pair-wise treatment comparisons (excision *vs* ED&C, Mohs surgery *vs* ED&C, and Mohs surgery *vs* excision). These propensity scores were determined using a logistic regression model for treatment in which independent variables included all patient, tumor, and care characteristics that were associated with actual treatment choice in bivariable analyses, or that we thought might likely be associated with treatment choice. These variables were patient age, gender, income, history of previous NMSC, baseline Skindex Emotions subscale score, tumor type, tumor diameter, tumor location in the H-zone of the face, presence of histological risk factors for tumor recurrence (NCCN, 2005), whether the patient had more than one NMSC, whether the biopsy was performed by an attending physician, resident physician, or nurse practitioner, and whether the practice setting was the private or the VA site. For each of the three pair-wise comparisons, we created matched pairs of patients based on propensity score, using a Greedy 5-to 1 digit-matching algorithm (Parsons, 2001). We then compared change in Skindex-16 scores in the groups of matched pairs.

Statistical analyses were performed using Stata Statistical Software, Release 9.

CONFLICT OF INTEREST

The authors state no conflict of interest.

ACKNOWLEDGMENTS

This work was supported by an Investigator-Initiated Research Grant (IIR 97010-2) and the Health Services Research Enhancement Award Program (REAP) of the Health Services Research and Development Service of the Department of Veterans Affairs, and by an Independent Scientist Award (No. K02 AR 02203-01) from the National Institute of Arthritis and Musculoskeletal and Skin Diseases, National Institutes of Health.

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