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Socioeconomic status, human papillomavirus, and overall survival in head and neck squamous cell carcinomas in Toronto, Canada

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ABSTRACT

Background: Despite universal healthcare in some countries, lower socioeconomic status (SES) has been associated with worse cancer survival. The influence of SES on head and neck cancer (HNC) survival is of immense interest, since SES is associated with the risk and prognostic factors associated with this disease.

Patients and methods: Newly diagnosed HNC patients from 2003 to 2010 ($n=2124$) were identified at Toronto's Princess Margaret Cancer Centre. Principal component analysis was used to calculate a composite score using neighbourhood-level SES variables obtained from the 2006 Canada Census. Associations of SES with overall survival were evaluated in HNC subsets and by p16 status (surrogate for human papillomavirus).

Results: SES score was higher for oral cavity ($n=423$) and p16-positive oropharyngeal cancer (OPC, $n=404$) patients compared with other disease sites. Lower SES was associated with worse survival [HR 1.14 (1.06–1.22), $p=0.0002$], larger tumor staging ($p<0.001$), current smoking ($p<0.0001$), heavier alcohol consumption ($p<0.0001$), and greater comorbidity ($p<0.0002$), but not with treatment regimen ($p>0.20$). After adjusting for age, sex, and stage, the lowest SES quintile was associated with the worst survival only for OPC patients [HR 1.66 (1.09–2.53), $n=832$], primarily in the p16-negative subset [HR 1.63 (0.96–2.79)]. The predictive ability of the prognostic models improved when smoking/alcohol was added to the model (*c*-index 0.71 vs. 0.69), but addition of SES did not (*c*-index 0.69).

Conclusion: SES was associated with survival, but this effect was lost after accounting for other factors (age, sex, TNM stage, smoking/alcohol). Lower SES was associated with greater smoking, alcohol consumption, comorbidity, and stage.

1. Introduction

Head and neck cancers (HNC) comprise a diverse set of patients that differ by tumor biology, exposure history, and social environments. Lower socioeconomic status (SES) is associated with worse prognosis amongst various cancer groups, including HNC [1–5]. The relationship between SES and survival is multifactorial, as many factors associated with SES are also associated with HNC incidence and survival, such as smoking and alcohol consumption, anatomic subsite, comorbidity, and more recently, with tumours testing positive for human papillomavirus (HPV) [6–10].

Patients with lower SES may present with larger tumours at diagnosis and may receive treatment different from similar patients with higher SES [11–13]. Canadians have access to universal health care, which might reduce a component of the socioeconomic disparities that accompany other healthcare systems. However, evidence from countries with a similar healthcare system to Canada (i.e. The Netherlands) suggests that SES can continue to affect outcomes [12,14,15], yet the underlying causes may differ from those in privatized healthcare systems.

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Although SES has been shown to be prognostic in various cancer cohorts [5,12], few studies have reported on the predictive performance of survival models that include SES compared to similar models without SES [16], and thus, whether or not it is an important factor to consider in making clinically-relevant survival predictions.

Understanding the role of SES with cancer prognosis and uncovering potential reasons for such relationships is important for public health and informing health policy. This is particularly important for HNC, where sociodemographic risk factors have changed over recent years, particularly with HPV [17]. The oropharyngeal subset of HNC (OPC) patients with HPV infection has risen over the past decade [17,18]. In particular, HPV-positive OPCs are associated with higher SES, lower alcohol and tobacco exposures, and smaller tumours (but larger nodal metastases) whose outcomes are significantly better than their stage would otherwise suggest [5,19]. How SES and these changing demographics and lifestyle factors are related to outcomes in this new era of HNC is of great interest.

The first goal of this study was to evaluate the prognostic value of SES on overall survival in a HNC population in the era of HPV-associated OPC using both prognostic and predictive models. The

Table 1
Patient demographics by subsite (all head and neck cancers) and p16 status (in oropharyngeal cancers). Summary of the HNC population, including demographic, clinical, and social history.

Variable	Missing data	All head and neck cancers by disease site				Oropharyngeal cancer by known p16 status			
		OPC (n = 832)	Non-OPC[b] (n = 1292)	OPC vs. other HNC		p16-positive (n = 404)	p16-negative (n = 151)	p16+ vs. p16 − OPC	
				aOR[c]	p-Value			aOR[c]	p-Value
Sex	0 (0%)								
Female		182 (22%)	288 (22%)	1.0	0.78	77 (19%)	40 (26%)	1.0	0.03
Male		650 (78%)	1004 (78%)	1.04 (0.79–1.36)		327 (81%)	111 (74%)	2.11 (1.08–4.13)	
Age at diagnosis (years)[a]	0 (0%)	60.4 (10.3)	65.3 (11.8)	0.75 (0.68–0.83)	<.0001	58.0 (9.72)	64.2 (9.92)	0.61 (0.45–0.81)	0.0006
Marital status	58 (7%)								
Married		554 (72%)	836 (72%)	1.0	0.92	284 (73%)	93 (71%)	1.0	0.06
Not married		220 (28%)	320 (28%)	1.01 (0.80–1.29)		103 (26%)	38 (29%)	1.76 (0.98–3.17)	
Residence status	(0%)								
Urban		726 (87%)	1159 (90%)	1.0	0.44	355 (88%)	126 (83%)	1.0	0.15
Rural		106 (13%)	133 (10%)	1.14 (0.82–1.56)		49 (12%)	25 (17%)	0.60 (0.29–1.21)	
Charlson Comorbidity Score	(0%)								
0		449 (54%)	604 (47%)	1.0	0.61	243 (60%)	68 (45%)	1.0	0.66
1		243 (29%)	397 (31%)	0.90 (0.71–1.15)		120 (30%)	45 (30%)	1.18 (0.65–2.12)	
2+		140 (17%)	291 (22%)	0.89 (0.66–1.20)		41 (10%)	38 (25%)	0.82 (0.40–1.72)	
Treatment	7 (1%)								
Chemoradiation		306 (37%)	379 (29%)	1.0	<.0001	157 (39%)	50 (33%)	1.0	0.98
Radiation only		208 (25%)	399 (31%)	1.37 (1.04–1.81)		90 (22%)	51 (34%)	0.83 (0.43–1.60)	
Surgery + adjuvant		292 (35%)	401 (31%)	1.28 (0.99–1.65)		155 (38%)	49 (33%)	1.00 (0.54–1.84)	
Surgery only		15 (2%)	105 (8%)	1.18 (0.09–0.35)		1 (0%)	0 (0%)	–	
Overall TNM stage	3 (<1%)								
I		18 (2%)	260 (20%)	–	–	5 (1%)	8 (5%)	–	–
II		57 (7%)	247 (19%)			16 (4%)	23 (15%)		
III		110 (13%)	223 (17%)			45 (11%)	24 (16%)		
IV		644 (78%)	559 (44%)			336 (84%)	95 (63%)		
Tumor stage	3 (<1%)								
T3/T4		415 (50%)	597 (46%)	1.0	0.72	175 (44%)	81 (54%)	1.0	0.04
T1/T2		414 (50%)	692 (54%)	1.04 (0.84–1.29)		227 (56%)	69 (46%)	1.74 (1.04–2.91)	
Nodal stage	3 (<1%)								
N0/N1		229 (28%)	861 (67%)	1.0	<.0001	77 (19%)	70 (47%)	1.0	0.01
N2/N3		600 (72%)	427 (33%)	5.36 (4.28–6.73)		325 (81%)	80 (53%)	2.06 (1.15–3.66)	
Smoking status	2 (<1%)								
Current		352 (42%)	654 (51%)	1.0	<.0001	123 (31%)	99 (66%)	1.0	<.0001
Former		285 (35%)	405 (32%)	1.76 (1.37–2.26)		143 (35%)	40 (27%)	2.78 (1.56–4.94)	
Never		193 (23%)	219 (17%)	1.78 (1.31–2.41)		137 (34%)	11 (7%)	6.17 (2.59–14.7)	
Alcohol consumption	15 (2%)								
Heavy		255 (31%)	378 (31%)	1.0	0.65	73 (18%)	83 (56%)	1.0	<.0001
Moderate		99 (12%)	162 (13%)	0.86 (0.61–1.22)		52 (13%)	16 (11%)	3.39 (1.55–7.44)	
Non/light		463 (57%)	686 (56%)	0.91 (0.70–1.18)		272 (69%)	48 (33%)	4.18 (2.28–7.65)	
Anatomic subsite (OPC)	(0%)								
Tonsil		447 (54%)	–	–	–	249 (62%)	67 (45%)	1.0	<.0001
Base of tongue		271 (33%)	–	–	–	136 (34%)	37 (24%)	0.99 (0.56–1.75)	
Other site		114 (14%)	–	–	–	18 (4%)	46 (31%)	0.17 (0.08–0.38)	

[a] Mean age (standard deviation), odds ratio represents 10-year increment in age.
[b] Comprised of 423 (32%) oral cavity, 715 (55%) laryngeal, and 154 (12%) hypopharyngeal cancer.
[c] Adjusted odds ratio (aOR), adjusted for all variables in table unless given by a dash (–).