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ORIGINAL ARTICLE

Days alive and out of hospital following primary surgery for oral cavity squamous cell carcinoma

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ABSTRACT

Background: Days Alive and Out of Hospital (DAOH) is a recently introduced, readily obtainable postoperative outcome measure method that expresses procedure and disease-associated morbidity and mortality. In this study, we evaluated DAOH with 30- and 365-days follow-up periods after primary surgery ($DAOH_{30}$ and $DAOH_{365}$, respectively) for patients with oral cavity squamous cell carcinoma (OSCC). The aim of this study is to identify patient-, procedure- and disease-associated risk factors for patients treated with primary surgery for primary OSCC.

Material and methods: This retrospective cohort study from a prospective collected database represents patients from Eastern Denmark surgically treated for primary OSCC in the period 2000–2014. $DAOH_{30}$ and $DAOH_{365}$ were calculated and associations with patient characteristics including comorbidity, tumor characteristics, clinical outcomes such as length of stay, readmission, and mortality were evaluated. Tests for difference and significance between groups were assessed with Mann–Whitney U test and quantile linear regression.

Results: We included 867 patients (63% males, median age: 63 years (IQR 56–70 years)). Median $DAOH_{30}$ and $DAOH_{365}$ after OSCC surgery were 25 days (IQR 21–27 days) and 356 days (IQR 336–360 days), respectively. Alcohol consumption had a significant association with a lower $DAOH_{365}$, $p < 0.01$, but not with $DAOH_{30}$. Advanced T-stage, adjuvant radiotherapy (RT) and increased Charlson Comorbidity Index (CCI) score was significantly associated with a lower $DAOH_{30}$ and $DAOH_{365}$.

Conclusion: In this population-based study in OSCC patients treated with primary surgery, we found that DAOH after 30 days was 25 days (83%), while DAOH after 365 days was 356 days (98%). Advanced T-stage acts as a predictor for significant $DAOH_{30}$ and $DAOH_{365}$ reduction while excessive alcohol consumption predicts a significant $DAOH_{365}$ reduction. Readmission within 30 days following surgery was associated with further readmission within one year.

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Introduction

Cancer of the oral cavity is one of the most frequent malignancies, and with 405,000 new cases per year, oral squamous cell carcinoma (OSCC) is the sixth most common malignancy worldwide [1–4]. Although surgical techniques and multimodal therapy have improved, the survival rates among patients undergoing OSCC surgery have not changed significantly in the last decade, with 5-year survival rates of 50% [5–7]. Peri- and postoperative complications are yet dominating factors impairing patient recovery resulting in prolonged hospital stay, hospital readmission, and reduced survival [8,9].

Postoperative complications occur in up to 28% of all patients undergoing surgery for OSCC [10]. A commonly used method to report postoperative complications is the Clavien-Dindo Classification system, where the complications are evaluated and graded from I-V according to severity [11]. However, simply grading postoperative complications is unlikely to capture the full patient experience and patients' recovery after surgery [12]. As a result, a variety of outcome measures have been proposed to quantify the patients perceived postoperative experience, and only a few provide a strong and patient-centered perspective of effective and efficient postoperative care needed in value-based healthcare [12–16]. Recent studies have documented that patients consider readmission due to postoperative complications as a major issue resulting in reduced quality of life and loss of independence, and is a strong predictor of postoperative mortality in elderly patients [9, 17–20].

Days Alive and Out of Hospital (DAOH) is a measure of days spent in the hospital following index surgery and has been shown to be a readily obtainable and efficient patient-centered outcome measure in perioperative clinical trials [8,

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21]. DAOH has previously been described in patients undergoing transoral robotic surgery for oropharyngeal cancer [22,23], but never in patients surgically treated for OSCC. DAOH was first introduced in studies on heart disease and stroke [24,25] but has also proved a strong correlation between postoperative complications and fewer days at home in patients undergoing a wide variety of surgical procedures [8,9, 21, 26–28]. DAOH provides a measure to detect clinically important differences in outcome, including primary length of hospital stay (LOS), readmission to hospital, and death [29,30]. DAOH is highly sensitive to comorbidity, differences in surgical risk, and the impact of perioperative complications and is also associated with mortality up to 1 year after surgery [9]. DAOH has been used to report on the postoperative course up to 30 and 90 days after surgery but rarely with 365 days follow-up.

The aim of this study was to evaluate DAOH following primary surgery for OSCC ($DAOH_{30}$ and $DAOH_{365}$) to describe the disease and procedure related morbidity and mortality. Further, the association between $DAOH_{30/365}$ and pre- and periprocedural factors, including comorbidity score, OSCC tumor stage, N-stage, adjuvant radiotherapy (RT), LOS, readmission, reoperation, and mortality, were analyzed.

Materials and methods

This retrospective cohort study was conducted on patients treated with primary surgery identified through the Copenhagen Oral Cavity Squamous Cell Carcinoma (COrCa) database [31]. The COrCa database contains information on all OSCC patients diagnosed in Eastern Denmark in the period 2000–2014. Additional patient information was obtained from the Central Population Registry (CPR), Danish National Patients Register (NPR), the Danish Cancer Registry (DCR), and the Danish Cause of Death Register (DAR). CPR contains information on gender, date of birth, and vital status linked to a unique civil registration number assigned to every individual in Denmark upon birth or immigration [32]. NPR contains information on all registered hospital contacts in Denmark since 1946, including inpatient consultations, medical and surgical procedures, and diagnosis codes in accordance with the International Classification of Disease, which was registered using the 10th edition (ICD-10) [33]. DAR contained information on the assumed causative cause of death among all citizens dying in Denmark, classified according to the ICD-10 codes, and was used in the analysis of $DAOH_{30/365}$. The quality of the information entered in the DAR relies upon the accuracy of the physician's notifications hence subject to uncertainty [34]. Data on patients treated with curative intent was extracted from the databases after required approvals from the Danish Data Protection Agency (Approval number: 05228), the Danish Health Data Authority (Approval number: 04280), and the Ethical Committee (Approval number: H-1-2014-053). Based on this data, $DAOH_{30/365}$ and Charlson Comorbidity Index scores (CCI) were calculated [35,36] for all patients. In Denmark, residents are treated at no personal cost in the public healthcare system financed through taxes, thus stressing the unique diversity in the national databases. Due to reimbursement and mandatory reporting, all hospital contacts are reported in NPR. By law, no cancer patients are treated within the private healthcare system.

The primary outcome was $DAOH_{30/365}$, and secondary outcomes were LOS, mortality, and readmissions within the 30- and 365-days follow-up period.

In order to carry out comparative testing, patients were divided into groups based on patient and tumor-specific factors listed in Table 1. Patients were grouped based on gender, age, number of pack-years of smoking, daily units of alcohol, and CCI score at the time of index surgery. Patients were further grouped according to T-stage [37], UICC-stage (8th edition) [38], and according to treatment modality, i.e., surgery or surgery + adjuvant RT. Patients were also grouped according to their LOS following primary surgery (<3 days, 3–5 days, 6–8 days, or more than eight days), whether they were readmitted to the hospital within the first 30 days following surgery, had recurrence, and whether reoperation was performed. Finally, patients were categorized according to the occurrence of death within the study period.

Statistical analysis

Categorical data are presented as numbers with relative percentages. Continuous data are presented as means with 95% confidence intervals (CI) or medians with 25th and 75th interquartile range (IQR). Differences between groups were assessed with Mann–Whitney U test. Quantile linear regression modeling was performed to test for differences between groups with non-parametric continuous data. Statistical analyses were performed in the statistical environment R statistics version 3.5.2 [39]. $p < 0.05$ was considered statistically significant.

DAOH is a composite measure incorporating hospital length of stay following the index surgery (day 0), readmission to either the index or any other hospital, and deaths after surgery into a single outcome metric [8]. DAOH was calculated using hospitalization and mortality data from the date of the primary surgery (day 0) [29].

$DAOH_{30}$ was calculated by subtracting Days Alive and In Hospital within 30 days after surgery ($DAIH_{30}$) and Days Dead within 30 days after surgery (DD_{30}) from the follow-up period of 30 days.

$$DAOH_{30} = 30 \text{ days} - (DAIH_{30} + DD_{30})$$

$DAIH_{30}$ was defined as the aggregate of days with an overnight stay in hospital after the day of the primary surgery and in the follow-up period of 30 days. DD_{30} was defined as the number of days from death to the end of the 30-days follow-up period. $DAOH_{365}$ was calculated similarly to $DAOH_{30}$ as described above with 365 days instead of 30 days. Outpatient hospital visits, including adjuvant RT, were not included in the $DAOH_{30/365}$ calculation.

Readmission causes and postoperative complications

Readmission to the hospital within 30 and 365 days after surgery was categorized according to the cause leading to

Table 1. $DAOH_{30}$ and $DAOH_{365}$ of patient characteristics.

	$DAOH_{30}$			$DAOH_{365}$		
Variate	Count, *n* (%)	Median (IQR)	*p*-value	Count, *n* (%)	Median (IQR)	*p*-value
Gender						
Male	549 (63.3%)	24 (21–26)	Ref	549 (63.3%)	355 (330–360)	ref
Female	318 (36.7%)	25 (21–27)	0.125	318 (36.7%)	357 (340.25–361)	0.01
Age (at date of surgery)						
<50	92 (10.6%)	25 (23–27)	ref	92 (10.6%)	358 (343.75–361)	ref
50–59	238 (27.5%)	25 (21–27)	0.115	238 (27.5%)	355 (336–360)	0.16
60–69	305 (35.2%)	25 (21–26)	0.014	305 (35.2%)	356 (336–360)	0.136
≥70	232 (26.8%)	24 (20–26)	0.002	232 (26.8%)	354.5 (318–360)	0.045
Pack years						
0	108 (12.5%)	25 (21–27)	Ref	108 (12.5%)	357 (346.5–360)	ref
1–40	266 (30.7%)	24.5 (21–27)	0.82	266 (30.7%)	356 (338–360)	0.44
>40	266 (30.7%)	24 (20.25–26)	0.244	266 (30.7%)	354 (337.25–360)	0.084
Unknown	227 (26.2%)	25 (21–27)	0.068	227 (26.2%)	354 (320–361)	0.265
Daily units of alcohol						
0	261 (30.1%)	24 (21–27)	Ref	261 (30.1%)	355 (340–360)	ref
1–4	258 (29.8%)	25 (21–27)	0.775	258 (29.8%)	356.5 (341.25–360)	0.511
>4	198 (22.8%)	24 (20–26)	0.303	198 (22.8%)	352 (327.5–359)	0.039
Unknown	150 (17.3%)	25 (22–27)	0.195	150 (17.3%)	356.5 (300.5–360)	0.007
T-stage						
T1	311 (35.9%)	26 (24–27)	Ref	311 (35.9%)	359 (352–362)	ref
T2	293 (33.8%)	24 (21–26)	<0.001	293 (33.8%)	355 (321–359)	<0.001
T3	45 (5.2%)	21 (19–24)	<0.001	45 (5.2%)	345 (314–354)	<0.001
T4	107 (12.3%)	18 (12–21)	<0.001	107 (12.3%)	331 (253–351.5)	<0.001
Unknown	111 (12.8%)	26 (23–28)	<0.001	111 (12.8%)	356 (342–360)	0.017
N-stage						
N0	536 (61.8%)	25 (22–27)	Ref	536 (61.8%)	357 (346–361)	ref
N1	124 (14.3%)	24 (20–26)	0.011	124 (14.3%)	350 (308.5–358)	<0.001
Unknown	207 (23.9%)	24 (20–26)	0.028	207 (23.9%)	348 (313.5–358)	<0.001
UICC disease stage						
I	251 (29%)	26 (24–27)	Ref	251 (29%)	360 (355.5–362)	ref
II	188 (21.7%)	25 (22–26)	<0.001	188 (21.7%)	357 (344–360)	<0.001
III	121 (14%)	24 (21–26)	<0.001	121 (14%)	351 (314–358)	<0.001
IV	199 (23%)	20 (14.5–23)	<0.001	199 (23%)	336 (279.5–352)	<0.001
Unknown	108 (12.5%)	26 (23.75–28)	0.073	108 (12.5%)	356 (343.75–360)	<0.001
Treatment						
Surgery	497 (57.3%)	25 (23–27)	Ref	497 (57.3%)	358 (349–361)	ref
Surgery + RT	370 (42.7%)	22.5 (19–26)	<0.001	370 (42.7%)	347 (310.25–357)	<0.001
CCI at date of surgery						
2	531 (61.2%)	25 (21–27)	Ref	531 (61.2%)	357 (342–361)	ref
3	194 (22.4%)	24 (20–26)	0.034	194 (22.4%)	354 (323–359)	0.002
4	71 (8.2%)	24 (20.5–26.5)	0.12	71 (8.2%)	351 (321.5–360)	0.038
5	31 (3.6%)	22 (15–26.5)	0.074	31 (3.6%)	339 (282–356)	<0.001
>5	40 (4.6%)	24 (19.5–26)	0.012	40 (4.6%)	347.5 (223.3–357.3)	<0.001
LOS						
<3	151 (17.4%)	28 (28–28)	Ref	151 (17.4%)	361 (357–363)	ref
3–5	355 (40.9%)	26 (25–27)	<0.001	355 (40.9%)	359 (349–361)	<0.001
6–8	161 (18.6%)	23 (22–24)	<0.001	161 (18.6%)	353 (334–357)	<0.001
>8	200 (23.1%)	17 (12–20)	<0.001	200 (23.1%)	336 (248.75–350)	<0.001
Readmission <30 days						
No	730 (84.2%)	25 (21–27)	Ref			
Yes	137 (15.8%)	22 (18–24)	<0.001			
Readmission <365 days						
No				705 (81.3%)	357 (341–361)	ref
Yes				162 (18.7%)	347 (311–357)	<0.001
Re-surgery						
No	818 (94.3%)	25 (21–27)	Ref	799 (92.2%)	356 (336–360)	ref
Yes	49 (5.7%)	23 (18–24)	<0.001	68 (7.8%)	352 (332.25–358)	0.016
Recurrence						
No	862 (99.4%)	25 (21–27)	Ref	726 (83.7%)	357 (344–361)	ref
Yes	5 (0.6%)	22 (19–24)	0.14	141 (16.3%)	336 (275–352)	<0.001
Days dead						
0	861 (99.3%)	25 (21–27)	Ref	756 (87.2%)	357 (347–360)	ref
1–30	6 (0.7%)	0 (0–0)	<0.001			
1–180				73 (8.4%)	219 (172–261)	<0.001
>180				38 (4.4%)	49 (3.5–91.5)	<0.001

Count, *n* (%); IQR: Inter-quartile-range; UICC: Union for international Cancer Control; RT: Radiotherapy; CCI: Charlson Comorbidity Index; LOS: Length of (hospital) stay; Days dead: mortality and related DAOH within period.

hospital admission and the related diagnosis code(s) registered during hospitalization. Each in-hospital period for a patient included one or more registrations in LPR, and each registration was affiliated with a primary diagnosis code. Registered diagnosis codes include postoperative complications causes but could also be due to other concurrent diseases or already existing comorbidities. Diagnosis codes were grouped according to type and category into five major groups defined as (I) postoperative complications, (II) malignancy, (III) cardiopulmonary, (IV) digestive system disorders, and (V) other. In every major group, subgroups were included to further specify the cause of readmission. A weighting factor, expressing how much every single major group and subgroup contributed DAOH reduction, was calculated to determine the relative impact of every readmission cause in relation to the entire postoperative course [23].

$$\text{Relative impact} = \frac{\text{Number of readmissions (in group or subgroup)}}{\text{Total number of readmissions}} \times \text{Median length of readmission (group or subgroup)}$$

Most readmissions had the diagnosis code of their primary disease co-assigned concurrently with the cause of readmission, e.g., postoperative bleeding. In the case of reoperation, the diagnosis code assigned to the readmission was also the primary disease, often not further specified. The process above was performed for both the 30 days and 365 days follow-up periods. Postoperative complications were defined as any diagnosis codes associated with the surgery within 30 days following surgery, e.g., postoperative bleeding, infection, etc.

Results

A total of 867 patients with OSCC treated with primary surgery were included in this study. The median age at surgery was 63 years (IQR 56–70 years). Only 108 (12.5%) patients were registered with no smoking history, while 266 (30.7%) patients had a history of smoking for more than 40 pack-years (Table 1 and Figure 1). A total of 198 (22.8%) patients had a history of drinking more than four units of alcohol per day. A total of 137 (15.8%) patients were readmitted with an overnight stay within 30 days after surgery. During the first 30 days following index surgery, 49 (5.7%) patients underwent reoperation for their OSCC.

$DAOH_{30}$

The median $DAOH_{30}$ was 25 days (IQR 21–27 days) for the entire cohort. Patients aged above 60 years had a lower $DAOH_{30}$ than patients aged under 50 years, $p < 0.02$. This was further confirmed through a quantile linear regression model, which found a lower $DAOH_{30}$ with increasing age, $p < 0.001$, Table 2. No difference in $DAOH_{30}$ was found according to the number of pack-years of smoking or daily alcohol intake. Lower $DAOH_{30}$ was seen with increasing T-stage, Table 1 and Figure 1. Similarly, a lower $DAOH_{30}$ was seen with increasing UICC stages, Table 1 and Figure 1. Patients who underwent surgery without adjuvant RT had a median $DAOH_{30}$ of 25 days (IQR 23–27 days), while patients who received adjuvant RT had a median $DAOH_{30}$ of 22.5 days (IQR 19–26 days), $p < 0.001$. Only patients with a CCI score >5 had a significantly lower $DAOH_{30}$ than patients with CCI scores 2–5, $p = 0.012$. Concurrently, a quantile linear regression model found a significantly lower $DAOH_{30}$ with increasing T- or N-stage, and CCI, Table 2. Quantile linear regression modeling found lower $DAOH_{30}$ with increasing primary LOS, Table 2.

We found no significant $DAOH_{30}$ reduction in patients with residual malignant disease within 30 days after surgery. Patients who underwent reoperation (not further specified) for their OSCC had significantly lower $DAOH_{30}$ than patients who did not undergo reoperation, $p < 0.001$. Reduced $DAOH_{30}$ was significantly associated with six-month mortality, $p < 0.001$, Table 1 and Figure 1.

$DAOH_{365}$

The median $DAOH_{365}$ was 356 days (IQR 336–360 days) for the entire cohort. The fraction of patients with specified intervals of $DAOH_{365}$ is seen in Figure 1. Patients aged $\geq$ 70 years had a lower $DAOH_{365}$ than patients aged under 50 years, with median $DAOH_{365}$ of 354.5 days (IQR 318–360 days) and 358 days (IQR 344–361 days), respectively, $p = 0.045$. No difference in $DAOH_{365}$ was found between groups according to the number of pack-years of smoking. A significant reduction of 1.6 days in $DAOH_{365}$ was found between patients with and without alcohol consumption, and quantile linear regression modeling found a significantly lower $DAOH_{365}$ with increasing alcohol consumption, $p < 0.01$. A significant association was seen between advanced T-stages and lower $DAOH_{365}$ throughout all increasing T-stages, Table 1, and Figure 2; this was further confirmed with quantile linear regression, $p < 0.001$. In line with advancing T-stages, a significant association between advanced UICC stages and lower $DAOH_{365}$ was seen throughout all increasing UICC stages, Table 1 and Figure 2. Patients who solely underwent surgery had a median $DAOH_{365}$ of 358 days (IQR 349–361 days), while patients who underwent surgery with adjuvant RT had a median $DAOH_{365}$ of 347 days (IQR 310–357 days), $p < 0.001$. Patients with a CCI score $>$ 2 had a significantly lower $DAOH_{365}$ than patients with a CCI score $\leq$ 2. A quantile linear regression model found a consistently lower $DAOH_{365}$ with increasing CCI scores, Table 2.

$DAOH_{365}$ was significantly lower in patients with a primary LOS $>$ 3 days compared to patients discharged within three days of hospitalization after surgery, $p < 0.001$. Although non-significant, patients discharged on the same day of surgery had a lower $DAOH_{365}$ than patients discharged after 1 to 5 days after surgery, median $DAOH_{365}$ 356 days (IQR 342–365 days) and 361 days (IQR 357–363 days), $p = 0.394$. Quantile linear regression modeling found lower $DAOH_{30}$ with increasing primary LOS, after adjusting for the primary LOS (Table 2). Patients who had a recurrence within 365 days had a significantly lower $DAOH_{365}$ than patients with no recurrence, respectively 336 days (IQR 278–352 days) and 357 days (IQR 344–361 days), $p < 0.001$. Patients who underwent reoperation (not further specified) for their OSCC had

Figure 1. Boxplot of Median $DAOH_{30}$ for Patients- and Postoperative Characteristics. UICC: Union for international Cancer Control; CCI: Charlson Comorbidity Index; LOS: Length of (hospital) stay.

significantly lower DAOH than patients who did not undergo reoperation, $p = 0.016$. Reduced $DAOH_{365}$ was significantly associated with one-year mortality, $p < 0.001$ (Table 1 and Figure 2). Overall, 111 (12.8%) patients died within one year after surgery. Of these, 6 (0.7%) patients died within 30 days, 32 patients (3.7%) died within 180 days following surgery, while the remaining 73 patients (8.4%) died in the period 180–365 days after surgery.

Postoperative follow-up

The number of patients readmitted within 30 days following surgery was $n = 137$ (15.8%). Some patients had more than one readmission in the period, resulting in a total of $n = 277$ readmissions. The majority of readmissions, $n = 179$ (64.6%), within 30 days following surgery were due to a concurrent reason related to malignancy, with 172 (62.4%) readmissions

Table 2. Quantile linear regression of patient characteristics and $DAOH_{30}$ and $DAOH_{365}$.

	$DAOH_{30}$			$DAOH_{365}$		
Variable	Median (IQR)	Estimate	*p*-value	Median (IQR)	Estimate	*p*-value
Age	62.7 (62.7–62.7)	−0.08	<0.001	62.7 (62.7–62.7)	−1.02	<0.001
Pack years (smoking)	47 (47–47)	−0.01	0.24	47 (47–47)	−0.12	0.08
Daily units of alcohol	3 (3–3)	0	0.62	3 (3–3)	−0.21	<0.01
T-stage	2 (2–2)	0.02	<0.001	2 (2–2)	0.03	<0.01
N-stage	0 (0–0)	0.02	0.01	0 (0–0)	0.01	0.89
UICC stage	2 (2–2)	0.02	0.01	2 (2–2)	0.03	<0.01
Charlson Comorbidity Index (CCI)	2 (2–2)	−0.71	<0.001	2 (2–2)	−11.6	<0.001
Length of stay (LOS)	5 (5–5)	−0.97	<0.001	5 (5–5)	−2.14	<0.001

IQR: Inter-quartile-range stay; UICC: Union for international Cancer Control; CCI: Charlson Comorbidity Index; LOS: Length of (hospital); Estimate, regression model output for how much outcome (DAOH) changes per single change in variable grouping.

due to head and neck malignancy. Forty-one readmissions (14.8%) to the hospital within 30 days following surgery were registered as diagnoses that were likely to be postoperative complications. Among these postoperative complications, postoperative infection ($n = 18$, 6.5%) had the highest impact, followed by postoperative bleeding ($n = 12$, 4.3%) on $DAOH_{30}$ reduction. Other causes for readmission are listed in Table 3. The number of patients readmitted within 365 days following surgery was $n = 162$ (18.7%), resulting in a total of $n = 919$ readmissions. The majority of readmissions, $n = 368$ (40%) within 365 days after surgery were due to a concurrent reason related to malignancy, with head and neck malignancies being the most frequent, $n = 301$ (32.8%). The remaining readmission causes are seen in Table 3.

Discussion

This study found that the median $DAOH_{30}$ and $DAOH_{365}$ after OSCC surgery were 25 days (IQR 21–27 days) and 356 days (IQR 336–360 days), respectively.

While most studies have explored DAOH for a period of 30 to 90 days, several postoperative complications and poor survival manifest several months after surgery [18,40,41]. This study suggests that a combinatory exploration of 30- and 365-days follow-up periods after surgery offers important insight into patients' overall postoperative course and rehabilitation, including postoperative complications, recurrences, reoperation, and deaths. Where the period of 30 days provides an understanding of surgery-related factors affecting the postoperative course, the extended period of observation to 365 days captures the long-term complications after surgery that can impair quality of life [42]. Previous studies have argued that, given the potential for missing data and the weight of additional work, DAOH-assessment for more than 30 days has no significant additional benefit over DAOH for 30 days [9]. While other studies have argued that DAOH beyond 30 days is important in detecting time-cause differences in specific complications [21,40]. Databases and registries used in this study are established and maintained regional and nationwide, no additional work is required for follow-ups and the potential missing data is minimal. Therefore, we believe that a combined analysis of $DAOH_{30}$ and $DAOH_{365}$ yields a superior evaluation of the postoperative outcome in a well-defined timely manner. The risk of variations in overall hospital stay, from admission to discharge, can impact DAOH and can potentially constitute a bias, why standardized criteria for admission and discharge is of importance for overall trackability of the entire postoperative course.

Forty-nine patients underwent reoperation during the 30 days follow-up period. A substantial part of these are thought to be due to sentinel node biopsy (SNB), which is routinely performed at our institution and is positive in 20–30% of the patients [43] and when found to be positive leads to a subsequent neck dissection. However, the data derived from national registries do not allow for detailed information regarding the indication for reoperation.

Several studies have proven a relationship between alcohol and tobacco use and the risk of OSCC development as well as increased cancer-related mortality [44,45]. Although approximately one-third of the patients in this study were considered heavy smokers and categorized with heavy alcohol consumption, this study found no association between the use of alcohol and tobacco, including their respective quantity and $DAOH_{30}$. However, we found that alcohol consumption of more than four units per day was significantly associated with a lower $DAOH_{365}$. Advanced tumor stage was, as expected, found to be significantly associated with a lower $DAOH_{30}$ and $DAOH_{365}$, which may suggest differences in surgical approach and hence the risk of postoperative complications as well as diverse treatment plans with adjuvant treatment offered advanced tumor stages. Patients who underwent adjuvant RT had a significant reduction in both $DAOH_{30}$ and $DAOH_{365}$, reflecting a higher tumor stage or deviating surgery-related factors such as positive margins and/or extracapsular spread in cervical lymph nodes. Treatment with adjuvant RT was counted as outpatient visit since the treatment is not given under hospitalization. Hence, RT treatment did not impact DAOH itself, as no DAIH was added to the calculation of DAOH, but the multimodal therapy treatment was significantly associated with lower $DAOH_{30/365}$. Postoperative RT has also been shown to significantly reduce the quality of life of OSCC patients [46], i.e., an indirect parameter in the measure of DAOH [8].

Primary LOS was found to be significantly associated with both $DAOH_{30}$ and $DAOH_{365}$. Although the definition of DAOH does not allow adjustment for primary LOS, we found an association between the length of primary LOS and lower $DAOH_{30/365}$, most prominent for $DAOH_{365}$. Furthermore, we found that patients discharged on the same day of surgery had a slightly lower DAOH than patients discharged after 1–5 days which might suggest that too early discharge after

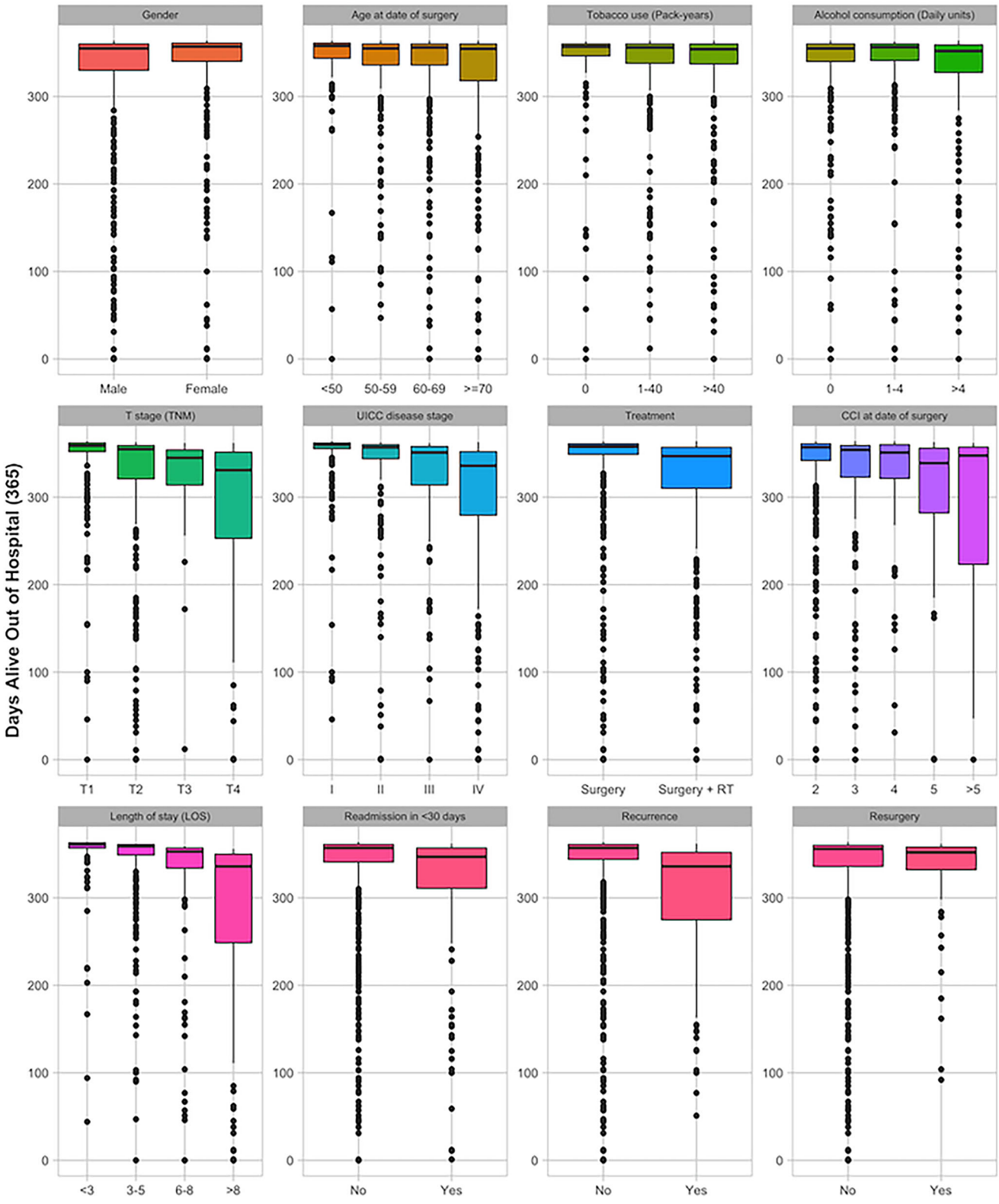

Figure 2. Boxplot of Median $DAOH_{365}$ for Patients- and Postoperative Characteristics. UICC: Union for international Cancer Control; CCI: Charlson Comorbidity Index; LOS: Length of (hospital) stay.

surgery fails to capture potential postoperative complications.

Quantile linear regression found that tumor specific factors (such as TNM- and UICC-stage) affect both $DAOH_{30}$ and $DAOH_{365}$. Comorbidities, as measured by CCI, impacted both $DAOH_{30\&365}$. Comorbidity has consistently been found to have an adverse impact on treatment effectiveness and cancer survival, where studies have reported higher rates of complications in cancer patients with comorbidity [47,48].

We found that patients with OSCC recurrence had a significantly reduced $DAOH_{365}$. Patients readmitted within 30 days after surgery had an average of approximately two

Table 3. Readmission causes within 30- and 365 days following surgery.

	Readmission within 30 days			Readmission within 365 days		
Category	Admission count (%)	Median inpatient days (IQR)	Relative impact	Admission count (%)	Median inpatient days (IQR)	Relative impact
Postoperative complication	41 (14.8%)	4 (2–6)	0.592	158 (17.2%)	5 (2–8)	0.86
Bleeding	12 (4.3%)	2.5 (2–4.25)	0.108	18 (2%)	2 (1.25–4)	0.039
Infection, other	9 (3.2%)	5 (4–8)	0.162	50 (5.4%)	4 (2–8)	0.218
Infection, respiratory	6 (2.2%)	5 (3.25–6.75)	0.108	29 (3.2%)	7 (5–13)	0.221
Infection, systemic	3 (1.1%)	3 (2.5–13)	0.032	13 (1.4%)	6 (3–12)	0.085
Other	11 (4%)	2 (1–4)	0.079	48 (5.2%)	4 (1–7)	0.209
Malignancy	179 (64.6%)	7 (3–11)	4.523	368 (40%)	8 (4–15)	3.203
Head and neck	172 (62.1%)	7 (3.75–11)	4.347	301 (32.8%)	8 (4–16)	2.62
Metastatic	6 (2.2%)	3 (1.5–3.75)	0.065	14 (1.5%)	9.5 (3.25–19.5)	0.145
Lung				29 (3.2%)	5 (3–7)	0.158
Other location	1 (0.4%)	4 (4–4)	0.014	24 (2.6%)	4.5 (3–9)	0.118
Cardiopulmonary	24 (8.7%)	4.5 (3–7.25)	0.39	101 (11%)	4 (2–9)	0.44
Circulatory disease	8 (2.9%)	3 (2–4.25)	0.087	40 (4.4%)	3.5 (2–5.25)	0.152
Heart disease	3 (1.1%)	8 (6–10.5)	0.087	16 (1.7%)	3.5 (2–6.5)	0.061
Pulmonary disease	13 (4.7%)	5 (3–13)	0.235	45 (4.9%)	5 (3–9)	0.245
Digestive system disorder	16 (5.8%)	2 (1–4)	0.116	98 (10.7%)	4 (2–9)	0.427
Acute	12 (4.3%)	2 (1–4)	0.087	56 (6.1%)	4 (2–7)	0.244
Other	4 (1.4%)	1.5 (1–4.5)	0.022	42 (4.6%)	4 (2–13.5)	0.183
Other	17 (6.1%)	4 (2–7)	0.245	194 (21.1%)	3 (2–8)	0.633
Benign tumor				19 (2.1%)	4 (2.5–6)	0.083
Intoxication				17 (1.8%)	3 (2–5)	0.055
Neurological				27 (2.9%)	2 (1–6)	0.059
Orthopedic	5 (1.8%)	4 (4–7)	0.072	29 (3.2%)	4 (3–12)	0.126
Other	12 (4.3%)	3 (1.75–5.5)	0.13	102 (11.1%)	3 (2–8)	0.333

Total number of readmissions within 30 days: $n = 277$. Total number of readmissions within 365 days: $n = 919$. Admission count, n (%), IQR: Inter-quartile-range.

readmissions per patient during the first month after surgery, while the average number of readmissions within one year was 5.7 readmissions per patient. Of all patients readmitted within one year, approximately 85% were also readmitted within the first month after surgery, suggesting readmission within the first month could be a predictor for further readmissions within one year, hence resulting in a further DAOH reduction.

Postoperative infections (other than respiratory or systemic infection) and postoperative hemorrhage had the highest impact among postoperative complications on $DAOH_{30}$ reduction and hence increased morbidity. This mandates closer attention to preventing these complications in future perioperative enhancement studies since prevention of these causes will lead to the most significant improvement in $DAOH_{30}$ and thereby improve treatment quality and efficiency, both from a patient-cohort and healthcare perspective. In addition, clinical attention should focus on patients with a CCI >2 (since median $DAOH_{365}$ is reduced with a median of 11.6 days with each increasing CCI score), patients with heavy alcohol consumption, and patients receiving adjuvant RT since these patients are at risk of increased morbidity according to $DAOH_{365}$. Future studies should strive to improve the long-term postoperative course for these patients.

The study has limitations. Since population databases and registries capture postoperative morbidity with varying accuracy and severity during the prospective registration process, the true incidence of complications might be higher. The diagnosis codes and data from the national registries might not reflect all specific complications developing under readmission, e.g., a patient readmitted with postoperative infection which develops irregular heart rhythm that prolongs the LOS will often only be registered as a postoperative infection if the patient is not transferred to another department, e.g., the cardiologic department. In cases where patients, during a continuous admission, were transferred between departments we used the diagnosis codes associated with each department to calculate the relative impact of a readmission diagnosis. Another limitation is the inability to filter out SNB followed by complete neck dissection. However, the strengths of this study include a well-described cohort of patients undergoing primary surgical treatment for primary OSCC with prospective registration of comorbidity and with a complete mandatory follow-up of hospital contacts through the regional and national databases.

In conclusion, the median $DAOH_{30}$ and $DAOH_{365}$ after OSCC surgery were 25 days (IQR 21–27 days) and 356 days (IQR 336–360 days), respectively. This was significantly reduced in patients with advanced tumor stages and in patients with a higher comorbidity score. Furthermore, the study found that alcohol consumption reduced $DAOH_{365}$ but not $DAOH_{30,}$ suggesting a long-term impact on recovery but less of an impact on short-term recovery. The most common postoperative complication causes of readmission within 30 days following surgery were postoperative bleeding and infection, with the latter having the highest relative impact on the reduction of $DAOH_{30}$.

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Data availability statement

Due to the nature of this research, participants of this study did not agree for their data to be shared publicly, so supporting data is not available.

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