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Comorbidity scores associated with limited life expectancy in the very elderly with nonmelanoma skin cancer

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Abstract

Background—There is controversy regarding nonmelanoma skin cancer (NMSC) treatment in the very elderly, with some suggesting that this population may not live long enough to benefit from invasive treatments. Tools to assess limited life expectancy (LLE) exist, but performance in the very elderly NMSC population has not been well-defined.

Objective—Define comorbidity scores associated with LLE in the very elderly presenting for management of NMSC.

Methods—A retrospective review of 488 patients aged 85 or older presenting for NMSC management between July 1999 through December 2014 was performed. Comorbidities were scored using Adult Comorbidity Evaluation-27 (ACE-27) and age-adjusted Charlson Comorbidity Index (ACCI). Dates of death, follow-up, and overall survival were determined.

Results—ACE-27 and ACCI scores were associated with overall survival: scores of 3 and 7+, respectively, were associated with <50% survival at 4 years. Mohs surgery patients survived a median of 20 months longer than non-Mohs patients.

Limitations—Retrospective study design. Referral bias.

Conclusions—ACE-27 and ACCI predicted LLE. The cohort presenting for MMS had improved survival, despite similar inter-cohort comorbidity. This suggests that additional factors contributed to survival, and that age and comorbidities alone are inadequate for making NMSC treatment decisions in the very elderly.

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Conflicts of Interest

None

Meeting Presentation

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IRB Approval

This study was approved by the Memorial Sloan Kettering Cancer Center IRB.

Keywords

skin cancer; Mohs micrographic surgery; comorbidity; NMSC; elderly; limited life expectancy

Introduction

Very elderly patients (defined as age 85 or older) account for approximately 20% of the 3.3 million people treated for nonmelanoma skin cancer (NMSC) each year in the United States.¹⁻⁴ The population 85 years and older is projected to increase from 5,887,000 in 2012 to 17,978,000 in 2050.⁵ Given the predilection for NMSC to develop in the older population due to cumulative sun exposure, the incidence of NMSC is also expected to increase.

Nonmelanoma skin cancer, most frequently basal cell carcinoma (BCC) and squamous cell carcinoma (SCC), is rarely fatal but without treatment may grow over time and become symptomatic.⁶⁻⁸ However, some have suggested that the very elderly population may not live long enough to benefit from treatment.⁹⁻¹² Defining limited life expectancy (LLE) in this population presents two challenges: First, what should be considered LLE in an elderly person presenting with NMSC? Various estimates from life expectancy <1 year to <5 years have been associated with this term, but there is no consensus among the dermatologic community. As the natural history of untreated BCC and low risk SCC have not been well-studied, clinicians cannot always predict which tumors will behave indolently and which will progress to cause problems for the patient. Secondly, while calculators and algorithms exist to better define life expectancy, the select population being referred and considered for treatment of NMSC may perform differently than other populations. To help guide management decisions in this population, a shared decision making approach, which includes the assessment of comorbidities, has been proposed.⁹ The Adult Comorbidity Evaluation-27 (ACE-27) and the Age-Adjusted Charlson Comorbidity Index (ACCI) are two validated indices used to predict survival in diverse cancer populations including the head and neck cancer and skin cancer populations.¹³⁻¹⁵ However, guidelines for use of the ACE-27 and the ACCI for predicting limited life expectancy have not been established in the very elderly presenting for skin cancer.

To guide the shared decision-making approach in the very elderly with NMSC, and for researchers studying this topic, this study was undertaken with the following objective: identify an ACCI and ACE-27 score that identifies patients age 85 years or older presenting for management of NMSC with LLE. For the purposes of this study, a conservative estimate of LLE will be defined as less than 50% expected survival in 4 years.

Methods

Patient Selection

This was a single center retrospective study of prospectively-collected patients aged 85 years or older who underwent Mohs micrographic surgery (MMS) for NMSC with three surgeons in a dermatologic surgery service between July 1999 and December 2014. A retrospective search using an institutional database was performed to identify patients who presented to

the service with NMSC and did not undergo MMS during that time period. Patient demographics, tumor characteristics, and surgical details were recorded following chart review. Tumor anatomic risk was defined using the National Comprehensive Cancer Network guidelines.¹⁶ For those patients who did not have MMS, reason for treatment choice was noted.

Comorbidity Assessment

Electronic medical records were reviewed and comorbidities were scored using the ACE-27 and the ACCI. Comorbidities recorded in the consult note were considered if diagnosed on or before the date of consult. For the ACE-27, 27 comorbidities were assessed by the following scale: grade 0 = no disease, grade 1 = mild decompensation, grade 2 = moderate decompensation, and grade 3 = severe decompensation. An overall comorbidity grade between 0–3 was determined. For the ACCI, a score was calculated based on age at date of surgery and on the presence or absence of 19 conditions, which are each assigned a different point value between 1–6. To age-adjust, for each decade over age 40, an additional point is added to the score. Therefore, our patient population of age 85 and above had between 4 and 5 points added to the original CCI score for age.

Follow-up and Survival

An institutional database search was conducted to collect last follow-up with a dermatologist, last follow-up at MSKCC, and date of death. For patients who had MMS, time began at date of surgery. For patients who did not elect to have MMS, time began with the date of MMS consult. Elapsed time was calculated until death or last follow-up. Participants were considered censored if they were alive or lost to follow-up at the date of last assessment. Alpha was set at 5%, and all analyses were two-tailed. Analyses were performed using StataSE version 14.1 (College Station, TX, USA). Overall survival was determined for all participants. For univariate assessments of overall survival, Kaplan-Meier survival curves, stratified by MMS status, were created.

Patient characteristics were summarized by procedure status (MMS vs. no MMS). Student T-tests and χ^2 tests were used to assess differences in the distribution of patient characteristics, surgical procedure characteristics and patient comorbidity scores for continuously- and categorically-scaled variables. For univariate assessments of overall survival, Kaplan-Meier survival curves, stratified by MMS status, were created. Log-rank tests were used to assess the equality of the unadjusted survivor functions. In addition, Cox proportional hazards regression was used for the analysis of overall survival time.

Results

Patient and lesion characteristics

A total of 488 patients aged 85 years or older were included in the study. Of these, 371 of 10,103 total patients who presented for MMS were aged 85 years or older. An additional 117 patients aged 85 years or older were seen for MMS consultation but did not pursue MMS. Characteristics of the study participants and the presenting skin cancer are presented in Table 1. The mean age was 88.1 years and the majority were female (52.5%). The majority

of lesions were located on the head and neck (nose 19.7%, scalp 8.6%, ear 5.1%, periocular 4.5%, lip 3.5%, neck 2.1%, and other face 30.1%), followed by the extremity (16.6%) and trunk (6.4%).

Comorbidity

As listed in Table 2, the most frequent comorbidities according to the ACE-27 were hypertension (72.7%) followed by solid tumor malignancy (56.1%) and coronary artery disease (22.1%). The mean ACE-27 score was 1.47, while the mean ACCI score was 6.1. Patients who were seen for consult but did not undergo MMS had similar mean ACE-27 and ACCI scores as those who underwent MMS (1.47 vs. 1.47, $p=0.64$ and 6.2 vs. 6.1, $p=0.60$).

Survival

The patient cohort was followed for a total of 1631 person-years. During the follow-up period, 230 (47%) patients died with a mean age of death of 93.5 years. 54 (46%) patients died in the non-MMS group and 176 (47%) in the MMS group. The Kaplan Meier survival curves for MMS and non-MMS patients are presented in Figure 1. Patients who underwent MMS had a median survival of 67 months compared with 47 months in non-MMS patients, $p=0.004$. Both the ACCI and the ACE-27 scores were significantly associated with overall survival. Since ACCI and ACE-27 were highly correlated, separate Cox proportional hazard models were created.

After controlling for age, sex, anatomic site of tumor based on risk for recurrence, and comorbidities through ACCI, the patients in the MMS group had significantly better survival compared to the non-MMS group ($HR=0.63$, 95% CI:0.46–0.86). Similar results were observed for the Cox model substituting ACE-27 scores for ACCI ($HR=0.59$, 95% CI:0.43–0.81). Higher ACCI and ACE-27 were both significantly associated with poorer survival. Each one-point increase in ACCI score was associated with a 16% increase in mortality ($HR=1.16$, 95% CI:1.09–1.24), while each one point increase in ACE-27 was associated with a 21% increase in mortality ($HR=1.21$, 95% CI:1.13–1.30). The Cox models were assessed and met the assumption of proportionality. Hazard estimates for death based on their overall ACE-27 and ACCI scores are presented in Figures 2 and 3.

Discussion

Life expectancy is estimated to increase from 6 to 7 years in men, and from 7.1 to 8.5 years in women aged 85 years between 2012 and 2050.⁵ With life expectancy and the proportion of the very elderly population projected to increase in the United States, the management of non-life-threatening illnesses, such as skin cancer, will increasingly be relevant. In this study, patients presenting to a tertiary cancer center for MMS had a mean age of death of 93.5 years; longer than the predicted national life expectancies of 76.4 years for males and 81.2 years for females.¹⁷ This elderly group presenting for NMSC evaluation may be in better overall health than the general population. If patients are severely decompensated or managing several active comorbidities, prioritization of their health conditions may lead to skin cancer treatment being deferred.

While the definition of LLE varies, less than 50% survival at 4 years was seen in those patients with an ACE-27 score of 3, or ACCI score of 7+. Age and comorbidity status were strikingly similar between patients undergoing MMS and non-MMS patients, but MMS patients survived a median of 20 months longer. These results suggest that selection bias or a confounding factor such as high functional status was protective for those patients presenting for specialized surgical management. Functional status is evaluated by assessing Activities of Daily Living (ADL) in terms of self-care, communication, and mobility.¹⁸ It is often used as a measure of overall health, can be predictive of survival in older adults, and is independent of comorbidity status.^{19,20} Regula and colleagues previously showed that patients 75 years and older who underwent Mohs were generally high functioning.²¹ Although functional status was not systematically collected in this population, the patient's overall ability to perform ADL is informally assessed during the preoperative consultation. Patients may also have self-selected based on their own perceived ability to perform wound care, tolerate surgery and return for follow-up appointments.

The ACCI and ACE-27 were previously identified as the most commonly used formal comorbidity indices in the NMSC population.¹⁵ Our findings indicate that although comorbidity status alone does not explain the survival difference between the cohorts, it was predictive of overall survival. Previous studies have found conflicting results regarding comorbidity status and life expectancy in the very elderly.^{22,23} Additionally, the ACCI and the ACE-27 were shown to be similarly useful tools in determining limited life expectancy,²⁴ despite differences between the indices. Patients with the highest comorbidity grades had a median survival of less than 4 years compared with 7.2 years for those with the fewest comorbidities.

Linos and colleagues previously examined patient characteristics in those treated for NMSC and compared participants with and without limited life expectancy (definition included age 85 and older and/or non-age-adjusted-CCI score of 3 or greater) in individuals aged 65 or older. Their findings demonstrated no difference in rates of treatment modality used between these two groups including the use of MMS.¹⁰ In this study, patients presented for MMS predominantly with facial lesions and the majority only required one to two stages for negative margins. Most of the surgical wounds healed by secondary intention or primary closure, illustrating that the simplest and lowest risk healing approaches were used in this population. These results support prior studies showing that the 85 year and older population presenting for NMSC management is generally healthy and tolerates MMS.^{22,25,26} While various estimations of life expectancy should be components of shared decision making for NMSC interventions, the survival difference observed between MMS and non-MMS groups despite similar comorbidity scores in this study suggests that a broader view of limited life expectancy in this population should be evaluated and further studied.

There are limitations to this study including the retrospective, observational design. This patient population was also specific to a cancer center and may have a predilection for a different comorbidity profile than those at other medical centers. Nearly half of the patients in both cohorts had a solid organ malignancy or lymphoma, whereas only 10% had diabetes. Furthermore, patients were pre-screened by their referring dermatologist. Therefore, there

was implicit referral bias that may have impacted the improved comorbidity status and life expectancy seen in both cohorts compared with the general population.

Conclusions

Patients 85 years and older presenting to a dermatologic surgery service surpassed expected survival. Higher comorbidity scores were associated with decreased survival, and both the ACE-27 and ACCI were predictive of LLE at scores of 3 and 7+, respectively. Patients who underwent MMS survived longer, despite similarities in comorbidity profiles between groups, implying that additional factors selected for by patients and their physicians may significantly contribute to survival in this cohort. Age alone is inadequate for making NMSC treatment decisions in the very elderly, and a comprehensive approach to management, considering comorbidity, functional status, and anticipated life expectancy should be considered.

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References

1. Byfield SD, Chen D, Yim YM, Reyes C. Age distribution of patients with advanced non-melanoma skin cancer in the United States. *Arch Dermatol Res.* 2013; 305(9):845–850. [PubMed: 23604961]
2. Rogers HW, Weinstock MA, Feldman SR, Coldiron BM. Incidence estimate of nonmelanoma skin cancer (keratinocyte carcinomas) in the US population. *JAMA Dermatol.* 2015; 151(10):1081–1086. [PubMed: 25928283]
3. Lubeek SF, van Vugt LJ, vandeKerkhof PC, Gerritsen MP. The epidemiology and clinicopathological features of basal cell carcinoma in patients 80 years and older: a systematic review. *JAMA Dermatol.* 2017; 153(1):71–78. [PubMed: 27732698]
4. Hafner, K., Palmer, G. The New York Times. Health; 2017. Skin cancers rise, along with questionable treatments.
5. Ortman, JM., Velkoff, VA., Hogan, H. An aging nation: the older population in the United States. 2014. <http://www.census.gov/prod/2014pubs/p25-1140.pdf>. Accessed September 15, 2016
6. Batra RS, Kelley LC. Predictors of extensive subclinical spread in nonmelanoma skin cancer treated with Mohs micrographic surgery. *Arch Dermatol.* 2002; 138(8):1043–1051. [PubMed: 12164742]
7. Wu PA, Stern RS. How likely is another nonmelanoma skin cancer?: better informing patients and clinicians. *JAMA Dermatol.* 2015; 151(4):369–370. [PubMed: 25587795]
8. Thompson AK, Kelley BF, Prokop LJ, Murad MH, Baum CL. Risk factors for cutaneous squamous cell carcinoma recurrence, metastasis, and disease-specific death. *JAMA Dermatol.* 2016; 152(4): 419–428. [PubMed: 26762219]
9. Lee EH, Brewer JD, MacFarlane DF. Optimizing informed decision making for basal cell carcinoma in patients 85 years or older. *JAMA Dermatol.* 2015; 151(8):817–818. [PubMed: 26018032]
10. Linos E, Chren M, Stijacic-Cenzer I, Covinsky KE. Skin cancer in U.S. elderly adults: does life expectancy play a role in treatment decisions? *J Am Geriatr Soc.* 2016; 64(8):1610–1615. [PubMed: 27303932]
11. Linos E, Parvataneni R, Stuart SE, Boscardin WJ, Landefeld CS, Chren MM. Treatment of nonfatal conditions at the end of life: nonmelanoma skin cancer. *JAMA Intern Med.* 2013; 173(11):1006–1012. [PubMed: 23699934]

12. Linos E, Schroeder SA, Chren M. Potential overdiagnosis of basal cell carcinoma in older patients with limited life expectancy. *JAMA*. 2014; 312(10):997–998. [PubMed: 25203077]
13. Charlson ME, Pompei P, Ales KL, Mackenzie CR. A new method of classifying prognostic comorbidity in longitudinal studies: development and validation. *J Chronic Dis*. 1987; 40(5):373–383. [PubMed: 3558716]
14. Paleri V, Wight RG. A cross-comparison of retrospective notes extraction and combined notes extraction and patient interview in the completion of a comorbidity index (ACE-27) in a cohort of United Kingdom patients with head and neck cancer. *J Laryngol Otol*. 2002; 116(11):937–941. [PubMed: 12494924]
15. Connolly KL, Jeong JM, Barker CA, Hernandez M, Lee EH. A systematic review of comorbidity indices used in the nonmelanoma skin cancer population. *J Am Acad Dermatol*. 2017; 76(2):344–346. [PubMed: 28088996]
16. Miller SJ, Alam M, Andersen J, et al. Basal cell and squamous cell skin cancers. *J Natl Compr Canc Netw*. 2010; 8(8):836–864. [PubMed: 20870631]
17. Arias E, Heron M, Xu J. United States Life Tables. National Vital Statistics Reports. 2017; 66(3): 1–64.
18. Pincus T, Summey JA, Soraci SA, Wallston KA, Hummon NP. Assessment of patient satisfaction in activities of daily living using a modified stanford health assessment questionnaire. *Arthritis Rheum*. 1983; 26(11):1346–1353. [PubMed: 6639693]
19. Keeler E, Guralnik JM, Tian H, Wallace RB, Reuben DB. The impact of functional status on life expectancy in older persons. *J Gerontol A Biol Sci Med Sci*. 2010; 65(7):727–733. [PubMed: 20363833]
20. Extermann M, Overcash J, Lyman GH, Parr J, Balducci L. Comorbidity and functional status are independent in older cancer patients. *J Clin Oncol*. 1998; 16(4):1582–1587. [PubMed: 9552069]
21. Regula C, Alam M, Behshad R, et al. Functionality of Patients 75 Years and Older Undergoing Mohs Micrographic Surgery: A Multicenter Study. *Dermatol Surg*. 2017; 43(7):904–910. [PubMed: 28328703]
22. Delaney A, Shimizu I, Goldberg LH, MacFarlane DF. Life expectancy after Mohs micrographic surgery in patients aged 90 years and older. *J Am Acad Dermatol*. 2013; 68(2):296–300. [PubMed: 23200199]
23. Pascual JC, Belinchon I, Ramos JM. Mortality after dermatologic surgery for nonmelanoma skin cancer in patients aged 80 years and older. *J Am Acad Dermatol*. 2013; 69(6):1051–1052. [PubMed: 24238160]
24. Hines RB, Chatla C, Bumpers HL, et al. Predictive capacity of three comorbidity indices in estimating mortality after surgery for colon cancer. *J Clin Oncol*. 2009; 27(26):4339–4345. [PubMed: 19652054]
25. MacFarlane DF, Pustelny BL, Goldberg LH. An assessment of the suitability of Mohs micrographic surgery in patients aged 90 years and older. *Dermatol Surg*. 1997; 23(5):389–392. [PubMed: 9179250]
26. Charles AJ, Otley C, Pond G. Prognostic factors for life expectancy in nonagenarians with nonmelanoma skin cancer: Implications for selecting surgical candidates. *J Am Acad Dermatol*. 2002; 47(3):419–422. [PubMed: 12196753]
27. Basal cell and squamous cell skin cancers (Version 1.2017). National Comprehensive Cancer Network; 2017.

Capsule Summary

- Controversy exists over nonmelanoma skin cancer treatment in the very elderly (>85 years).
- In the current study, both the Adult Comorbidity Evaluation-27 and Age-Adjusted Charlson Comorbidity Index predicted limited life expectancy. Patients who underwent Mohs surgery had improved survival.
- Management decisions should include consideration of comorbidity, functional status, and anticipated life expectancy.

Figure 1.
Kaplan Meier survival for Mohs and non-Mohs cases.

Figure 2.
Probability of death by Adult Comorbidity Evaluation-27 scores

Figure 3.
Probability of death by Age-Adjusted Charlson Comorbidity Index scores

Table 1

Study categorical variables by Mohs surgery

	Mohs N=371	No Mohs N=117	Total N=488	P-value
	mean (SD)	mean (SD)	Overall, mean (SD)	
Age	87.9 (2.7)	88.8 (3.4)	88.1 (2.9)	0.005
Gender	n (%)	n (%)	n (%)	
Female	182 (49.1)	74 (63.3)	256 (52.5)	0.007
Male	189 (50.9)	43 (36.8)	232 (47.5)	
Diagnosis				
BCC	204 (55.0)	54 (46.2)		
SCC	162 (43.7)	51 (43.6)		
Other NMSC	5 (1.3)	12 (10.3)		
Anatomic Location Risk *				
Low	58 (15.6)	40 (34.2)	98 (20.1)	<0.001
Medium	141 (38)	31 (26.5)	172 (35.3)	
High	172 (46.4)	46 (39.3)	218 (44.7)	
Mohs Stages				
1	108 (29.2)	n/a	108 (29.2)	n/a
2	159 (43)	n/a	159 (43)	
3	79 (21.4)	n/a	79 (21.4)	
4	24 (6.5)	n/a	24 (6.5)	
Wound management				
Second intent	112 (30.2)	n/a	112 (30.2)	
Primary closure	156 (42.0)	n/a	156 (42.0)	
Flap	63 (17.0)	n/a	63 (17.0)	
Graft	33 (8.9)	n/a	33 (8.9)	
Other (e.g., combined; referred)	7 (1.9)	n/a	7 (1.9)	

* Anatomic risk profile categorized according to National Comprehensive Cancer Network guidelines.²⁷

Table 2

Frequency of most common individual comorbidities.

	Mohs N=371	No Mohs N=117	Total N=488	P-value
	n (%)	n (%)	n (%)	
Hypertension	275 (74.1)	80 (68.4)	355 (72.7)	0.22
Cancer - solid tumor	215 (58.0)	59 (50.4)	274 (56.1)	0.15
Cardiovascular - CAD	88 (23.7)	20 (17.1)	108 (22.1)	0.13
Cardiovascular - rhythm	74 (19.9)	31 (26.5)	105 (21.5)	0.13
Diabetes	38 (10.2)	12 (10.2)	50 (10.2)	0.99
Stroke	35 (9.4)	11 (9.4)	46 (9.4)	0.99
Cancer - lymphoma	28 (7.5)	5 (4.3)	33 (6.8)	0.22