

Squamous cell carcinoma of the head and neck – screening in patients who misuse alcohol and tobacco in Switzerland: a prospective pilot study

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Abstract

Squamous cell carcinoma (SCC) of the head and neck is the sixth most common cancer worldwide. It is preceded by early asymptomatic lesions which, if identified early enough and removed, would prevent malignant transformation or avoid delaying diagnosis to advanced stages. Our aim was to evaluate the feasibility of a screening programme for SCC of the head and neck in a group of high-risk patients, and to investigate their addiction profile. Patients admitted to an inpatient alcohol addiction centre (n = 101) were prospectively enrolled and asked to fill in a questionnaire about their use of tobacco and alcohol, and the presence of warning symptoms for SCC of the head and neck from 23 June 2014 to 21 January 2016. Participants in the study had a physical examination by an alcohol addiction physician followed by a full examination of the head and neck by an otorhinolaryngologist to rule out premalignant or malignant lesions of the upper aerodigestive tract. Of the 101 patients, 62 (60%) had at least one warning symptom. Alcohol addiction physicians identified leukoplakia in six (6%) and erythroplakia in two. No pre-malignant or malignant lesions were confirmed on examination by the otolaryngologist.

We were unable to draw conclusions about the cost-effectiveness or the yield of the screening programme. Despite our negative findings, we may need further investigation to clarify the relevance of such a programme on health-related outcome given the high compliance rate and minimal delay that was achieved by taking advantage of an in-patient alcohol rehabilitation centre.

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Introduction

Squamous cell carcinoma (SCC) of the head and neck is the sixth most common cancer, and the eighth cause of death from cancer, worldwide.¹ Patients with early stage (I and II) dis-

ease have a 60% to 90% chance of cure, whereas patients with more advanced disease have more than a 50% risk of failure of treatment.² Numerous studies have shown that the overuse of tobacco, together with alcohol, are major risk factors for the development of SCC of the head and neck.³ Tobacco and alcohol increase the risk in a dose-response and synergistic fashion,⁴ with heavy drinkers and smokers having 38 times the risk of developing SCC than the general population.⁵ In Switzerland, 25% of the population smoked cigarettes in 2016 (29.5% of men and 21% of women),⁶ and 17% of men and 9% of women consumed alcohol daily. Given the syn-

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ergistic effect of tobacco and alcohol on the risk of SCC, patients who present with disorders of tobacco and alcohol use can be considered particularly at risk.

Screening is based on the hypothesis that malignant tumours are preceded by early asymptomatic lesions which, if identified early enough and removed, can either prevent malignant transformation or avoid diagnosis in the advanced stages. Most SCC are preceded by visible lesions, known as potentially malignant disorders that show signs of epithelial dysplasia,⁷ the most common of which is leukoplakia,⁸ in which the rate of dysplastic progression is not uniform and varies both from site to site and within the same lesion.⁸ It is estimated that the overall malignant lifetime transformation rate for oral leukoplakia is of approximately 5%.⁹ It has been shown that targeting high-risk patients could result in a significant increase in quality-adjusted-life-years, and that any associated stage shift could produce appreciable cost savings.¹⁰

In Switzerland most patients with disorders of alcohol use are treated as outpatients, and specialised inpatient units deal with the most severe cases. Several studies have shown that patients who misuse alcohol have a higher prevalence of tobacco use than the general population, and they are also more at risk of tobacco dependence. In the same way, people dependent on tobacco are more likely to misuse alcohol.¹¹ In Switzerland, patients with a pattern of risky drinking (>20 g/day for women/>40 g/day for men) are 1.7 times more likely to be susceptible to smoking. The patients in the inpatient unit of the alcohol treatment centre may therefore be at high risk of developing SCC of the head and neck, and therefore are well suited to take part in a screening programme.

In this study we aimed to assess prospectively the feasibility of a screening programme for SCC of the head and neck in an inpatient unit for people who misused alcohol, while characterising their profiles of alcohol and tobacco misuse.

Methods

Recruitment

In this prospective pilot study all patients admitted to the inpatient unit at the alcohol treatment centre of the CHUV University Hospital of Lausanne (Tamaris), Switzerland were considered for enrollment. The inclusion period ran from 23 June 2014 to 21 January 2016. The inclusion criteria were: ≥ 40 years old, tobacco use of 15 pack/years or more, and a diagnosis of current alcohol dependence (World Health Organization (ICD-10) codes F10.2x).¹² The exclusion criteria were a current or history of SCC of the head and neck or psychological instability. The research was approved by the Ethics Committee for Clinical Research in the Canton de Vaud, 20 February, 2014 (Protocol 358/2013).

A research assistant met all new patients admitted over the recruitment period, assessed their eligibility criteria, and informed the eligible patients about the study. Participants

who provided written informed consent were included in the study.

Measurements

The alcohol addiction physician completed a list of the ICD-10 criteria for alcohol dependence and made a clinical examination to rule out the presence of premalignant or malignant lesions of the head and neck region. Patients were also asked to fill in a questionnaire about the use of tobacco and alcohol as well as the presence of warning symptoms for SCC. The questionnaire had been developed by alcohol addiction, smoking cessation, and ENT specialists from the participating organisations.

The following warning symptoms of SCC of the head and neck were part of the survey: pain or difficulty to swallow (odynophagia or dysphagia); change in voice (dysphonia); unintended weight loss or unexplained tiredness; the presence of blood in the saliva or sputum; mobility of the teeth; limitation of mouth opening; ear pain on swallowing; any chronic oral lesion, or swelling or numbness of the face or neck; or recent misadjustment of a dental prosthesis.

Regarding the alcohol misuse profile, we included questions covering their drinking habits over the past three months. Participants were provided with visual aids indicating what is a standard drink. The frequency of heavy episodic drinking during the past 30 days was also assessed. Participants were asked at what age they first drank alcohol regularly, at what age they had their first drink, and when they first became intoxicated. They were also asked to state if they had had any periods of abstinence between the time they started to drink regularly and when they entered the study.

The quantity and frequency of smoking (including cigarettes, smokeless tobacco, cannabis, cigar, or pipe) were also self-reported, together with the age at which they started smoking. The severity of tobacco dependence was assessed from the heaviness of the smoking index, and the number of smoking pack-years.¹³ Participants were classified in three categories according to the heaviness of smoking index: very low dependence (score = 1–2), moderate dependence (score = 3–4), and high dependence (score ≥ 5).¹³ Finally, ex-smokers were asked when they stopped smoking.

Care of study participants by ENT physician

The otolaryngologist examined the oral cavity and the oropharynx with a microscope, and the hypopharynx and larynx with a nasofibroscope. Finally, the oesophagus and hypopharynx were assessed using brush cytology (Oesotest[®], Biondesca). If a precancerous or cancerous lesion was suspected on clinical examination, it was biopsied under local anaesthesia whenever possible; otherwise, an examination under general anaesthesia with biopsy was planned. If the biopsy specimen or the cytological smear indicated the presence of dysplastic or malignant cells, the patient left the study to follow our standard treatment for SCC of the head and neck.

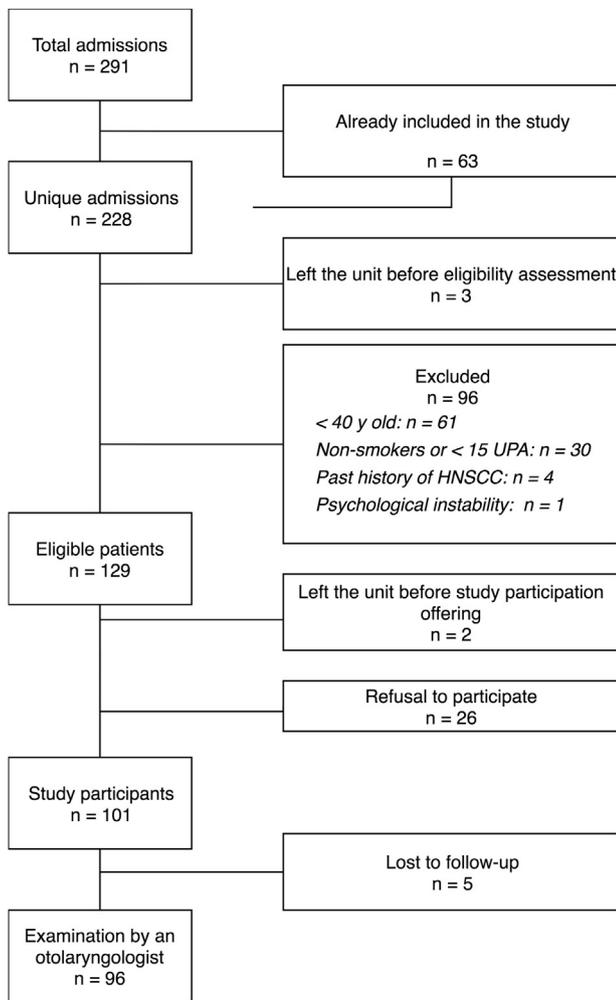


Fig. 1. Flow chart of the study.

Statistics

The sample size was estimated based on a previously reported prevalence of premalignant lesions of the upper aerodigestive tract of 3%, in a similar group.¹⁴ The binomial distribution function was used to calculate the probability of not finding any premalignant or SCC cells in the study sample, and 95% CI for mean and proportion were computed by the Wald method. Statistics were analysed in the R programming language (version 3.4.2.).

Results

Patients

Between November 2014 and June 2016, 228 patients were admitted to the inpatient unit of the alcohol treatment centre of the CHUV University Hospital of Lausanne (Tamaris), Switzerland. Fig. 1 shows the enrollment process. One hundred and one participants were enrolled in the study, and

reasons for refusal were: “lack of utility of a head and neck exam” (n = 10 (38.5%) 95% CI 28.7% to 48.2%); “fear of the head and neck exam” (n = 2 (8%) 95% CI 2.4% to 13%); and “too many medical examinations” (n = 6 (23%) 95% CI 14.6% to 31.5%). In the remaining 10 cases, no specific reason was recorded. Of the 101 study participants, 96 (95%) were examined by the otolaryngologist, and five left the unit before the examination could be planned. The mean (SD) age of the study participants was 53 (8.5) years, and 71% were men. Fig. 1 provides the study flowchart while Table 1 describes the study participants, their background, and clinical findings.

Discussion

We report for the first time to our knowledge the feasibility of a screening programme for high-risk patients for SCC of the head and neck, and show that such a programme can be followed through with a high compliance rate.

The patients included reported considerable misuse of tobacco and alcohol. Patients were over 40 years old, and therefore were at high at risk of SCC of the head and neck. Indeed, coexisting high consumption of tobacco (>20 cigarettes/day) and alcohol (>5 drinks/day) results in a 38-fold increase risk in SCC of the head and neck compared with that in a group who reported consumption of less alcohol or tobacco.⁵

SCC of the head and neck is usually preceded by a premalignant phase, followed by early-stage malignant lesions,⁸ after which survival rates are higher than when the SCC is diagnosed in the advanced stages. A randomised control study reported appreciable reduction in mortality by a targeted screening programme in a high-risk population.¹⁶ However, to date, we know of no study that has replicated such findings in incidental countries. The lower incidence of SCC of the head and neck in well-developed countries is partly responsible for this. Most screening programs conducted in Europe, Japan, or in the USA between 1980 and 2000 involved low-risk groups. One way to improve the yield of such a screening programme is to focus on a high-risk group of patients.¹⁷

Depending on the target group, acceptance rates vary between 26% and 78%.¹⁸ Our acceptance rate was 79.5% (95% CI 71.5% to 87.6%), and our results indicate that the recruitment of these patients within an in-patient unit for alcohol use disorder treatment is feasible and is an option to reach this specific group.

Diagnostic delays have been shown to contribute to the progression of the disease and are associated with a worse prognosis,¹⁹ as well as an overall delay of over six weeks, with poorer survival.²⁰ Our overall delay was only 12 days, which further highlights the advantage of coordinating a targeted screening programme within an in-patient unit.

The prevalence of leukoplakia in the general population is reported to be between 0.25% and 0.3%²¹ whereas rates

Table 1
Participants in the study and summary of the results.

Variable	Mean (SD) or No. (%)	95% CI
Demographic (n = 101):		
Age (years)	53 (8.5)	
Sex:		
Male	72 (71%)	62.2% to 80.3%
Female	29 (29%)	19.7% to 37.8%
Alcohol habits (n = 101):		
Age of first alcoholic drink (years)	15 (3.78)	
Age of first intoxication (years)	18 (6.49)	
Age of regular alcohol consumption	27 (9.65)	
Duration of alcohol consumption (years)	23 (14.68)	
No. of days/week alcohol consumed	6.5 (1.15)	
No. of alcohol units/day	17 (9.9)	
No. of alcohol units/week	110 (71.55)	
No. of maximum alcohol unit/day	27 (18.54)	
Alcohol abstinence time (months)	22 (31.32)	
Tobacco habits (n = 101):		
No. of ancient smokers	10 (10%)	4% to 16%
No. of actual smokers	90 (89%)	82.7% to 95.3%
No. of consumers of smokeless tobacco	2 (2%)	–0.8% to 4.8%
No. of cannabis consumers	19 (19%)	11.2% to 26.8%
No. of cigar or pipe consumers	10 (10%)	4% to 16%
No. of cigarettes/day	23 (10.43)	
Pack-year	44 (21.87)	
Age of the beginning of cigarette consumption	15 (5)	
Duration of tobacco consumption (years)	34 (14.99)	
Timing of first cigarette after waking up:		
<5 minutes	68 (67%)	57.6% to 76.4%
5–30 minutes	16 (16%)	8.7% to 23.3%
30–60 minutes	2 (2%)	–0.8% to 4.8%
>60 minutes	3 (3%)	–0.4% to 6.4%
Heavy smoking index:		
Low addiction	13 (13%)	6.3% to 19.7%
Medium addiction	57 (56%)	46.1% to 65.9%
Heavy addiction	30 (30%)	20.8% to 39.2%
Intensity of weaning symptoms:		
Absent or minimal	19 (19%)	11.2% to 26.8%
Moderate	38 (38%)	28.3% to 47.7%
Strong	27 (27%)	18.1% to 35.9%
Very strong	16 (16%)	8.7% to 23.3%
At least one smoke arrest >48 hours	62 (61%)	51.2% to 70.8%
Tobacco abstinence time (months)	26 (61.92)	
Examination at Tamaris (n = 101):		
Symptoms		
Odynophagia	7 (7%)	1.9% to 12.1%
Dysphagia	13 (13%)	6.3% to 19.7%

Table 1 (Continued)

Variable	Mean (SD) or No. (%)	95% CI
Aliments being swallowed the wrong way	22 (22%)	13.7% to 30.3%
Ear pain while swallowing	3 (3%)	–0.4% to 6.4%
Dysphonia	13 (13%)	6.3% to 19.7%
Blood in saliva or expectoration	9 (9%)	3.3% to 14.7%
Chronic mouth lesion	3 (3%)	–0.4% to 6.4%
Face or neck swelling	9 (9%)	3.3% to 14.7%
Limitation of mouth opening	2 (2%)	–0.8% to 4.8%
Face, neck or mouth numbness	7 (7%)	1.9% to 12.1%
Difficulty to move the tongue or chew	3 (3%)	–0.4% to 6.4%
Jaw pain independent of eating or mouth opening	4 (4%)	0.1% to 7.9%
Mobility of the teeth	15 (15%)	7.9% to 22.1%
Badly-fitted dental prosthesis	7 (7%)	1.9% to 12.1%
Unexplained tiredness	32 (32%)	22.7% to 41.3%
Involuntary weight loss	16 (16%)	8.7% to 23.3%
Physical examination:		
Erythroplakia	2 (2%)	–0.8% to 4.8%
Enlarged neck lymph node	8 (8%)	2.6% to 13.4%
Leukoplakia	6 (6%)	1.2% to 10.8%
Poor dental hygiene	6 (6%)	1.2% to 10.8%
No. of suspicious lesions:		
1	6 (6%)	1.2% to 10.8%
2	2 (2%)	–0.8% to 4.8%
Specialist examination (n = 96):		
Suspicious mucosal lesion	4 (4%)	0.1% to 7.9%
Enlarged neck lymph node	0	0% to 0%
Indication on panendoscopy	2 (2%)	–0.8% to 4.8%
Local biopsy	4 (4%)	0.1% to 7.9%
Confirmed cancerous lesion	0	0% to 0%

of erythroplakia are lower, and vary between 0.02% and 0.83%.²² Other studies that have focused on the targeted screening of oral lesions in high-risk patients have reported a prevalence of dysplasia that ranges from 3% to 9.5%,²³ whereas the prevalence of malignant lesions varied from 0.2% to 2%.¹⁴ We found a prevalence of erythroplakia of 2% (95% CI –0.8% to 4.9%), and of leukoplakia of 6% (95% CI 1.4% to 11.1%), respectively. This result is in line with those of other studies.^{14,23} However, none of these lesions could be confirmed as premalignant or malignant on examination by the otolaryngologist or after tissue biopsy. This could be partially explained by the greater experience of the otolaryngologist in upper aero-digestive tract examination as well as by an insufficient sample size of patients enrolled in the study. Indeed, a post hoc analysis showed that the probability of not finding any premalignant or malignant lesion in our study sample was 5% (95% CI 0.9% to 9.9%).

Although the results are promising our study has several limitations. The small sample size did not allow us to measure the yield of premalignant or malignant lesions, the survival, the morbidity, or the stage-shift in this high-risk population. The mean age of the study group was also less than the mean age of patients who develop SCC of the head and neck, and therefore may well explain why we did not find any cancerous lesions in our study.¹

In conclusion, the small sample size did not allow us to draw conclusions about either the cost-effectiveness or the yield of the screening programme. Despite the negative findings, it may call for further investigation to clarify the relevance of such a programme to health-related outcome, given the high compliance rate and minimal delay that was achieved by taking advantage of an in-patient alcohol rehabilitation unit.

Conflict of interest

We have no conflicts of interest.

Ethics statement/confirmation of patients' permission

The research was approved by the Ethics Committee for Clinical Research in the Canton de Vaud, and we obtained the patients' permission for participation in the study.

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Disclosure

Actimed S.A. had no role in the design of the study or on the decision to publish the study results.

Meetings at which the manuscript was presented

None.

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References

- Vigneswaran N, Williams MD. Epidemiological trends in head and neck cancer and aids in diagnosis. *Oral Maxillofac Surg Clin North Am* 2014;**26**:123–41.
- Brockstein B, Haraf DJ, Rademaker AW, et al. Patterns of failure, prognostic factors and survival in locoregionally advanced head and neck cancer treated with concomitant chemoradiotherapy: a 9-year, 337-patient, multi-institutional experience. *Ann Oncol* 2004;**15**:1179–86.
- Macfarlane GJ, Zheng T, Marshall JR, et al. Alcohol, tobacco, diet and the risk of oral cancer: a pooled analysis of three case-control studies. *Eur J Cancer B Oral Oncol* 1995;**31B**:181–7.
- Lubin JH, Purdue M, Kelsey K, et al. Total exposure and exposure rate effects for alcohol and smoking and risk of head and neck cancer: a pooled analysis of case-control studies. *Am J Epidemiol* 2009;**170**:937–47.
- Blot WJ, McLaughlin JK, Winn DM, et al. Smoking and drinking in relation to oral and pharyngeal cancer. *Cancer Res* 1988;**48**:3282–7.
- Gmel G, Kuendig H, Notari L, et al. *Monitoring Swiss addictions: consumption of alcohol, tobacco and illegal drugs in Switzerland, 2016*. Lausanne, Switzerland: Addiction Suisse; 2017 (book in French).
- Warnakulasuriya S, Johnson NW, van der Waal I. Nomenclature and classification of potentially malignant disorders of the oral mucosa. *J Oral Pathol Med* 2007;**36**:575–80.
- Napier SS, Speight PM. Natural history of potentially malignant oral lesions and conditions: an overview of the literature. *J Oral Pathol Med* 2008;**37**:1–10.
- Scully C, Bagan J. Oral squamous cell carcinoma overview. *Oral Oncol* 2009;**45**:301–8.
- Brocklehurst P, Kujan O, Glennly AM, et al. Screening programmes for the early detection and prevention of oral cancer. *Cochrane Database Syst Rev* 2010:CD004150.
- Guydish J, Passalacqua E, Pagano A, et al. An international systematic review of smoking prevalence in addiction treatment. *Addiction* 2016;**111**:220–30.
- The ICD-10 Classification of Mental and Behavioural Disorders. *Diagnostic criteria for research*. Geneva: World Health Organization; 1993.
- Kozłowski LT, Porter CQ, Orleans CT, et al. Predicting smoking cessation with self-reported measures of nicotine dependence: FTQ, FTND, and HSI. *Drug Alcohol Depend* 1994;**34**:211–6.
- Duhamel O, Bell G, Granger V, et al. Cancers of the upper aerodigestive tract. Importance of systematic screening during alcohol withdrawal cures. *Alcoologie Addictologie* 2005;**27**:277–80 (paper in French).
- Sankaranarayanan R, Ramadas K, Thomas G, et al. Effect of screening on oral cancer mortality in Kerala, India: a cluster-randomised controlled trial. *Lancet* 2005;**365**:1927–33.
- Shuman AG, Entezami P, Chernin AS. Demographics and efficacy of head and neck cancer screening. *Otolaryngol Head Neck Surg* 2010;**143**:353–60.
- Ikeda N, Downer MC, Ishii T, et al. Annual screening for oral cancer and precancer by invitation to 60-year-old residents of a city in Japan. *Community Dent Health* 1995;**12**:133–7.
- Allison P, Franco E, Black M, et al. The role of professional diagnostic delays in the prognosis of upper aerodigestive tract carcinoma. *Oral Oncol* 1998;**34**:147–53.
- Pitchers M, Martin C. Delay in referral of oropharyngeal squamous cell carcinoma to secondary care correlates with a more advanced stage at presentation, and is associated with poorer survival. *Br J Cancer* 2006;**94**:955–8.
- Mehanna HM, Rattay T, Smith J, et al. Treatment and follow-up of oral dysplasia—a systematic review and meta-analysis. *Head Neck* 2009;**31**:1600–9.
- Reichart PA, Philipsen HP. Oral erythroplakia—a review. *Oral Oncol* 2005;**41**:551–61.
- Vacher C, Legens M, Rueff B, et al. Screening of cancerous and precancerous lesions of the oral mucosa in an at-risk population. *Rev Stomatol Chir Maxillofac* 1999;**100**:180–3.