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Title

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

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Abstract

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

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

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

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

Key words

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

Abbreviations

95%CI = 95% Confidence Interval

ACE-27 = Adult Comorbidity Evaluation 27

ADL = Activities of Daily Living

BCC = Basal Cell Carcinoma

BMI = Body Mass Index

CGA = Comprehensive Geriatric Assessment

CM = Cutaneous Melanoma

G8 = Geriatric 8

GDS-15 = Geriatric Depression Scale 15

GFI = Groningen Frailty Indicator

IADL = Instrumental Activities of Daily Living

MCC = Merkel Cell Carcinoma

MMSE = Mini Mental State Examination

MUST = Malnutrition Universal Screening Tool

NL = Netherlands

NMSC = Non-melanoma Skin Cancer

OR = Odds Ratio

SCC = Squamous Cell Carcinoma

SD = Standard Deviation

SES = Socioeconomic Status

TUG = Timed Up and Go

UMCG = University Medical Center Groningen

Introduction

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

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

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

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

Materials and methods

Study design

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

Study population

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

Data collection

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

(G8).[19,20] Postoperative complications occurring within 30 days after surgery were assessed from medical files using the Clavien-Dindo classification.[32]

Statistical analysis

Patient characteristics were presented as mean ± standard deviation, median (range) or value (percentage). Univariable logistic regression analyses were performed to identify factors associated with postoperative complications. Analyses yielded odds ratios (ORs) with 95% confidence intervals (95%CIs). For multivariable logistic regression analysis with step backward method, variables with $p<0.10$ were included. When collinearity was present between variables using Pearson and Spearman correlation coefficients, only clinically most relevant variables were selected. For variables eligible for multivariable analysis, missing values were imputed using multiple imputation. The multivariable model was fitted using a stepwise selection of predictors. All statistical analysis was performed with SPSS Statistics 23.0 software (IBM, Armonk, New York, United States of America). P-value <0.05 was considered statistically significant.

Results

Study selection

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

Patient characteristics

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

Univariable analysis of predictors for postoperative complications

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

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

Independent predictors of postoperative complications

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

Discussion

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

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

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

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

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

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

From all individual geriatric domains, polypharmacy and malnutrition were most significantly related with post-operative complications in our population. These domains are both well represented in the G8 as well. Polypharmacy is related to frailty and comorbidities, but also associated with outcome parameters such as postoperative complications, delirium, (chemo)radiation toxicity, increased hospital stay and mortality.[23] Across literature, however, polypharmacy lacks definition and cut-off values range largely, with ≥5 being the mostly used.[23] Whether certain specific medications such as anticoagulants were related to postoperative complications, just like in the study of Amici et al., was not possible to investigate using the current dataset.[37] Malnutrition is very common and undertreated in elderly.[52] Evaluation of the nutritional status is therefore important in preoperative screening. Higher risk of malnutrition using MUST is associated with postoperative complications, increased hospital stay and mortality.[53–55] Often, the body mass index (BMI) is used as an indicator for nutritional status, just as in MUST. However, normal values of 18.5-24.9 kg/mm^2 are based on mortality risk within a young and healthy population.[56] For older patients, a BMI <23 kg/mm^2 is already associated with increased mortality, and may therefore be a better cut-off value for underweight. The 7.9% of patients having risk of malnutrition measured by MUST in our cohort may be an underestimation of the real prevalence of malnutrition. Identification of such deficits is particularly important, as a geriatrician or a dietary consultant may be able to respectively manage polypharmacy or prevent malnutrition, lowering the risk of complications.

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

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

Limitations of our study may include that it is a single center study in a tertiary care hospital. As a result, the cohort contains a high percentage of complex cases, regarding tumor and treatment characteristics. Furthermore, the population was heterogenic, also in terms of tumor characteristics, like histopathology. However, as we were primarily investigating patient-related factors, this seemed to be less relevant in our study. Lastly, most complications have only temporary effect on the patients' lives. Other outcome parameters, 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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465 **Figure 1**

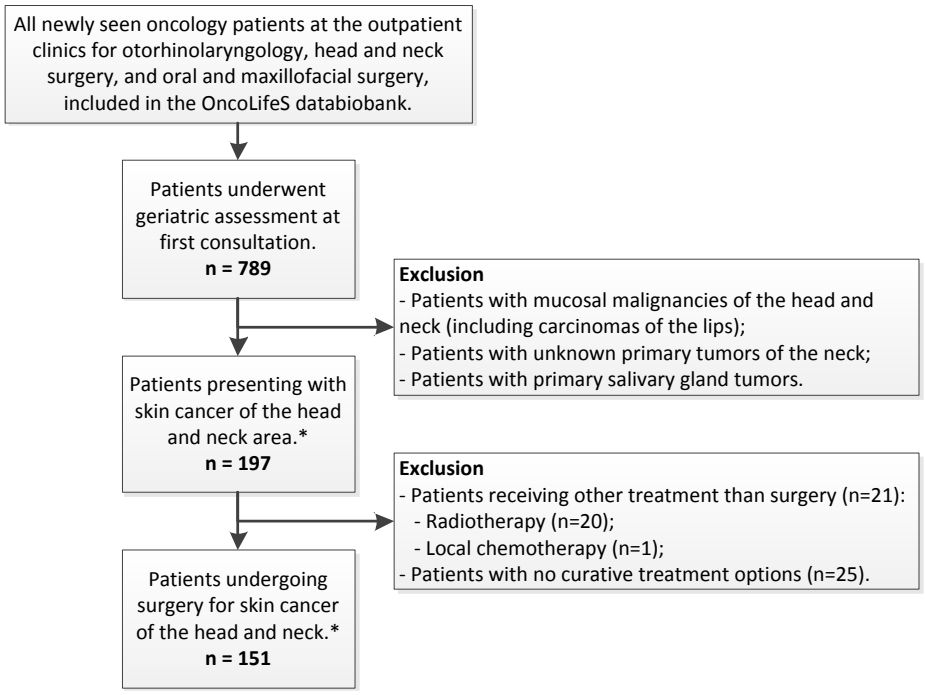

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Figure 1. Flowchart diagram representing the inclusion of patients into the final cohort of 151 patients who were surgically treated for cutaneous head and neck malignancies. * Cohorts showed no significant differences in age and sex throughout exclusion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

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** n=151
No complications	89 (58.9%)
Grade I	22 (14.6%)
Grade II	25 (16.6%)
Grade III	13 (8.6%)
Grave IV	2 (1.3%)
Grade V	0 (0.0%)

518
519

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 ± SD, y	78.9 ± 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**
≥ 40mm	13 (10.7%)	**3.89 (1.12-13.51)**	**< 0.05**
Invasion depth			
Mean ± SD, mm	5.2 ± 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			

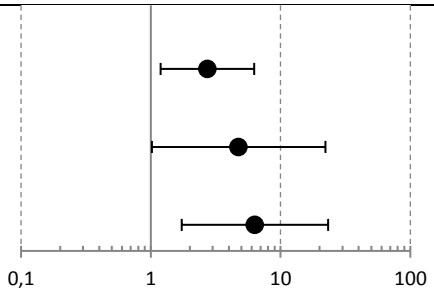
< 5 medications	95 (65.1%)	1	
≥ 5 medications	51 (34.9%)	**2.36 (1.11-5.07)**	**< 0.05**
Nutritional status			
MUST			
Low risk	128 (92.1%)	1	
Medium to high risk	11 (7.9%)	3.46 (0.99-12.07)	0.05
Functional status			
ADL			
No restrictions (< 1)	114 (82.6%)	1	
Restrictions (≥ 1)	24 (17.4%)	1.69 (0.65-4.39)	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

526

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]			
Minor		1	
Major		**2.73 (1.19-6.26)**	**< 0.05**
Anesthesia			
Local anesthesia		1	
General anesthesia		**4.74 (1.02-22.17)**	**< 0.05**
Frailty on G8			
Non-frail (> 14)		1	
Frail (≤ 14)		**6.34 (1.73-23.25)**	**< 0.01**



539

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