

Psychosocial factors and their association with reflux oesophagitis, Barrett's oesophagus and oesophageal adenocarcinoma

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Abstract

AIM: To investigate the role of psychological characteristics as risk factors for oesophageal adenocarcinoma (OAC), as well as the reflux-mediated precursor pathway.

METHODS: An all-Ireland population-based case-control study recruited 230 reflux oesophagitis (RO), 224 Barrett's oesophagus (BO) and 227 OAC patients and 260 controls. Each case/control group completed measures of stress, depression, self-efficacy, self-esteem, repression and social support. A comparative analysis was undertaken using polytomous logistic regression adjusted for potential confounders.

RESULTS: Compared to controls, OAC patients were almost half as likely to report high stress levels over their lifetime ($P = 0.010$, OR 0.51; 95%CI: 0.29-0.90)

and 36% less likely to report having experienced depression (OR 0.64; 95%CI: 0.42-0.98). RO patients reported significantly higher stress than controls particularly during middle- and senior-years (P for trends < 0.001). RO patients were 37% less likely to report having been highly emotionally repressed (OR 0.63; 95%CI: 0.41-0.95). All case groups (OAC, RO and BO) were more likely than controls to report having had substantial amounts of social support (OR 2.84; 95%CI: 1.63-4.97; OR 1.97; 95%CI: 1.13-3.44 and OR 1.83; 95%CI: 1.03-3.24, respectively).

CONCLUSION: The improved psychological profile of OAC patients may be explained by response shift. The role of psychological factors in the development of OAC requires further investigation.

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Key words: Reflux oesophagitis; Barrett's oesophagus; Oesophageal adenocarcinoma; Adjustment; Psychological; Psychosocial factors

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INTRODUCTION

Gastro-oesophageal reflux comprises a series of chronic symptoms caused by abnormal reflux of gastric and intestinal digestive juice^[1] which may cause inflammation of the oesophageal mucosa reflux oesophagitis (RO)^[2] or cause a squamous to columnar cell metaplasia within the

distal oesophagus Barrett's oesophagus (BO)^[3]. Prevalence rates for gastro-oesophageal reflux disease in western countries range from 10%-20%^[4,5]. Incidence of BO in Northern Ireland is 567/100 000 of the population (unpublished data, Northern Ireland BO Registry). Although the absolute risk remains low (0.5% per patient per year)^[6], BO confers an increased risk of developing oesophageal adenocarcinoma (OAC)^[7], the incidence of which has increased by 600% in western countries in recent decades^[8]. The incidence rate for oesophageal cancer in Northern Ireland is similar to rates reported elsewhere^[9].

Previous studies have found associations between hypothesized risk factors including diet, obesity and smoking^[10-14] and the development of OAC though the demographic distribution of risk factors does not fully align with OAC incidence^[15]. Stress appears to affect the neuroendocrine and immune systems as well as the sympathetic nervous system^[16,17]. In population-based studies, job strain-related stress has been positively associated with symptomatic reflux and an increased risk of OAC^[17-19]. However, the role of psychosocial factors in the development of OAC and its precursor lesions has not been investigated.

Data from an all-Ireland population-based, case-control study (the FINBAR Study) was used to investigate the nature and extent to which different psychosocial factors (*e.g.*, stress and depressed mood) affected the development of OAC, including the influence such factors may have on the reflux-mediated precursor pathway.

MATERIALS AND METHODS

The FINBAR study was an all-Ireland population-based case-control study comprising three patient groups with (1) OAC; (2) long-segment BO; and (3) RO and a group of normal population controls. All participants were Caucasian and aged between 35-85 years. The design of the FINBAR Study has been described elsewhere^[10,20]. Briefly, OAC cases had histological confirmation of adenocarcinoma within the oesophagus. They were identified using electronic pathology records from all pathology laboratories in Northern Ireland and from the main hospitals involved in the treatment of oesophageal cancer in the Republic of Ireland. BO patients had histological confirmation of specialized intestinal metaplasia within the oesophagus and at least 3 centimeters of BO observed at endoscopy. RO patients were those diagnosed with macroscopically visible erosive oesophagitis (grades 2-4 in the Savary Miller/Hetzel-Dent classification or grades B, C or D in the Los Angeles classification) at upper gastro-intestinal (GI) endoscopy. BO and RO patients were frequency matched (within 5-year age- and sex-strata) to the distribution of OAC patients. Control subjects had no history of oesophageal or other GI cancer or BO. They were frequency matched by sex, and 5-year age bands to OAC patients.

For the psychosocial assessment patients were asked to reflect on their life as a whole when answering the

questions. Self-perceived stress or daily strain was assessed using the 4-item Reed Stress Inventory. Responses to items were scored as follows: 0, no response on one or more statements; 1, "not at all" for all four statements; 2, "not at all" for any three statements with any other response for the fourth; 3, "not at all" for any two statements with "hardly true" for the other two; 4, "not at all" for any one or two statements with any other responses for the remainder but not those for a score of 3; 5, all other response sets not specified under 0, 1, 2, 3, 4, 6, 7 or 8; 6, "moderately true" to all four statements, or "moderately true" for three statements with "exactly true" for the fourth; 7, "exactly true" for any three statements with "moderately true" or "hardly true" for the fourth; and 8, "exactly true" in response to all four statements. Scores from 1 to 8 were categorised as representing high (6-8), medium (4-5), or low (1-3) levels of stress.

A 4-part item was used to assess self-reported stress across the lifespan from: (1) childhood/teenager (up to 19 years); (2) young adulthood (20-39 years); (3) midlife (40-59 years); and (4) senior or later years in life (60-85 years). Each life period was considered a separate variable in the analyses in order to gauge approximately the extent to which any particular developmental period in an individual's life had been stressful and to assess its significance for patients compared to controls.

Depressed mood was assessed using an adapted 2-item case-finding instrument^[21]. A score of 1-2 on either question indicated a "not depressed" status while a score of 3-4 on either question indicated that the respondent was likely to be "depressed" or to have a depressed mood.

Self-efficacy and coping ability were measured using a 10-item scale designed to assess the extent to which a respondent had a self-belief that they had the capacity to overcome difficult tasks and cope with adversity. Responses on the 4-point likert scale were summed yielding a score of between 10 and 40 in the direction of increasing self-efficacy and coping ability. Self-efficacy was categorized as low (scores of 10-29), medium (30-34) and high (35-40) based on the tertile distribution of scores among the controls.

A single-item was used to measure self-esteem with a score of 1-2 indicating low self-esteem and a score of 3-4 indicating high self-esteem.

A single-item was used to assess emotional repression. A high score (3-4) indicated a tendency to share feelings and emotions relatively easily and a low score (1-2) was endorsed by respondents who were reticent or repressive in nature.

The responses to three questions on social support and loneliness were summed and categorized as indicating varying degrees of support from hardly any (scores 0-8), some (score 9), moderate (score 10) and substantial (scores 11-12) based on the quartile distribution of scores among the control group.

Ethical approval

Ethical approval for the FINBAR study was obtained

Table 1 Characteristics of participants

Variables	Controls	RO		BO		OAC	
	n (%)	n (%)	P value	n (%)	P value	n (%)	P value
Gender							
Male	220 (84.6)	189 (82.2)	0.47	185 (82.6)	0.55	192 (84.6)	0.99
Female	40 (15.4)	41 (17.8)		39 (17.4)		35 (15.4)	
Age (yr)	63.0	61.7	0.22	62.4	0.57	64.2	0.28
Education (yr)	12.0	10.8	< 0.001	11.3	0.01	10.7	< 0.001
Job type							
Manual	119 (48.0)	107 (48.2)	0.71	130 (59.1)	0.02	128 (59.5)	0.01
Non-manual	129 (52.0)	115 (51.8)		90 (40.9)		87 (40.5)	
GOR symptoms							
Never	211 (81.2)	140 (60.9)	< 0.001	60 (26.8)	< 0.001	117 (51.5)	< 0.001
Ever	49 (18.8)	90 (39.1)		164 (73.2)		110 (48.5)	
Smoking status							
Never	102 (40.2)	109 (48.4)	0.03	87 (39.2)	0.40	45 (20.4)	< 0.001
Ex-smoker	107 (42.1)	68 (30.2)		85 (38.3)		99 (44.8)	
Current	45 (17.7)	48 (21.3)		50 (22.5)		77 (34.8)	
Alcohol (g/d)	26.1	22.0	0.15	22.3	0.21	19.2	0.01
Body mass index (kg/m ²)	27.0	27.8	0.05	27.0	0.90	28.7	< 0.001
Reed stress inventory, mean ± SD							
Mean score (range 2-8)	4.50 ± 2.08	4.11 ± 1.88	0.014	4.28 ± 2.08	0.187	3.80 ± 2.09	< 0.001
Stress teenage years							
Mean score (range 1-5)	1.80 ± 1.05	1.67 ± 0.95	0.146	1.86 ± 1.18	0.539	1.85 ± 1.17	0.655
Stress young adulthood							
Mean score (range 1-5)	2.45 ± 1.23	2.67 ± 1.11	0.301	2.34 ± 1.25	0.328	2.37 ± 1.24	0.486
Stress midlife							
Mean score (range 1-5)	2.49 ± 1.26	3.33 ± 1.20	< 0.001	2.75 ± 1.34	0.038	2.50 ± 1.33	0.928
Stress senior years							
Mean score (range 1-5)	2.07 ± 1.17	2.80 ± 1.42	< 0.001	2.34 ± 1.35	0.08	2.33 ± 1.37	0.088
Depression							
Mean score (range 2-8)	4.11 ± 1.74	4.42 ± 2.37	0.107	4.38 ± 2.25	0.147	3.82 ± 2.31	0.109
Self efficacy							
Mean score (range 10-40)	32.0 ± 4.76	33.8 ± 4.32	< 0.001	31.8 ± 5.52	0.794	34.3 ± 4.89	< 0.001
Self esteem							
Mean score (range 1-4)	2.95 ± 0.81	2.93 ± 1.10	0.828	2.76 ± 1.04	0.022	3.13 ± 0.97	0.034
Repression							
Mean score	2.80 ± 0.89	2.64 ± 1.17	0.097	2.86 ± 1.05	0.501	2.86 ± 1.17	0.554
Social support							
Mean score (range 1-4)	3.57 ± 0.60	3.82 ± 0.50	< 0.001	3.62 ± 0.63	0.40	3.76 ± 0.48	< 0.001

RO: Reflux oesophagitis; BO: Barrett's oesophagus; OAC: Oesophageal adenocarcinoma; GOR: Gastroesophageal reflux.

from the Research Ethics Committee of the Queen's University Belfast, the Clinical Research Ethics Committee of the Cork Teaching Hospitals and the Research Ethics Committee Board of St. James's Hospital, Dublin.

Statistical analysis

Group *t*-tests and Pearson χ^2 tests were used to compare cases and controls. Polytomous multivariate logistic regression was used to compare the psychosocial factors in each case group with the control group, adjusting for potential confounders including gender, age, years of full-time education, job type (manual, non-manual), Gastroesophageal reflux (GOR) symptoms (never, ever), smoking status (never, ex-smoker, current smoker), alcohol consumption (g/d) and BMI (self-reported weight 5-years before interview divided by height measured at

interview).

RESULTS

In total, 227 OAC patients, 224 BO patients, 230 RO patients and 260 controls were recruited into the study with participation rates of 64%, 82%, 69% and 42% respectively. Case groups and controls were similar regarding gender and age due to frequency matching. Other characteristics are displayed in Table 1.

There were no significant trends between reported stress levels as measured by the Reed Stress Inventory and risk of RO or BO (Table 2). However, OAC patients were half as likely to report high stress than controls (OR 0.51; 95%CI: 0.29-0.90). Stress levels were similar during childhood/teenage years for RO, BO, OAC cases and

Table 2 Self-reported stress levels during lifetime

Stress levels	Controls	RO		BO		OAC	
	<i>n</i> (%)	<i>n</i> (%)	AOR (95%CI)	<i>n</i> (%)	AOR (95%CI)	<i>n</i> (%)	AOR (95%CI)
Reed stress inventory levels							
Low	45 (17.6)	63 (27.9)	1.00	60 (27.2)	1.00	81 (36.3)	1.00
Medium	154 (60.2)	122 (54.0)	0.92 (0.51-1.63)	102 (46.2)	0.51 (0.31-0.86)	91 (40.8)	0.37 (0.23-0.61)
High	57 (22.3)	41 (18.1)	1.43 (0.64-3.22)	59 (26.7)	0.60 (0.33-1.09)	51 (22.9)	0.51 (0.29-0.90)
			<i>P</i> for trend 0.48		<i>P</i> for trend 0.10		<i>P</i> for trend 0.010
Teenage years							
1	135 (52.7)	132 (58.7)	1.00	122 (55.5)	1.00	127 (57.5)	1.00
2	67 (26.1)	53 (23.6)	1.05 (0.64-1.71)	42 (19.1)	0.73 (0.43-1.23)	32 (14.5)	0.63 (0.37-1.06)
3	31 (14.1)	26 (11.6)	0.77 (0.40-1.49)	31 (14.1)	1.06 (0.57-1.96)	42 (19.0)	1.50 (0.84-2.67)
4	16 (6.3)	11 (4.9)	0.67 (0.26-1.70)	14 (6.4)	0.75 (0.31-1.79)	9 (4.1)	0.58 (0.23-1.48)
5	7 (2.7)	3 (1.3)	0.28 (0.06-1.26)	11 (5.0)	0.76 (0.25-2.29)	11 (5.0)	1.18 (0.40-3.48)
			<i>P</i> for trend 0.10		<i>P</i> for trend 0.55		<i>P</i> for trend 0.85
Young adulthood							
1	64 (25.0)	38 (16.9)	1.00	76 (34.7)	1.00	70 (32.3)	1.00
2	67 (26.2)	61 (27.1)	2.04 (1.11-3.76)	47 (21.5)	0.59 (0.34-1.04)	52 (24.0)	0.80 (0.47-1.38)
3	82 (32.0)	75 (33.3)	1.92 (1.06-3.49)	57 (26.0)	0.47 (0.27-0.81)	55 (25.4)	0.67 (0.39-1.14)
4	32 (12.5)	39 (17.3)	2.65 (1.27-5.55)	23 (10.5)	0.46 (0.22-0.96)	24 (11.1)	0.71 (0.35-1.44)
5	11 (4.3)	12 (5.3)	3.20 (1.07-9.55)	16 (7.3)	0.86 (0.33-2.28)	16 (7.4)	1.22 (0.47-3.18)
			<i>P</i> for trend 0.01		<i>P</i> for trend 0.05		<i>P</i> for trend 0.49
Midlife							
1	68 (28.7)	20 (9.1)	1.00	52 (25.0)	1.00	58 (27.9)	1.00
2	57 (24.1)	38 (17.2)	2.56 (1.22-5.37)	39 (18.8)	0.87 (0.48-1.59)	62 (29.8)	1.25 (0.73-2.16)
3	55 (23.2)	50 (22.6)	4.04 (1.97-8.25)	48 (23.1)	1.07 (0.59-1.94)	38 (18.3)	0.95 (0.53-1.71)
4	41 (17.3)	76 (34.4)	8.50 (4.14-17.46)	47 (22.6)	1.23 (0.65-2.30)	25 (12.0)	0.70 (0.36-1.36)
5	16 (6.8)	37 (16.7)	9.82 (4.11-23.45)	22 (10.6)	1.27 (0.55-2.89)	25 (12.0)	1.60 (0.72-3.53)
			<i>P</i> for trend 0.001		<i>P</i> for trend 0.33		<i>P</i> for trend 0.97
Senior years							
1	64 (42.4)	30 (24.4)	1.00	47 (39.2)	1.00	47 (37.3)	1.00
2	38 (25.1)	28 (22.8)	1.76 (0.86-3.61)	23 (19.2)	0.71 (0.35-1.45)	32 (25.4)	1.08 (0.56-2.09)
3	30 (19.9)	22 (17.9)	1.77 (0.82-3.83)	22 (18.3)	0.93 (0.44-1.96)	19 (15.1)	0.84 (0.40-1.78)
4	12 (8.0)	23 (18.7)	4.28 (1.72-10.67)	18 (15.0)	2.15 (0.85-5.43)	14 (11.1)	1.71 (0.67-4.35)
5	7 (4.6)	20 (16.3)	5.92 (1.72-16.77)	10 (8.3)	1.48 (0.48-4.54)	14 (11.1)	2.35 (0.82-6.70)
			<i>P</i> for trend 0.001		<i>P</i> for trend 0.20		<i>P</i> for trend 0.14

RO: Reflux oesophagitis; BO: Barrett's oesophagus; OAC: Oesophageal adenocarcinoma; 1: Low; 2-4: Medium; 5: High; AOR: Adjusted odds ratio.

controls, respectively. Regarding young adulthood, there was a significant trend between having RO and reported stress; RO cases also reported significantly much higher stress during middle- and senior-years than controls (almost 10-fold and 6-fold more, respectively) with a significant linear trend (*P* for trend < 0.001) observed for each point on the life-span stress scale.

OAC cases were 36% less likely than controls to report depression; no significant association was observed between depression and BO or RO (Table 3). Self-efficacy levels were 3-times higher in RO patients and 2-times higher in OAC patients compared to controls. No significant association was observed for self-efficacy and BO. OAC patients were 58% more likely than controls to report high self-esteem though the association was not statistically significant (95%CI: 0.99-2.52). Self-esteem did not differ significantly between RO or BO cases respectively and controls. RO patients were 37% less likely than controls to report being repressed; significant associations were not observed between repression and BO or OAC status. RO, BO and OAC patients were more likely to report high levels of social support than controls.

DISCUSSION

This is the first study to investigate psychological characteristics of RO, BO and OAC patients as possible risk factors for the development of these conditions. OAC patients compared to controls reported significantly lower stress levels throughout their life in contrast to comparisons between RO and BO patients and controls. RO patients reported significantly higher stress levels in later life. OAC patients were also less likely than controls to report depression and to have higher (albeit non-significant) self-esteem and significantly better coping skills. All three case groups reported more social support than controls.

It has been hypothesized that psychosocial factors such as stress and social support may mediate or moderate cancer risk through, for example, influencing neuroendocrine and immune functioning^[22]. Long-term exposure to stress causes persistent activation of the hypothalamic-pituitary-adrenal axis reducing tumour suppressor capability and suppressing DNA repair functions^[23-26] through suppression of lymphocyte activity^[27] and cytotoxic T-cell

Table 3 Psychosocial factors by group status

	Controls	RO		BO		OAC	
	n (%)	n (%)	AOR (95%CI)	n (%)	AOR (95%CI)	n (%)	AOR (95%CI)
Depression							
No	163 (63.7)	131 (58.0)	1.00	118 (52.2)	1.00	147 (65.9)	1.00
Yes	93 (36.3)	95 (42.0)	0.92 (0.61-1.40)	104 (46.9)	1.12 (0.74-1.70)	76 (34.1)	0.64 (0.42-0.98)
Self-efficacy							
Low	84	35	1.00	79	1.00	43	1.00
Medium	74	55	1.65 (0.92-2.98)	54	0.61 (0.36-1.05)	49	1.06 (0.60-1.87)
High	97	135	3.14 (1.86-5.31)	86	0.78 (0.48-1.27)	128	2.17 (1.32-3.57)
Self-esteem							
Low	67 (26.2)	63 (27.9)	1.00	77 (35.0)	1.00	46 (20.6)	1.00
High	189 (73.4)	163 (72.1)	0.93 (0.59-1.47)	143 (65.0)	0.76 (0.48-1.18)	177 (79.4)	1.58 (0.99-2.52)
Repression							
Low	83 (32.4)	100 (44.4)	1.00	71 (32.0)	1.00	72 (32.3)	1.00
High	173 (67.6)	125 (55.6)	0.63 (0.41-0.95)	151 (68.0)	1.20 (0.78-1.86)	151 (67.7)	1.10 (0.72-1.67)
Social support							
Hardly any	89	78	1.00	77	1.00	60	1.00
Some	89	53	0.72 (0.43-1.21)	61	1.12 (0.67-1.86)	58	1.28 (0.77-2.14)
Moderate	37	30	0.93 (0.49-1.77)	30	1.26 (0.66-2.39)	38	1.89 (1.02-3.48)
Substantial	41	64	1.97 (1.13-3.44)	54	1.83 (1.03-3.24)	67	2.84 (1.63-4.97)

RO: Reflux oesophagitis; BO: Barrett's oesophagus; OAC: Oesophageal adenocarcinoma; AOR: Adjusted odds ratio.

and natural killer cell activity^[28,29]. However, perceived stress over one's lifetime appeared to be significantly lower in OAC patients. Other factors such as recall bias and response shift may explain these reported lower levels of stress. Retrospective reporting may be skewed by recall bias as patients may lose their memory trace with time and their salience following a cancer diagnosis. Also, the current study identified an overall positive psychological profile among OAC patients including less depression, higher self-efficacy, higher self-esteem and more social support. The phenomenon of "response shift" may help to explain the findings in so far as a perceptual adjustment may occur in how a patient views stress or adversity and friends; and family tend to be sympathetic, caring and more likely to offer support at times of illness^[30-32]. Furthermore, a "cancer experience" has the potential to effect positive psychological change or post-traumatic growth (PTG)^[33]. For example, studies have found that PTG is inversely associated with emotional distress^[34] and positively associated with happiness^[35]. The majority of studies that have investigated the role of PTG have been conducted with patients with breast cancer, a form of cancer which has relatively high survival rates. In Europe, five and ten year survival rates of women diagnosed with breast cancer between 2000 and 2002 were 82% and 72%, respectively^[35]. In contrast, survival rates for OAC patients are much lower between 13% and 17% for males and females, respectively, in Ireland^[36]. A diagnosis of a cancer such as OAC with a poor prognosis and survival rate might be expected to result in despair, pessimism, reduce active coping and increase dependence on more an emotional-based style; and, in turn, these factors might be expected to reduce potential for PTG. In addition, OAC presents a unique symptom complex and the psychosocial issues and disabilities that arise from the treatment modalities involved with this cancer might be expected

to influence a patient's benefit finding ability and diminish their capacity for PTG. However, this study - the first to investigate PTG and response shift in OAC patients - suggests that benefit finding and positive well-being may be experienced by OAC patients despite the often hopeless prognosis. High levels of self-efficacy reported by OAC patients may serve to regulate the stress process, relieve depression and improve cancer symptoms^[37,38]. For example, OAC patients were less depressed than controls (OR 0.64; 95%CI: 0.42-0.98).

Perceived stress was higher in RO patients (particularly among older patients) in line with other studies [that demonstrate a link between psychosocial factors and gastro-oesophageal reflux disease (GORD)^[19,39]] even though RO patients were more likely than controls to report high self-efficacy. The association between GORD and somatisation disorder and depression reported elsewhere^[40] was not supported by the results of this study. The voluntary self-selection to participate in the study may have led to a form of ascertainment bias, whereby individuals with lower self-efficacy may have been less likely to participate in the study. Also, recall bias may have over-reported prior levels of self-efficacy, based on their current ability to cope with adversity.

Repression has been linked with poor health and cancer^[41-45]. However, there was no significant association found between repression and OAC. The single-item measure of repression used in this study may not have been sufficiently sensitive^[46]. RO patients were less likely than controls to report high repression. This relationship may have been moderated by social support - RO patients were more likely than controls to report that they had good social support.

This is a large, all-Ireland, population-based study, for which there was a relatively high response rate among case groups. The low control group response rate (42%),

however, merits a cautious approach to the interpretation of results (*e.g.*, representativeness of the population) though adjusted analyses were performed on potential confounders such as GOR, gender, age at interview, smoking status, alcohol consumption, occupation and BMI.

The retrospective nature of this study meant that it was susceptible to recall bias; this problem may be overcome by using a prospective study design. The resource-heavy nature, however, of these kinds of studies means that a retrospective study design, which can generate large data sets relatively quickly and efficiently, is usually more practicable. In any case, the incidence of OAC is still relatively low^[8] and the sample population is not large enough for a prospective study.

In conclusion, our results suggest that there may be a complex interaction between psychological factors regarding the development of RO, BO and OAC. Furthermore, the results presented here indicate that these conditions have significant psychological health consequences. Further research with enhanced methodological rigor is required to clarify the role of psychological factors in the development of OAC.

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COMMENTS

Background

Incidence of oesophageal adenocarcinoma (OAC) is rising more rapidly than that of any other form of cancer in the western world. The causes of OAC are largely unknown. Psychological factors are thought to mediate cancer risk for other forms of malignancies, but have not been investigated with regards to OAC or the conditions predisposing to it, including reflux oesophagitis (RO) and Barrett's oesophagus (BO).

Research frontiers

Several risk factors for OAC have been investigated, including diet, obesity and smoking. These factors mediate cancer risk in a variety of ways and have been shown to confer an increased risk of OAC. These risk factors, however don't fully explain the dramatic increase that has been seen over the last three decades (600% in Western countries) and psychosocial factors are thought to play a role.

Innovations and breakthroughs

Stress has been shown to mediate immune function, and subsequently cancer

risk in several forms of cancer, through the hypothalamic-pituitary-adrenal axis. Other psychosocial risk factors for cancer, such as depression, anxiety and job strain have also been investigated, but it remains unclear to what extent these factors are influencing the risk of OAC; either independently or through RO or BO.

Applications

Survival rates for OAC patients are relatively low and the comorbidities and treatment regimens for this form of cancer can greatly diminish quality of life in these patients. Identification of unambiguous risk factors for both OAC itself as well as the premalignant, reflux-mediated pathway, would provide the potential for early intervention and greatly improve survival and quality of life for RO, BO and OAC patients.

Terminology

Oesophageal adenocarcinoma is a cancer of the oesophagus that originates in the glandular tissue of the epithelium. Barrett's oesophagus is a squamous to columnar cell metaplasia within the distal oesophagus and is the main risk factor for OAC. Reflux oesophagitis is an inflammation of the oesophageal mucosa and is caused by abnormal gastro-oesophageal reflux; it also increases the risk of developing OAC.

Peer review

This is a very well written original manuscript assessing relationship between psychosocial factors and reflux esophagitis, Barrett's esophagus and esophageal adenocarcinoma.

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