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Geriatric assessment of patients treated for cutaneous head and neck malignancies in a tertiary referral center

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1 Title

2 Geriatric assessment of patients treated for cutaneous head and neck malignancies in a tertiary referral center:
3 predictors of postoperative complications

4

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37

38 **Abstract**

39 Introduction: As cutaneous head and neck malignancies are highly prevalent especially in older patients, the
40 risk of surgical complications is substantial in this potentially vulnerable population. The objective of this study
41 was to evaluate the value of geriatric assessment of this population with respect to postoperative
42 complications.

43
44 Methods: Patients were prospectively included in OncoLifeS, a databiobank. Before surgery, patients
45 underwent a geriatric assessment including multiple validated screening tools for frailty, comorbidity,
46 polypharmacy, nutrition, functional status, social support, cognition and psychological status. Postoperatively,
47 complications (Clavien-Dindo \geq grade II) were registered. Uni- and multivariable logistic regression analyses
48 were performed yielding odds ratios (ORs) and 95% confidence intervals (95% CIs).

49
50 Results: 151 patients undergoing surgery for cutaneous head and neck malignancies were included in this study
51 (mean age 78.9 years, 73.5% male). In a multivariable analysis, frailty measured by the Geriatric 8 (G8)
52 (OR=6.34; 95%CI:1.73-23.25) was the strongest independent predictor of postoperative complications, among
53 other predictors such as major treatment intensity (OR=2.73; 95%CI:1.19-6.26) and general anesthesia
54 (OR=4.74; 95%CI:1.02-22.17), adjusted for age and sex.

55
56 Conclusion: Frailty, measured by G8, is the strongest predictor of postoperative complications in patients
57 undergoing surgery for cutaneous head and neck malignancies in addition to treatment intensity and type of
58 anesthesia. Geriatric screening on multiple domains is recommended for patients with cutaneous malignancies
59 undergoing head and neck surgery is recommended, as this population includes old patients and frequently
60 suffers postoperative complications.

61
62 **Key words**

63 Geriatric screening, frailty, skin malignancy, head and neck surgery, postoperative complications.

64 Abbreviations

- 65 95%CI = 95% Confidence Interval
- 66 ACE-27 = Adult Comorbidity Evaluation 27
- 67 ADL = Activities of Daily Living
- 68 BCC = Basal Cell Carcinoma
- 69 BMI = Body Mass Index
- 70 CGA = Comprehensive Geriatric Assessment
- 71 CM = Cutaneous Melanoma
- 72 G8 = Geriatric 8
- 73 GDS-15 = Geriatric Depression Scale 15
- 74 GFI = Groningen Frailty Indicator
- 75 IADL = Instrumental Activities of Daily Living
- 76 MCC = Merkel Cell Carcinoma
- 77 MMSE = Mini Mental State Examination
- 78 MUST = Malnutrition Universal Screening Tool
- 79 NL = Netherlands
- 80 NMSC = Non-melanoma Skin Cancer
- 81 OR = Odds Ratio
- 82 SCC = Squamous Cell Carcinoma
- 83 SD = Standard Deviation
- 84 SES = Socioeconomic Status
- 85 TUG = Timed Up and Go
- 86 UMCG = University Medical Center Groningen

87 Introduction

88 Skin cancer is the most common type of cancer worldwide.¹ In the United States, the incidence of non-
89 melanoma skin cancer (NMSC) and cutaneous melanoma (CM) is estimated to be at least over 5.5 million
90 annually.^{2,3} The incidence of both NMSC and CM are dramatically on the rise,⁴⁻⁶ with especially the proportion
91 of older patients increasing.⁷ This results from the expanding older population in general and also due to older
92 patients' higher cumulative sun exposure. Possibly, associated diseases,^{8,9} use of immunosuppressive
93 medications,¹⁰ or exposure to prior radiation therapy,¹¹ contribute to this as well.

94 Cutaneous malignancies of the head and neck occur more frequently^{12,13} and are at higher risk for
95 metastasis than other subsites.¹⁴ The cornerstone of treatment in most of the cases is surgery, ranging from a
96 straightforward local excision to extended resections with neck dissections and even complex reconstructive
97 surgery. If radical surgery is beyond possibilities, because of expected functional or cosmetic impairments or
98 foreseen complications in older patients, radiotherapy is an effective treatment modality both as primary
99 therapy or as an adjuvant therapy.¹⁵ With surgery remaining the primary choice of treatment, the risk of
100 postoperative complications is substantial in this elderly and possibly vulnerable population, like previously
101 described after head and neck oncological surgery.¹⁶

102 Comprehensive Geriatric Assessment (CGA) by a geriatrician or specialized nurse is the gold standard
103 to expose vulnerabilities in older patients, which may be treated to prevent perioperative complications.¹⁷ CGA
104 focuses on multiple geriatric domains such as comorbidities, polypharmacy, nutritional status, functional
105 status, social support and psychological status.¹⁸ Because of its time consuming nature, screening tools such as
106 the Groningen Frailty Indicator (GFI) and the Geriatric 8 (G8) have been developed to detect vulnerable
107 patients who may benefit from a CGA.^{19,20}

108 The role of geriatric screening is established in many oncological patient populations, but not in
109 cutaneous malignancies, even though this population is relatively old. Therefore, in the present study, we
110 evaluated the role of geriatric assessment and frailty screening with respect to postoperative complications in
111 surgically treated patients for cutaneous head and neck malignancies in a tertiary center.

112 **Materials and methods**

113 *Study design*

114 The present cohort study included patients who were enrolled in OncoLifeS, a prospective oncological
115 databiobank at the University Medical Center Groningen. Study protocol was approved by the OncoLifeS
116 scientific board.

117

118 *Study population*

119 Between October 2014 and October 2018 all consecutive patients referred for a cutaneous malignancy to the
120 Department of Otorhinolaryngology, Head and Neck Surgery were included, regardless of age. Treatment
121 strategies were according to national guidelines and discussed within the multidisciplinary head and neck
122 tumor board and melanoma board, if applicable. If curative treatment was not possible or if patients received
123 other primary treatment than surgery, patients were excluded from this study.

124

125 *Data collection*

126 Patient, tumor- and treatment characteristics were obtained from the electronic medical record and OncoLifeS
127 database. Tumor stage was defined according to the seventh edition of the Union for International Cancer
128 Control TNM Classification.²¹ At the first day of consultation, patients underwent a geriatric assessment at the
129 outpatient clinic of our department, including the following geriatric domains: comorbidities, polypharmacy,
130 nutritional status, functional status, social support, cognition and psychological status. Comorbidities were
131 graded using the Adult Comorbidity Evaluation (ACE-27) as *none, mild, moderate or severe*.²² Polypharmacy
132 was defined as the prescription of five or more medications on a daily basis.²³ Nutritional status was assessed
133 using the Malnutrition Universal Screening Tool (MUST).²⁴ Functional status consisted of Activities of Daily
134 Living (Katz-ADL), Instrumental Activities of Daily Living (IADL), Timed Up & Go (TUG) and history of falls.²⁵⁻²⁷
135 Social support was based on patient reported questionnaires. Socioeconomic status (SES) scores are publicly
136 available scores, based on income, employment rate and educational status of postal code areas.²⁸ Cognition
137 was assessed by the Mini Mental State Examination (MMSE) and presence of risk factors for delirium.^{29,30}
138 Psychological status was scored using the Geriatric Depression Scale (GDS-15).³¹ Furthermore, two frailty
139 screening instruments were completed including the Groningen Frailty Indicator (GFI) and the Geriatric 8

140 (G8).^{19,20} Postoperative complications occurring within 30 days after surgery were assessed from medical files
141 using the Clavien-Dindo classification.³²

142

143 *Statistical analysis*

144 Patient characteristics were presented as mean \pm standard deviation, median (range) or value (percentage).

145 Univariable logistic regression analyses were performed to identify factors associated with postoperative

146 complications. Analyses yielded odds ratios (ORs) with 95% confidence intervals (95% CIs). For multivariable

147 logistic regression analysis with step backward method, variables with $p < 0.10$ were included. When collinearity

148 was present between variables using Pearson and Spearman correlation coefficients, only clinically most

149 relevant variables were selected. For variables eligible for multivariable analysis, missing values were imputed

150 using multiple imputation. The multivariable model was fitted using a stepwise selection of predictors. All

151 statistical analysis was performed with SPSS Statistics 23.0 software (IBM, Armonk, New York, United States of

152 America). P-value < 0.05 was considered statistically significant.

153 **Results**

154 *Study selection*

155 Between October 2014 and October 2018, 197 patients with cutaneous head and neck malignancies were
156 included in the OncoLifeS databiobank. After exclusion of patients treated with other primary treatment
157 modalities than surgery and patients with no curative treatment options, a total of 151 patients remained
158 eligible for analysis (Figure 1). There were no significant age and sex differences after exclusion.

159

160 *Patient characteristics*

161 Patient characteristics are presented in Table 1. The mean age of the patients was 78.9 years, ranging from
162 46.6 to 96.7 years. In this tertiary referral center, less than half of patients were referred with a primary tumor
163 (49.7%), and others with residual tumor after recent treatment (29.8%) or recurrent tumor (20.5%). Most
164 frequent histopathological subtypes of malignancies were squamous cell carcinoma (SCC; 59.6%), basal cell
165 carcinoma (BCC; 18.5%), cutaneous melanoma (CM; 11.3%) and Merkel cell carcinoma (MCC; 6.0%).

166

167 *Univariable analysis of predictors for postoperative complications*

168 Occurrence of postoperative complications is listed in Table 2. Forty patients (26.5%) experienced
169 complications grade II and higher according to the Clavien-Dindo classification. Factors associated with
170 postoperative complications are shown in Table 3. Age was not a significant predictor (OR 0.98; 95%CI 0.94-
171 1.02). Tumor characteristics, such as advanced tumor stage (OR 6.53; 95%CI 1.86-22.99) and large tumor
172 diameter (OR 3.89; 95%CI 1.12-13.51) significantly predicted postoperative complications. Treatment
173 characteristics, including locoregional surgery (OR 4.38; 95%CI 1.98-9.68), major treatment intensity (OR 3.46;
174 95%CI 1.62-7.39) and general anesthesia (OR 7.70; 95%CI 1.75-33.81), were also significantly related to
175 postoperative complications.

176 Among the individual domains of geriatric assessment, only polypharmacy (OR 2.36; 95%CI 1.11-5.07)
177 predicted postoperative complications respectively significantly (Table 3). Comorbidities, or impairments in
178 functional status, social support, cognitive status or psychological status alone were not significantly associated
179 with postoperative complications. Of the frailty screeners, the G8 was a strong, significant predictor of
180 complications (OR 5.83; 95%CI 1.68-20.26) and GFI was not (OR 1.43; 95%CI 0.63-3.26).

181

182 *Independent predictors of postoperative complications*

183 A multivariable model was fitted with eligible variables (Table 4). Within the multivariable model, adjusted for
184 age and sex, major treatment intensity (OR 2.73; 95%CI 1.19-6.26), surgery under general anesthesia (OR 4.74;
185 95%CI 1.02-22.17) and frailty, measured by G8 (OR 6.34; 95%CI 1.73-23.25) were the most significant
186 independent predictors of postoperative complications grade II and higher.

187 Discussion

188 Patients with complex cutaneous head and neck malignancies are old and frequently experience postoperative
189 complications. To our knowledge, this is the first study evaluating the value of geriatric assessment in a cohort
190 of patients with cutaneous head and neck malignancies. Key findings show that frailty, measured by G8, is the
191 strongest predictor of postoperative complications. Furthermore, tumor features, such as tumor size and stage,
192 and treatment related predictors, such as treatment intensity and type of anesthesia seem to be related to
193 postoperative complications.

194 With a mean age of nearly 80 years, the population of patients with cutaneous head and neck
195 malignancies being referred to our tertiary hospital was remarkably aged. However, age did not predict
196 postoperative complications within this population. This corresponds with other dermatological cohorts with
197 head and neck skin malignancies.^{33–35} Pascual et al. showed that complications did not significantly differ
198 between patients younger and older than 80 years, except for hemorrhagic complications.³⁶ This finding is in
199 line with a large prospective cohort of Amici et al., showing more hemorrhagic complications in the elderly as
200 well.³⁷ As significance disappears after correcting for use of anticoagulant medications, the higher amount of
201 hemorrhagic complications is probably related to the increased use of anticoagulants with aging, and not to
202 age itself. Just as age does not predict postoperative complications, it neither affects prognosis of patients with
203 skin cancer.³⁸ Moreover, the majority of patients with a lower life expectancy, defined as age 85 years and
204 older or a Charlson Comorbidity Index of 3 or higher, die of other causes than NMSC.³⁹ Whilst this does not
205 apply directly to our cohort with much more complex cases, it does call the attention to the dilemma of “time
206 to benefit”, referring to a clinical prediction, estimating whether the patient will live long enough to benefit
207 from the treatment.³⁷ It is suggested that a comprehensive approach towards treatment decisions should at
208 least include consideration of comorbidity, functional status and anticipated life expectancy in this specific
209 population.⁴⁰

210 Complications after surgery of cutaneous head and neck malignancies performed by a dermatologist
211 are usually rare. Percentages of the largest cohorts range between 3 and 6%.^{37,41–43} With 26.5% of patients
212 suffering postoperative complications in our cohort, these outcomes seem much worse. However, our cohort
213 suffers from a negative bias; higher tumor stage, more complex locations, more often lymph node metastasis,
214 and consequently more major surgeries under general anesthesia. Furthermore, referral to a tertiary center
215 may include more residual or recurrent tumor, which was the case in more than half of the patients. Clinical

216 research on tertiary cohorts of cutaneous head and neck malignancies are rarely reported; therefore
217 comparison is difficult.

218 Our results show that tumor features such as histopathological type, tumor size and stage, and
219 treatment characteristics, such as treatment intensity, adjuvant neck dissection and type of anesthesia, predict
220 postoperative complications. Many of these variables are closely related to each other. After all, increased
221 tumor size and more aggressive histopathological tumor type lead to more advanced stage, requiring extended
222 surgery, possibly including neck dissection and general anesthesia. As a result, only the strongest predictors
223 were included in multivariable analysis. Treatment intensity, defined as surgery time more than 120 minutes or
224 3 or more stages of Mohs micrographic surgery, and surgery under general anesthesia were found to be the
225 most important predictors of postoperative complications. Length of surgery and neck dissection has been
226 proven to predict postoperative complications in general head and neck oncological surgery as well.^{16,44-46} Even
227 in case of excision under local anesthesia, length of surgery predicts postoperative complications in skin cancer
228 surgery.³⁷

229 Frailty, measured by G8, was mostly associated with postoperative complications in this cohort. As far
230 as we know, frailty has never been examined in a cohort undergoing surgery for cutaneous malignancies.
231 Valdatta et al. investigated the FRAIL index in a cohort undergoing *reconstructive surgery* after NMSC
232 excision.⁴⁷ A higher score on the FRAIL index was associated with more moderate to severe complications.
233 Furthermore, Bras et al. included 45 patients with skin malignancies in their cohort of head and neck
234 oncological patients.⁴⁵ The domain *health problems* of the GFI significantly predicted postoperative
235 complications; however, subgroup analysis for patients with skin malignancies was not performed in that study.
236 Interestingly, in our analysis, GFI showed no prognostic value. Comparing these studies is difficult, as there are
237 large differences among frailty screening tools.⁴⁸ Domains that are covered by the G8 are nutritional status,
238 polypharmacy, neuropsychological status and mobility. The G8 has been proven to be a useful tool in liver and
239 colorectal surgery as a predictor of surgical complications.^{49,50} However, the value of G8 remains questionable,
240 as the majority of our patients scored frail on the G8 (73.3%). This is in line with Pottel et al. and Hamaker et al.
241 evaluating the G8 and other screening tools.^{48,51} They found that the G8 is very *sensitive* but not very *specific*
242 with respect to its gold standard, a CGA. Referring all frail patients, based on G8 to a geriatrician for a CGA
243 would be infeasible.

244 From all individual geriatric domains, polypharmacy and malnutrition were most significantly related
245 with post-operative complications in our population. These domains are both well represented in the G8 as
246 well. Polypharmacy is related to frailty and comorbidities, but also associated with outcome parameters such
247 as postoperative complications, delirium, (chemo)radiation toxicity, increased hospital stay and mortality.²³
248 Across literature, however, polypharmacy lacks definition and cut-off values range largely, with ≥ 5 being the
249 mostly used.²³ Whether certain specific medications such as anticoagulants were related to postoperative
250 complications, just like in the study of Amici et al., was not possible to investigate using the current dataset.³⁷
251 Malnutrition is very common and undertreated in elderly.⁵² Evaluation of the nutritional status is therefore
252 important in preoperative screening. Higher risk of malnutrition using MUST is associated with postoperative
253 complications, increased hospital stay and mortality.⁵³⁻⁵⁵ Often, the body mass index (BMI) is used as an
254 indicator for nutritional status, just as in MUST. However, normal values of 18.5-24.9 kg/mm² are based on
255 mortality risk within a young and healthy population.⁵⁶ For older patients, a BMI <23 kg/mm² is already
256 associated with increased mortality, and may therefore be a better cut-off value for underweight. The 7.9% of
257 patients having risk of malnutrition measured by MUST in our cohort may be an underestimation of the real
258 prevalence of malnutrition. Identification of such deficits is particularly important, as a geriatrician or a dietary
259 consultant may be able to respectively manage polypharmacy or prevent malnutrition, lowering the risk of
260 complications.

261 Based on our results, it seems that G8 is a very predictive screening tool. However, lack of specificity
262 does not make it possible to adequately select vulnerable patients. Meanwhile, individual geriatric domains
263 such as polypharmacy or malnutrition are too incomprehensive to point out patients at risk for surgical
264 complications. The question arises what would then be an adequate screening strategy for elderly patients with
265 cutaneous malignancies. As a recommendation, a two-step approach may bring a solution to this problem. The
266 first step would be a short geriatric screening by a trained nurse, gathering information on all geriatric domains
267 including comorbidities, polypharmacy, nutritional status, functional status, social support, cognition and
268 psychological status, using short screening instruments. Then, the patients' screening information is discussed
269 within a multidisciplinary team for elderly patients, in which the nurse, a geriatrician, and head and neck
270 surgeon are present. The geriatrician may then already advise on perioperative management, or indicate a CGA
271 and start pre-treatment optimization (second step). In this way, all potentially vulnerable patients have been
272 reviewed prior to treatment, efficiently with respect to limited capacity of geriatric health care.

273 A strength of this work is the broad range of validated geriatric instruments and screening tools that
274 were used to assess patients at baseline. Besides, many patient, tumor and treatment characteristics were
275 available to adjust for existing differences between patients. Furthermore, patients were prospectively
276 included and the selection of the study population was done carefully with respect to changes through
277 exclusion process.

278 Limitations of our study may include that it is a single center study in a tertiary care hospital. As a
279 result, the cohort contains a high percentage of complex cases, regarding tumor and treatment characteristics.
280 Furthermore, the population was heterogenic, also in terms of tumor characteristics, like histopathology.
281 However, as we were primarily investigating patient-related factors, this seemed to be less relevant in our
282 study. Lastly, most complications have only temporary effect on the patients' lives. Other outcome parameters,
283 such as health related quality of life may be of more value to this specific population and should be studied.

284 **Conclusion**

285 Frailty, measured by G8, is the strongest factor associated with postoperative complications in patients
286 undergoing surgery for cutaneous head and neck malignancies, besides treatment related predictors, such as
287 treatment intensity and type of anesthesia. Geriatric screening on multiple domains is recommended in
288 patients with cutaneous head and neck malignancies, as this population includes old patients and frequently
289 suffers postoperative complications.

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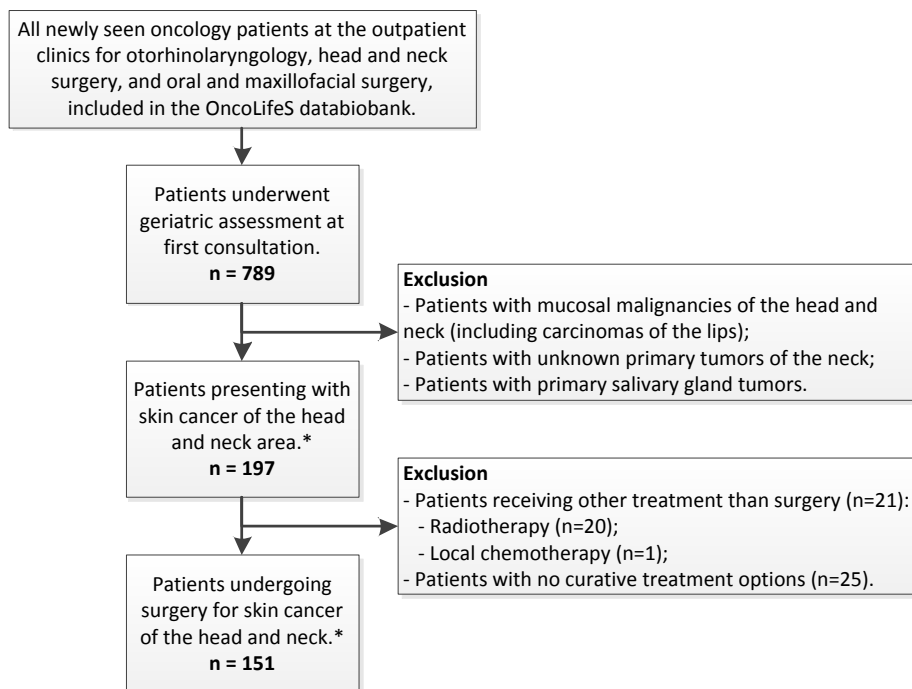
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464

465 **Figure 1**

466

467 **Figure 1.** Flowchart diagram representing the inclusion of patients into the final cohort of 151 patients who
468 were surgically treated for cutaneous head and neck malignancies. * Cohorts showed no significant differences
469 in age and sex throughout exclusion process.

470 **Table 1**

Variable	Value n=151
Age	
Mean ± SD, y	78.9 ± 9.0
Median (range), y	78.9 (46.6-96.7)
Categories	
< 70	27 (17.9%)
70-80	55 (36.4%)
80-90	53 (35.1%)
≥ 90	15 (10.6%)
Sex	
Male	111 (73.5%)
Female	40 (26.5%)
Reason for referral	
Primary tumor	75 (49.7%)
Residual tumor	45 (29.8%)
Recurrent tumor	31 (20.5%)
Primary tumor location	
Frontal	9 (6.0%)
Scalp	33 (21.9%)
Temporal	10 (6.6%)
Ear	56 (37.1%)
Cheek	9 (6.0%)
Peri-orbital	7 (4.6%)
Nose	21 (13.9%)
Peri-oral	3 (2.0%)
Neck	3 (2.0%)
Histopathology	
Basal cell carcinoma	28 (18.5%)
Squamous cell carcinoma	90 (59.6%)
Malignant melanoma	17 (11.3%)
Merkel cell carcinoma	9 (6.0%)
Other ^a	7 (4.6%)
Stage of disease	
Stage I	59 (39.1%)
Stage II	53 (35.1%)
Stage III	25 (16.6%)
Stage IV	14 (9.3%)
Immunocompromised^b	
No	130 (86.1%)
Yes	21 (13.9%)

511 **Table 1.** Characteristics of surgically treated patients with cutaneous malignancies of the head and neck area,
512 seen in a tertiary referral head and neck oncology center. ^a Included malignancies were angiosarcoma, atypical
513 fibroxanthoma, malignant adnexal tumor, pleomorphic dermal sarcoma, dermatofibrosarcoma protuberans
514 and adenoid cystic carcinoma. ^b Immunosuppression included patients who have been using long-term
515 immunosuppressive medication e.g. post transplantation, chronic lymphocytic leukemia, Non-Hodgkin's
516 lymphoma, severe rheumatism and Crohn's disease.

517 **Table 2**

Clavien-Dindo	Value	518
	n=151	510
No complications	89 (58.9%)	
Grade I	22 (14.6%)	
Grade II	25 (16.6%)	
Grade III	13 (8.6%)	
Grade IV	2 (1.3%)	
Grade V	0 (0.0%)	

523 **Table 2.** Postoperative complications in patients undergoing surgery for cutaneous head and neck
524 malignancies.

525 **Table 3**

Variable	Value (%) n=151	Univariable analysis Odds ratio (95% CI)	p-value
Patient characteristics			
Age			
Mean \pm SD, y	78.9 \pm 9.0	0.98 (0.94-1.02)	0.27
Median (range), y	78.9 (46.6-96.7)		
Sex			
Male	111 (73.5%)	1	
Female	40 (26.5%)	0.90 (0.39-2.06)	0.80
Immunocompromised ^a			
No	130 (86.1%)	1	
Yes	21 (13.9%)	1.89 (0.72-4.96)	0.20
Tumor characteristics			
Reason for referral			
Primary tumor	75 (49.7%)	1	0.71
Residual tumor	45 (29.8%)	0.95 (0.41-2.25)	0.91
Recurrent tumor	31 (20.5%)	1.40 (0.56-3.51)	0.47
Stage			
Stage I	59 (39.1%)	1	< 0.05
Stage II	53 (35.1%)	1.93 (0.78-4.78)	0.15
Stage III	25 (16.6%)	1.91 (0.63-5.76)	0.25
Stage IV	14 (9.3%)	6.53 (1.86-22.99)	< 0.01
Tumor diameter			
< 20 mm	72 (59.5%)	1	< 0.05
20-40 mm	36 (29.8%)	2.57 (1.04-6.36)	< 0.05
\geq 40mm	13 (10.7%)	3.89 (1.12-13.51)	< 0.05
Invasion depth			
Mean \pm SD, mm	5.2 \pm 3.3	1.13 (0.99-1.29)	0.06
Median (range), mm	4.7 (0.3-19.5)		
Histopathology			
Basal cell carcinoma	28 (18.5%)	1	0.23
Squamous cell carcinoma	90 (59.6%)	3.96 (1.11-14.20)	< 0.05
Malignant melanoma	17 (11.3%)	3.47 (0.71-16.99)	0.13
Merkel cell carcinoma	9 (6.0%)	1.04 (0.10-11.47)	0.97
Other ^b	7 (4.6%)	3.33 (0.44-25.39)	0.25
Treatment characteristics			
Primary treatment			
Local surgery	113 (74.8%)	1	
Locoregional surgery	38 (25.2%)	4.38 (1.98-9.68)	< 0.01
Treatment intensity ^c			
Minor	96 (63.6%)	1	
Major	55 (36.4%)	3.46 (1.62-7.39)	< 0.01
Anesthesia			
Local anesthesia	34 (22.5%)	1	
General anesthesia	117 (77.5%)	7.70 (1.75-33.81)	< 0.01
Reconstructive surgery			
No reconstructive surgery	45 (29.8%)	1	0.10
Intraoperative reconstruction	81 (53.6%)	1.07 (0.45-2.56)	0.88
Subsequent reconstructive surgery	25 (16.6%)	2.75 (0.96-7.92)	0.06
Intoxications			
Smoking			
Never or former	113 (86.3%)	1	
Current	18 (13.7%)	2.03 (0.72-5.74)	0.18
Drinking			
None or mild	117 (88.6%)	1	
Heavy (> 2/day)	15 (11.4%)	2.78 (0.93-8.35)	0.07
Comorbidities			
ACE-27			
None or mild	53 (35.1%)	1	
Moderate or severe	98 (64.9%)	1.61 (0.73-3.55)	0.24
Polypharmacy			
Medication count			

< 5 medications	95 (65.1%)	1	
≥ 5 medications	51 (34.9%)	2.36 (1.11-5.07)	< 0.05
Nutritional status			
MUST			
Low risk	128 (92.1%)	1	
Medium to high risk	11 (7.9%)	3.46 (0.99-12.07)	0.05
Functional status			
ADL			
No restrictions (< 1)	114 (82.6%)	1	
Restrictions (≥ 1)	24 (17.4%)	1.69 (0.65-4.39)	0.28
IADL			
No restrictions (< 1)	100 (69.4%)	1	
Restrictions (≥ 1)	44 (30.6%)	1.07 (0.48-2.38)	0.87
TUG			
Mean ± SD, s	11.4 ± 6.7	1.04 (0.98-1.11)	0.19
Median (range), s	10 (5-70)		
History of falls			
No	124 (91.2%)	1	
Yes	12 (8.8%)	0.96 (0.24-3.76)	0.95
Social support			
Education			
Low level of education	60 (48.8%)	1	0.64
Middle level of education	38 (30.9%)	1.52 (0.61-3.76)	0.37
High level of education	25 (20.3%)	1.04 (0.35-3.10)	0.95
Marital status			
In a relationship	89 (67.9%)	1	0.69
Widow	32 (24.4%)	1.38 (0.60-3.37)	0.47
Single	10 (7.6%)	0.76 (0.15-3.86)	0.74
Social Economic Statusscore (SES)			
Below average (NL)	119 (79.3%)	1	
Above average (NL)	31 (20.7%)	0.99 (0.40-2.44)	0.98
Cognitive status			
MMSE			
Normal cognition (> 24)	108 (76.6%)	1	
Declined cognition (≤ 24)	33 (23.4%)	0.83 (0.34-2.05)	0.69
Risk of delirium			
No	113 (77.4%)	1	
Yes	33 (22.6%)	0.85 (0.35-2.08)	0.72
Psychological status			
GDS-15			
No depression (< 6)	113 (81.3%)	1	
Depression (≥ 6)	26 (18.7%)	1.17 (0.45-3.09)	0.75
Frailty screeners			
G8			
Non-frail (> 14)	39 (26.7%)	1	
Frail (≤ 14)	107 (73.3%)	5.83 (1.68-20.26)	< 0.01
GFI			
Non-frail (< 4)	98 (70.5%)	1	
Frail (≥ 4)	41 (29.5%)	1.43 (0.63-3.26)	0.40

527 **Table 3.** Patient-, tumor- and treatment characteristics and domains of geriatric assessment in a univariable
528 logistic regression predicting postoperative complications grade II and higher. Abbreviations: CI=Confidence
529 Interval, SD=Standard Deviation, ACE-27=Adult Comorbidity Evaluation 27, MUST=Malnutrition Universal
530 Screening Tool, ADL=Activities of Daily Living, IADL=Instrumental Activities of Daily Living, TUG=Timed Up and
531 Go, NL=Netherlands, MMSE=Mini Mental State Examination, GDS-15=Geriatric Depression Scale 15,
532 G8=Geriatric 8, GFI=Groningen Frailty Indicator. ^a Immunosuppression included patients who have been using
533 long-term immunosuppressive medication e.g. post transplantation, chronic lymphocytic leukemia, Non-
534 Hodgkin's lymphoma, severe rheumatism and Crohn's disease. ^b Included malignancies were angiosarcoma,
535 atypical fibroxanthoma, malignant adnexal tumor, pleomorphic dermal sarcoma, dermatofibrosarcoma
536 protuberans and adenoid cystic carcinoma. ^c Defined as surgery > 120 minutes or three or more stages of Mohs
537 micrographic surgery.

538 **Table 4**

Variable	← No complications Complications →		Multivariable model ^a	
			Odds ratio (95% CI)	p-value
Treatment intensity ^b			1	
Minor			2.73 (1.19-6.26)	< 0.05
Major				
Anesthesia			1	
Local anesthesia				
General anesthesia			4.74 (1.02-22.17)	< 0.05
Frailty on G8			1	
Non-frail (> 14)				
Frail (≤ 14)			6.34 (1.73-23.25)	< 0.01

539

540 **Table 4.** Multivariable logistic regression model predicting postoperative complications grade II and higher
541 patients receiving in surgery for cutaneous head and neck malignancies. ^a Adjusted for age and sex. ^b Defined as
542 surgery > 120 minutes or three or more stages of Mohs micrographic surgery.