

Does recreational drug use influence survival and morbidity associated with laryngeal cancer

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Original Article

Abstract

Background: The use of opioids is considered a risk factor for laryngeal cancer. A retrospective study was performed to explore the relationship between recreational drug exposure and laryngeal cancer.

Methods: Patients diagnosed between the 1st of January 2013 and the 31st of December 2017 using ICD-10 CD-32 coding were identified from the Head and Neck Multidisciplinary Team database. We divided the study population into two cohorts (RD and non-RD) and compared the demographics, morbidity, and outcomes of these two populations. In addition, we performed case-matched analysis to control for potential confounding factors including gender, alcohol use and cigarette smoking.

Findings: 329 patients in Glasgow, Scotland were included with a mean age of 64.96 ± 10.94 and a follow-up of 24 ± 13.91 months. Of these, 39 reported recreational drug use (RD). RD was associated with younger age (53.0 vs. 66.6 , $p < 0.001$) at diagnosis with laryngeal cancer. A greater proportion of tumours occurred in the supraglottic subsite ($p = 0.041$). Furthermore, these patients were more likely to undergo tracheostomy (RR=2.50, 95% CI: 1.41-4.44, $p = 0.008$) and laryngectomy (RR=2.25, 95% CI: 1.57-3.21, $p < 0.001$). Recreational drug users were more likely to require enteral feeding support (RR= 1.44, 95% CI: 1.13-1.84, $p = 0.02$) during oncological treatment. No survival differences were noted at 1, 2, or 3-years ($p_{\log\text{-rank}} = 0.83$). Case matched analysis correcting for smoking, alcohol and gender confirmed that recreational drug users were younger at diagnosis with a predilection for the supraglottic subsite.

Conclusion: Recreational drug use is associated with an increased burden of disease and morbidity in laryngeal cancer. We suggest that clinicians view recreational drug exposure as a red flag in those with suspected laryngeal cancer regardless of patient age.

Keywords: Head and Neck neoplasms; Laryngeal neoplasms; Substance-related disorders; Analgesics, Opioid, Illicit drugs

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Introduction

Head and neck cancer (H&NC) is the 8th most common cancer in the United Kingdom with laryngeal cancer accounting for 19.7% of these.¹ 1-year and 5-year survival rates are as low as 84.6% and 64.8% respectively¹ and treatment frequently results in significant morbidity, including enteral feeding support, tracheostomy or laryngectomy. The West of Scotland has an incidence rate of 7.3 per 100000, higher than the Scottish average.² Cigarette and alcohol use are known risk factors for laryngeal cancer.³⁻⁶ However, opioids have also been implicated in the development of cancer and are associated with younger age at presentation.⁷⁻¹²

The impact of recreational drug (RD) use such as cannabis, cocaine and benzodiazepines on the development of H&NC cancer is debatable, partly due to the numerous issues in their analysis. Often the use is mixed and under-reported, and accurate dose determination is impossible.^{6, 10, 11} In addition, patterns of drug-related behaviour differ widely around the world, making it difficult to apply research results on a large scale. Regardless, drug use is thought to contribute to at least 90 causes of death, with drug-related deaths increasing over time.¹³ Therefore, several mechanisms for RD in carcinogenesis have been proposed.

Polycyclic aromatic hydrocarbons in opioid smoke are believed to be carcinogens.¹⁰ The μ -opioid receptor stimulation increases cell proliferation and promotes angiogenesis, increasing the risk of malignant transformation.^{14, 15} It has also been found to impair macrophage, T-cell and natural killer cell function which have carcinoprotective effects.⁸ When smoked, cannabis contains the same number of carcinogens as cigarettes, but with triple the amount of tar and smoke retention.^{14, 16} Cocaine's carcinogenic properties have not been fully established and its effect on laryngeal cancer has not been explored.¹⁴ Benzodiazepines, on the other hand, are thought to impact tobacco related cancer.¹⁷ Given that drug use is often heterogeneous, there is value in examining these drugs together in laryngeal cancer.

The United Nations Office on Drugs and Crime (UNODC) estimated that around 5.5% of people aged 15-64 used drugs at least once during the year 2016.¹⁸ Whereas, the same figure for Scotland from the same source in 2014 was 10.33%.¹⁹ Additionally, opiate drug-related death in 2016 in Scotland was highest in the region being managed by^{2, 20, 21}. This epidemiological study presents a unique

opportunity to evaluate the relationship between RD use and laryngeal cancer with regard to oncological outcomes and treatment morbidity.

Methods

Based on the Medical Research Council toolkit, ethical application was not required but local approval from the Queen Elizabeth University Hospital, Glasgow, Scotland Otolaryngology Head and Neck Surgery Department was obtained.

This was a retrospective cohort study. Patients diagnosed with pathologically confirmed squamous cell carcinoma of the larynx between the 1st of January 2013 and the 31st of December 2017 using ICD-10 CD-32 coding were identified from the West of Scotland Head and Neck Multidisciplinary database. All those with a tumour type other than squamous cell carcinoma were excluded.

Clinical information was compiled from patients' digital case record. The use of RD was identified based on patient-reported exposures to opioids, cannabis, cocaine and "street" benzodiazepines. All tumour staging was based on TNM7.

Follow-up time was calculated from the date of multi-disciplinary team discussion to the date of death or final clinic review. The date of multi-disciplinary team discussion was chosen for this time point as it was more reliable than the date of treatment completion. Socio-deprivation was analysed with the Scottish Index of Multiple Deprivation (SIMD16).²² Which ranks 6,976 data zones with regard to their deprivation based on 7 domains: income, employment, education, and health, access to services, crime, and housing.

We divided the study population into two cohorts (RD and non-RD) and compared the demographics, morbidity, and outcomes of these two populations. Continuous variables were tested for normality. Normally distributed variables were analysed with Welch's Two-Sample T-Test. Categorical data were analysed with Pearson's chi-squared (χ^2) test if conditions were met, otherwise Fisher's Exact Test (f) was used. Kaplan-Meier analysis (KM) and Log-rank test were performed for univariate survival analysis. This was reported as the median survival if this survival level was reached. A p-value of ≤ 0.05 on univariate analysis was required for entry into the multivariate cox proportional hazard analysis. Cigarette smoking and alcohol use were also included in the multivariate analysis as they are well established risk factors for laryngeal cancer.

Schoenfeld residuals were used to test the assumption of proportional hazards. Effect size estimates were reported as relative risk (RR).

In addition to the above analyses, case-matched analysis was also completed to control for potential confounding factors including gender, alcohol use and cigarette smoking. Age and Performance Status (PS) were not used as a criterion for case-matching as the RD cohort was assumed to be younger at

diagnosis with better PS. (Appendix Table A).

Computer-generated anonymised case matching for RD exposure was completed. Four patients from the RD cohort were excluded as no appropriate case matches were available. The result included 70 patients: 35 for each arm.

No power analysis was conducted. R, version 3.6.2 (2019-12-12) was used for all statistical analyses.

Appendix Table A. Confounding Adjustment for Case-Matching

	No N=35	Yes N=35	p.overall
Gender			1.000
Female	13 (37.1%)	13 (37.1%)	
Male	22 (62.9%)	22 (62.9%)	
Cigarette			1.000
Non-Smoker	1 (2.86%)	1 (2.86%)	
Ex-Smoker	3 (8.57%)	3 (8.57%)	
Smoker	31 (88.6%)	31 (88.6%)	
Alcohol			1.000
Non-Drinker	11 (31.4%)	11 (31.4%)	
Ex-Drinker	3 (8.57%)	3 (8.57%)	
Drinker	21 (60.0%)	21 (60.0%)	

Results

Initially, 339 patients were identified. Ten were excluded: 2 neuroendocrine cancer, 4 carcinoma-in-situ, 1 indeterminate cancer and 3 for inadequate documentation. Overall, 329 patients were analysed (Table 1). There were 39 (11.9%) patients in the RD cohort and 290 (88.1%) in the non-RD cohort. The mean age was 64.96 ± 10.94 (range 35-96) years with median follow-up of 24 ± 13.91 (range 0-55) months. 20 (51.3%) patients used opioids, 13 (33.3%) used cannabis, 5 (12.8%) used cocaine and 20 (51.3%) used street benzodiazepines. The most common opioid used was methadone (n=11, 55%). 13(33%) patients reported multiple substance use with the most common combination being opioids and benzodiazepines.

There was no difference between cohorts regarding gender distribution, follow-up duration, BMI, American Society of Anaesthesiologists' (ASA) classification, or alcohol use (Table 1). The RD cohort had a significantly greater proportion of current smokers (84.6% vs. 59%, $p=0.007$). RD use was also associated with a greater degree of socio-economic deprivation ($p=0.035$). A total of 14 patients (4.3%) had an

associated blood borne virus infection (BBV).

One had HIV, 2 had hepatitis B and 11 had hepatitis C. A significantly higher proportion of patients with BBV were in the RD cohort (28.2% vs. 1.0%, RR 27.26, $p<0.001$).

RD users were, on average, younger when diagnosed with laryngeal cancer (53.0 vs. 66.6, $p<0.001$). On subanalysis, this remained true for opioid ($p<0.001$), cannabis ($p=0.004$) and benzodiazepine use ($p=0.002$), but not cocaine use ($p=0.058$). Notably, smoking ($p<0.001$), BBV infection ($p <0.001$), and deprivation ($p=0.032$) also had statistically significant differences for age at presentation.

RD users were also more likely to have higher tumour stage at diagnosis ($p<0.001$). On subanalysis, opioid (RR 1.86; 95% CI: 1.68-2.06, $p=0.001$) users, but not cannabis ($p=0.06$), cocaine ($p=0.145$) or benzodiazepine ($p=0.076$) users were more likely to have stage 3 and 4 disease. BBV infection (RR 1.69, 95% CI: 1.42-2.02, $p=0.023$) and smoking (RR 1.29 95% CI: 1.04 - 1.59, $p=0.020$) but not SIMD16 ($p=0.413$) were more likely to have stage 3 or 4 disease.

In the RD cohort, a greater proportion of tumours occurred at the supraglottic subsite, and

a lower proportion in the glottic subsite ($p=0.041$). Although all individual RDs had the highest proportion of tumours at the supraglottic subsite, only opioids had a significantly increased proportion of supraglottic tumours (RR: 1.78, 95% CI: 1.34 - 2.37, $p=0.008$). This effect was independent of smoking ($p=0.294$), BBV infection ($p=0.464$), and SIMD16 for deprivation ($p=0.749$).

Oncological treatment was equally likely to have the same therapeutic objectives between groups ($p=0.988$) but those in the RD cohort were more likely to receive multimodal treatment ($p=0.002$). Adjuvant treatment following initial surgery was completed in 39 patients overall; 30 (77%) of these underwent radiotherapy and 9 (23%) underwent chemoradiotherapy. 12(30.8%) patients from the RD cohort underwent adjuvant treatment compared to 27 (9.3%) in the non-RD cohort. Those in the RD cohort were 1.5 times as likely to require enteral feeding support during treatment ($p=0.02$).

A summary of outcomes is provided in Table 2. Patients in the RD cohort were more likely to undergo tracheostomy (RR 2.5, $p=0.008$) or laryngectomy (RR 2.25, $p<0.001$). Of the tracheostomies, 30 were for palliative reasons, 5 were prior to laryngectomy, 1 was pre-treatment, 1 was during treatment, 9 were post-treatment and 1 was for intubation prior to cardiothoracic intervention. There was no difference in aspiration rates (based on either clinical or radiological evidence) between cohorts ($p=0.867$). Overall, recurrence occurred in 53 patients (Local: 36 (68%), Regional: 13 (24.5%), Distal: 4 (7.5%)). There was no significant difference in recurrence rates (16.1% vs. 21.2%, $p=0.672$) and time to recurrence (8 ± 4.90 vs. 11.6 ± 7.93 months, $p=0.3245$) between cohorts. There was no difference between the cohorts regarding salvage surgery rates (3(60%) vs. 26(54.2%), $p=1$).

Overall, the median survival was 58 months. Disease free survival rates were 94%, 77%, and 34% at 1-year, 2-years, and 3-years respectively.

From Kaplan-Meier analysis, there was no significant difference in survival rates between

cohorts ($p_{\text{log-rank}}=0.83$) or in any subgroup of RD use (opioid $p_{\text{log-rank}}=0.3$, cannabis $p_{\text{log-rank}}=0.1$, cocaine $p_{\text{log-rank}}=0.8$, benzodiazepine $p_{\text{log-rank}}=0.07$). Gender ($p_{\text{log-rank}}=0.54$), current smoking ($p_{\text{log-rank}}=0.72$), deprivation status ($p_{\text{log-rank}}=0.34$), BBV exposure ($p_{\text{log-rank}}=0.28$), and BMI ($p_{\text{log-rank}}=0.088$) had no impact on survival duration. Furthermore, the need for enteral feeding support ($p_{\text{log-rank}}=0.79$) or laryngectomy ($p_{\text{log-rank}}=0.13$) did not impact survival duration. Older age at diagnosis was associated with poorer survival duration. Those with age 55-70 had a median survival of 29 months as compared to 9 months in those older than 70 ($p_{\text{log-rank}}<0.0001$). In addition, those older than 70 were more likely to undergo palliative treatment compared to those aged 55-70 years (40% vs. 13.1%). Poorer ASA score ($p_{\text{log-rank}}<0.0001$), higher tumour stage ($p_{\text{log-rank}}<0.0001$), aspiration occurrence ($p_{\text{log-rank}}=0.005$), and the need for tracheostomy ($p_{\text{log-rank}}<0.001$) were associated with poorer survival. Current alcohol use was associated with improved survival on univariate analysis ($p_{\text{log-rank}}=0.0059$). This was also visible on multivariate analysis ($p=0.048$). On univariate analysis, supraglottic subsite has the worst survival rates ($p_{\text{log-rank}}<0.0001$) although on multivariate analysis this did not remain significant when compared to subglottic tumours ($p=0.464$).

In the multivariate analysis of factors predicting survival, ASA was excluded as 100 (30.4%) of the data were missing. Cigarette smoking ($p=0.223$) and age at diagnosis were not significantly associated with survival (Figure 1). Interestingly, alcohol use was significantly associated with improved survival (HR 0.68, 95% CI: 0.461-1.00, $p=0.048$). Stage 3 (HR 2.55, 95% CI: 1.131-5.75, $p=0.024$) or 4 (HR 5.44, 95% CI: 2.383-12.4, $p<0.001$) of the disease was associated with poorer survival and any number of treatment modalities was associated with improved survival ($p<0.001$). The Schoenfeld diagnostic test was performed to test the assumption of proportional hazards and had a p value of 0.2297.

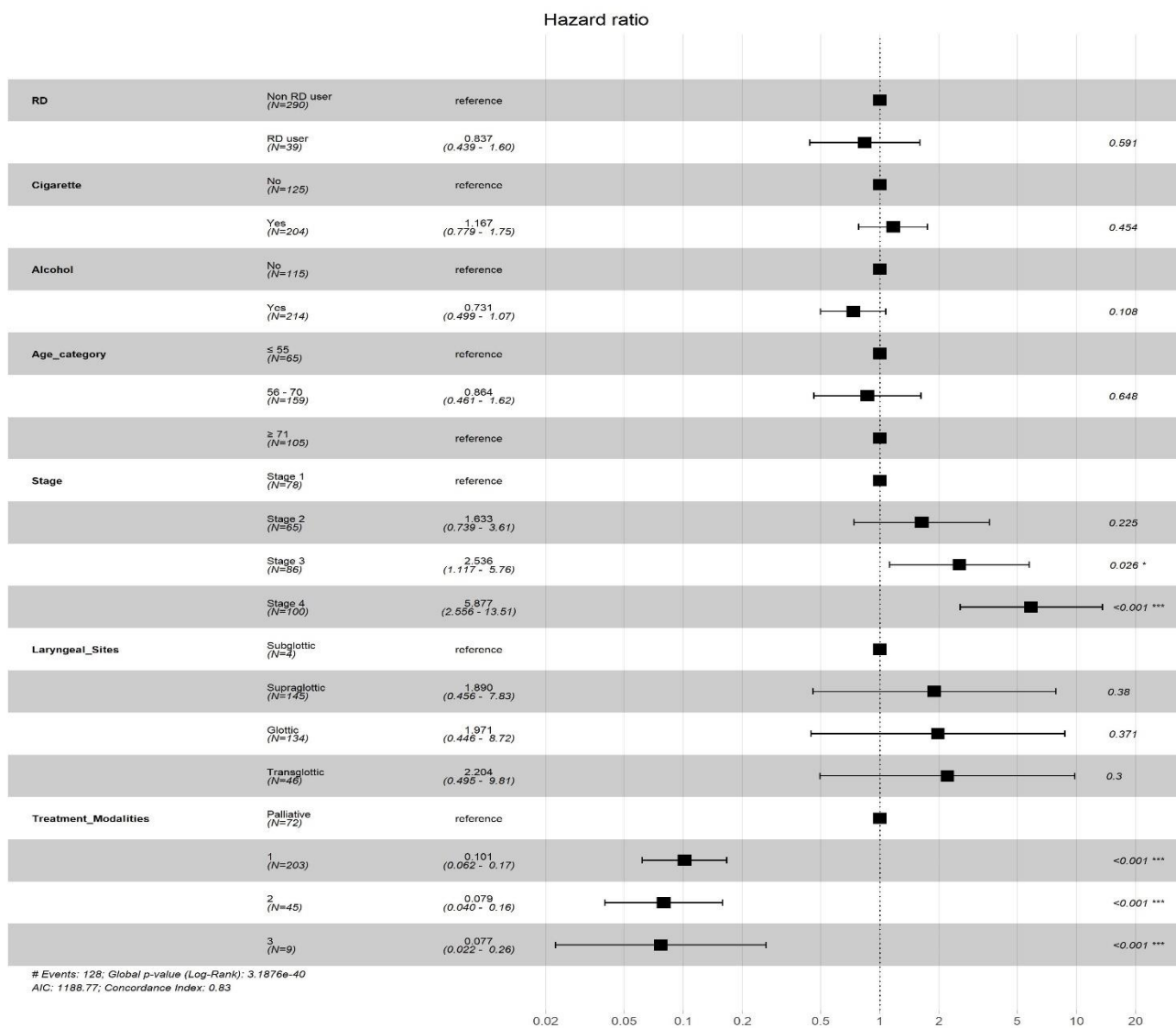


Figure 1. Forrest Plot for multivariate analysis of factors predicting survival

Given the higher proportion of smokers in the RD cohort, it was hypothesised that this factor contributed to the younger age and higher stage observed at diagnosis with laryngeal cancer in the RD cohort. Therefore, case-matched analysis was completed to correct for the confounding factors of

gender, smoking, and alcohol use. 35 patients were included in each arm and each arm consists of 13 (37.1%) females and 22 (62.9%) males, 31 (88.6%) smokers and 21 (60%) alcohol drinkers (Appendix Table A).

Table 1. Patient Demographics and Risk Factors for Laryngeal Cancer

Variables	Non-RD N=290	RD N=39	RR(95% CI)	p-value
Sex				
• Male	226 (77.9%)	25 (64.1%)	0.82 (0.65-1.05)	0.088 ^{X2}
• Female	64 (22.1%)	14 (35.9%)	1.63(1.01-2.61)	
Follow-up month (IQR)	24.0 (11.0, 31.0)	24.0 (10.0, 35.5)	Not relevant	0.800 ^{mann-whitney}
Age (SD)	66.6 (9.86)	53.0 (11.2)	-	<0.001 ^{wech t-test}
• <55	38 (13.1%)	27 (69.23%)	5.28(3.68-7.59)	
• 55-70	152 (52.4%)	7 (17.95%)	0.34(0.17-0.68)	<0.001 ^{X2}
• >70	100 (34.5%)	5 (12.82%)	0.37(0.16-0.86)	
BMI kg/m² (IQR)	25.0 (22.0, 29.0)	24.0 (20.8, 27.2)	-	0.202 ^{mann-whitney}
• <18.5	19 (7.20%)	5 (13.9%)	1.93(0.77-4.85)	
• 18.5-30	203 (76.9%)	26 (72.2%)	0.94(0.76-1.16)	0.378 ^{X2}
• >30	42 (15.9%)	5 (13.9%)	0.87(0.37-2.06)	
ASA				0.201 ^f
• 1	13 (6.5%)	0 (0.00%)	Not available	
• 2	60 (30.2%)	8 (26.7%)	0.88(0.47-1.66)	
• 3	119 (59.8%)	19 (63.3%)	1.06(0.79-1.42)	
• 4	7 (3.5%)	3 (10.0%)	2.84(0.78-10.40)	
SIMD16 Quintile Grouping				
• 1+2	204 (73.65%)	35 (92.1%)	1.25(1.11-1.41)	0.035 ^f
• 3	20 (7.22%)	1 (2.63%)	0.36(0.05-2.64)	
• 4+5	53 (19.13%)	2 (5.26%)	0.28(0.07-1.08)	
Cigarette use				0.007 ^{fisher exact}
• No	26 (8.96%)	1 (2.6%)	Not available	
• Ex	93 (32.07%)	5 (12.8%)	1.38 (0.17-11.3)	
• Yes	171 (58.97%)	33 (84.6%)	4.37 (0.62-30.7)	
Alcohol				0.214 ^{fisher exact}
• No	69 (23.79%)	14 (35.9%)	Not available	
• Ex	28 (9.66%)	4 (10.3%)	0.74 (0.26-2.08)	
• Yes	193 (66.55%)	21 (53.8%)	0.58 (0.31-1.09)	
BBV				<0.001 ^{X2}
• Negative	287 (99%)	28 (71.8%)	0.73(0.60-0.88)	
• Positive	3 (1.03%)	11 (28.2%)	27.26 (7.95-93.47)	
Stage				<0.001 ^{X2}
• 1	74 (25.51%)	4 (10.3%)	0.40(0.16-1.04)	
• 2	62 (21.37%)	3 (7.7%)	0.36(0.12-1.09)	
• 3	77 (26.56%)	9 (23.0%)	0.87(0.48-1.59)	
• 4	77 (26.56%)	23 (59.0%)	2.22(1.61-3.07)	
Laryngeal Cancer Subsite				0.041 ^{fisher exact}
• Glottic	125 (43.1%)	9 (23.1%)	0.54(0.30-0.96)	
• Subglottic	3 (1.03%)	1 (2.6%)	2.48(0.26-24.82)	
• Supraglottic	121 (41.73%)	24 (61.5%)	1.47(1.11-1.96)	
• Transglottic	41 (14.13%)	5 (12.8%)	0.91(0.38-2.16)	
Enteral Support				0.020 ^{X2}
• No	151 (52.1%)	12 (30.8%)	0.59(0.36-0.96)	
• Yes	139 (47.9%)	27 (69.2%)	1.44(1.13-1.84)	
Treatment Intention				0.988 ^{X2}
• Curative	226 (77.9%)	31 (79.5%)	1.02(0.86-1.21)	
• Palliative	64 (22.1%)	8 (20.5%)	0.93(0.48-1.79)	
Treatment Modalities				0.002 ^{X2}
• 1	185 (63.8 %)	18 (46.2%)	0.72(0.51-1.03)	
• 2	37 (12.8%)	8 (20.5%)	1.61(0.81-3.20)	
• 3	4 (1.38%)	5 (12.8%)	9.29(2.61-33.15)	
• Palliative	64 (22.1%)	8 (20.5%)	0.93(0.48-1.79)	

The overall mean age was 58.9 ± 12.1 - year-old. RD users were, on average, younger when diagnosed with LC (51.2 vs. 66.6 -year-old, $p < 0.001$, RR: 5.40 for being ≤ 55). On subanalysis, this remained true for opioids (46.3 vs. 63.9 -year-old, $p < 0.001$), cannabis (51.5 vs. 60.3- year-old, $p = 0.045$) and benzodiazepine use (51.9 vs. 61.1 -year-old, $p = 0.009$), but not for cocaine use (49.8 vs. 59.6 -year-old, $p = 0.172$). A significantly greater proportion of patients had a performance status of 0 (60% vs. 28.6%, $p = 0.016$).

On case-matched analysis, there was no significant difference in tumour stage ($p = 0.203$) between cohorts at diagnosis. On subanalysis, opioid users had a significantly increased risk of stage 3 and 4 of the disease (RR 1.72; 95% CI 1.36-2.18, $p = 0.001$), but this was not seen in cannabis (RR: 1.05; 95% CI 0.70-1.56, $p = 1$), cocaine (RR: 1.48, 95% CI 1.25-1.75, $p = 0.313$), or benzodiazepine (RR: 1.13; 95% CI 0.82-1.55, $p = 0.715$) users. Those in the RD cohort were more likely to present with supraglottic and transglottic tumours ($p = 0.011$).

Table 2. Comparison of patient outcomes between non-RD and RD cohort

Variables	Non-RD N=290	RD N=36	RR(95% CI)	p-value
Survival				
• 1-year	73.9%	69.2%	Not Relevant	0.83 ^{log-rank}
• 2-year	65.1%	61.5%		
• 3-year	58.4%	57.9%		
Tracheostomy				0.008 ^{fisher exact}
• No	184 (82.9%)	12 (57.1%)	0.69(0.47-1.00)	
• Yes	38 (17.1%)	9 (42.9%)	2.50(1.41-4.44)	
Laryngectomy				<0.001 ^{X2}
• No	184 (73.3%)	12 (38.7%)	0.55(0.35-0.85)	
• Yes	67 (26.7%)	19 (61.3%)	2.25(1.57-3.21)	
Recurrence				0.552 ^{X2}
• No	178 (78.8%)	26 (83.9%)	0.968(0.878-1.067)	
• Yes	48 (21.2%)	5 (16.1%)	1.306 (0.535-3.185)	
Aspiration Occurrence				0.867 ^{X2}
• No	242 (83.4%)	34 (87.2%)	1.03(0.89-1.19)	
• Yes	48 (16.6%)	5 (12.8%)	0.86(0.39-1.86)	

Discussion

In reviewing much of the available literature, we found no study in the UK to demonstrate a relationship between RD use and laryngeal cancer. In this study, those with RD exposure were, on average, younger when diagnosed with laryngeal cancer, although this association was not significant when analysing cocaine users individually. The association between opioid use and younger age at diagnosis with cancer has been observed in other studies, but not for other RD exposures.⁷⁻⁹ Of note, RD users had a significantly higher proportion of smoking, BBV infection, and deprivation than the control group, and notably, each of these factors were also significantly associated with younger age at presentation. However, case-matched analysis demonstrated that these effects are not explained by smoking. Case-

matching to include BBV infection and/or deprivation would have significantly reduced the number of patients included in the study rendering any analysis to be meaningless. The exact relationship between RD use and age at diagnosis has therefore not been fully established by this study and further large-scale studies would be required to establish this relationship in greater detail. However, RD should be regarded as a surrogate marker of exposure to risk factors which may predispose to earlier development of laryngeal cancer.

We initially showed that RD users were more likely to present with higher stage laryngeal cancer, however, case-matched analysis to correct for gender, smoking, and alcohol intake showed no significant difference in tumour stage at diagnosis

between cohorts. On subanalysis, opioid users had a significantly increased risk of stage 3 and 4 diseases in both methodologies. This contradicts the findings of a recent publication which indicated opioid users were more likely to present with Stage 1 or 2 supraglottic cancer compared to non-opioid users.⁸ Smoking and BBV infection have previously been shown to be associated with a higher stage at diagnosis.^{23, 24} These factors may therefore explain the discrepancy between our cohort study and case-matched analyses.

Interestingly, survival and recurrence rates were similar between the groups. However, patients with RD use were offered more aggressive and multimodal treatment regimens than those not exposed to RD, which may confound these observations.

We have demonstrated that RD use was associated with an increased risk of developing supraglottic tumours, with a relative reduced risk of glottic cancer when compared to the control group, independent of gender, smoking, alcohol, BBV status, and deprivation status (SIMD16). On subanalysis, this effect only remained significant for opioid use, in keeping with a previous study.⁸ It has been postulated that the supraglottis is relatively hypervascular when compared to the glottis, thus receiving greater exposure to the RD carcinogenic mediators.⁸

Patients in the RD cohort had higher laryngectomy and tracheostomy rates compared to those with no RD exposure, resulting in greater treatment-associated morbidity. Those with RD exposure also included a higher proportion of patients requiring enteral feeding support during treatment. We hypothesise that this may be secondary to more aggressive treatment regimens administered, as there was no significant difference in the mean BMI between cohorts prior to treatment commencement. Early dietetic input may benefit those with RD exposure, as ultimately 69% required enteral feeding support.

Of note, there was no significant difference between cohorts with regard to survival rate, survival duration, recurrence rate or time to recurrence. As mentioned, we believe this may be due to more aggressive treatment regimens offered to these younger patients, who may have fewer comorbidities.

An unexpected finding was that, on multivariate analysis, alcohol appeared to be significantly associated with improved survival. However,

alcohol has previously been shown to have an improved, but not statistically significant, impact on overall survival, disease-specific and disease-free survival in some subsites of oral cavity cancers and laryngopharyngeal cancer.²⁵ Low levels of alcohol consumption was also associated with significantly improved survival, in general, in a Swedish population.²⁶

RD is a significant risk factor for laryngeal cancer, with those exposed having a higher risk of laryngeal cancer at a younger age and a greater propensity for supraglottic cancers. There was co-existence of a greater proportion of smokers, BBV infection and deprivation in the RD cohort. Gender, smoking, and alcohol use were adjusted for using case-matched analysis. Further research is required to determine whether RD exposure is independent of BBV infection and deprivation in large-scale. Those in the RD cohort were more likely to suffer significant treatment morbidity such as tracheostomy formation or laryngectomy. Enteral feeding assistance was also more common in this group and early dietetic assessment should be considered.

The main strength of this paper is the relatively large patient cohort analysis, and the scarcity of data on the subject of RD use in laryngeal cancer to date. To this end, our RD cohort size is comparable with a recent publication.⁸

This study is subject to some weaknesses. First, we analysed several RDs together. Although this makes analysing the effects of individual substances challenging, we believe this study reflects actual exposure to RD, as the use is often mixed. Subanalysis of individual drugs was completed, but with small patient numbers, these results should be interpreted with caution. Another weakness is the retrospective nature of this study, meaning that data were not always available for example, quantities and duration of cigarettes, alcohol, and RD use were not always adequately documented. This may explain the unexpected findings of smoking giving no significant impact on survival and alcohol being associated with improved survival.

Conclusion

RD is associated with younger age at diagnosis with a predilection for the supraglottic subsite, and is also associated with increased treatment morbidity in laryngeal cancer. Patients with RD exposure will require early dietetic input. We suggest that clinicians consider RD exposure as a risk factor in those with suspected laryngeal cancer, regardless of patient age.

Conflict of Interests

None to declare.

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Stirling 2019.

Authors' Contribution

Study conception and design: MA MS, JM, CD Data Collection: Niall Woodley, MA MS, TT Analysis and interpretation of results: MA MS Draft Manuscript Preparation: Niall Woodley All authors reviewed the results and reviewed the final version of the manuscript.

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آیا مصرف تفریحی مواد مخدر بر بقا و عوارض مرتبط با سرطان حنجره تأثیر می‌گذارد؟

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مقاله پژوهشی

چکیده

مقدمه: استفاده از مواد افیونی به عنوان یک عامل خطر می‌تواند خطر ابتلا به سرطان حنجره را به صورت قابل ملاحظه‌ای افزایش دهد. یک مطالعه گذشته نگر برای بررسی رابطه بین قرار گرفتن در معرض مواد مخدر تفریحی و سرطان حنجره انجام شد.

مواد و روش‌ها: بیمارانی که بین ۱ ژانویه ۲۰۱۳ و ۳۱ دسامبر ۲۰۱۷ با استفاده از کدگذاری CD-32 ICD-10 تشخیص داده شده بودند، از یک پایگاه داده مربوط به بیماری‌های سر و گردن وارد مطالعه شدند. جمعیت مورد مطالعه به دو گروه مصرف‌کنندگان تفریحی مواد مخدر و غیر مصرف‌کنندگان تفریحی مواد مخدر (RD و غیر RD) تقسیم شدند و مقایسه جمعیت‌شناختی، عوارض و پیامدهای مصرف برای این دو جمعیت انجام شد. علاوه بر این، همسان‌سازی داده‌ها برای کنترل عوامل مخدوش‌کننده بالقوه از جمله جنسیت، مصرف الکل و سیگار کشیدن انجام شد.

یافته‌ها: ۳۲۹ بیمار در گلاسکو، اسکاتلند با میانگین سنی $۶۴/۹۶ \pm ۱۰/۹۴$ سال و پیگیری $۲۴ \pm ۱۳/۹۱$ ماه وارد مطالعه شدند. از این تعداد، ۳۹ مورد مصرف مواد مخدر تفریحی (RD) را گزارش کردند. RD با سرطان حنجره در سنین پایین‌تر ($۰/۵۳$ در مقابل $۰/۶۶/۶$ ، $p < ۰/۰۰۱$) در هنگام تشخیص همراه بود. نسبت بیشتری از تومورها در قسمت سوپر گلو ت قرار داشت ($p = ۰/۰۴۱$). علاوه بر این، بیشترین بیماران تحت درمان تراکتوستومی ($RR = ۲/۵۰$ ، ۹۵% فاصله اطمینان $۱/۴۱ - ۴/۴۴$ ، CI : $۱/۴۱ - ۴/۴۴$ ، $p = ۰/۰۰۸$) و لارنگکتومی ($RR = ۲/۲۵$ ، ۹۵% فاصله اطمینان $۱/۵۷ - ۳/۲۱$ ، CI : $۱/۵۷ - ۳/۲۱$)، قرار داشتند ($p < ۰/۰۰۱$ ، $RR = ۲/۲۵$ ، ۹۵% فاصله اطمینان $۱/۵۷ - ۳/۲۱$ ، CI : $۱/۵۷ - ۳/۲۱$). مصرف‌کنندگان تفریحی مواد مخدر در طول درمان انکولوژیک بیشتر به دنبال تغذیه حمایتی روده‌ای بودند ($RR = ۱/۴۴$ ، ۹۵% فاصله اطمینان $۱/۱۳ - ۱/۸۴$ ، CI : $۱/۱۳ - ۱/۸۴$ ، $p = ۰/۰۲$). هیچ تفاوتی در بقا در ۲ یا ۳ سال مشاهده نشد ($plog\text{-rank} = ۰/۸۳$). همسان‌سازی داده‌ها برای سیگار کشیدن، الکل و جنسیت نشان داد که مصرف‌کنندگان تفریحی مواد مخدر با تشخیص تومور در قسمت سوپر گلو ت جوان‌تر بودند.

نتیجه‌گیری: مصرف تفریحی مواد مخدر با افزایش بار بیماری و عوارض در سرطان حنجره همراه است. پیشنهاد می‌شود پزشکان استفاده تفریحی از مواد مخدر را به عنوان یک سیگنال خطر در افراد مشکوک به سرطان حنجره بدون توجه به سن بیمار در نظر داشته باشند.

واژگان کلیدی: نئوپلاسم‌های سر و گردن؛ نئوپلاسم‌های حنجره؛ اختلالات مرتبط با مواد؛ مسکن‌ها، مواد افیونی؛ داروهای غیرمجاز

ارجاع: وودلی نایل، مهد اسلیم مهد عفیق، تون ترانگ، مونتگومری جنی، داگلاس کاتریونا. آیا مصرف تفریحی مواد مخدر بر بقا و عوارض مرتبط با سرطان حنجره تأثیر می‌گذارد؟ مجله اعتیاد و سلامت ۱۴۰۱؛ ۱۴(۲): ۲۶-۱۱۴.

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