RESEARCH COMMUNICATION

Comparative Epidemiological Characteristics of Oesophageal Adenocarcinoma and other Cancers of the Oesophagus and Gastric Cardia

Anh-Minh Nguyen¹, Colin G Luke², David Roder³

Abstract

Secular trends and epidemiological characteristics of 1,581 oesophageal cancers, diagnosed in South Australian residents in 1977-2000, were analysed by histological type and diagnostic period, using multivariable Poisson regression and logistic regression. The age-adjusted incidence of squamous cell carcinoma did not vary significantly by diagnostic period, either in males (p=0.195) or females (p=0.087). By comparison, variations were observed for adenocarcinomas in males (p<0.001) and females (p=0.015), with an increase in age-adjusted incidence of 169% for males and 150% for females between 1977-81 and 1997-2000. Most of these increases occurred in the 1990s. Secular differences were not evident for tumours of other or unknown histological type. The ratio of adenocarcinomas to squamous cell carcinomas was higher in patients who were aged 80 years or more, male, residents of high socio-economic areas, and those born in the United Kingdom/Ireland. Conversely, relatively low ratios presented for patients born in Southern and other parts of Europe. These differences by country of origin accord with differences in secular trend and country of birth between adenocarcinomas of the oesophagus and gastric cardia suggest that they are not expressions of the same disease. Preventive implications of these results are discussed.

Key Words: Oesophageal cancer - secular trends - histological type.

Asian Pacific J Cancer Prev, 4, 225-231

Introduction

Marked increases in incidence of oesophageal adenocarcinoma have been recorded in many western populations since the 1970s, particularly in males (Lord et al., 1998; La Vecchia et al., 2002; Nyren and Adami, 2002; Wijnhoven et al., 2002). This has been attributed by some researchers to increased obesity and associated gastrooesophageal reflux, leading to Barrett's oesophagus (columnar cell metaplasia, often with ulceration), dysplasia and adenocarcinoma of the distal oesophageal mucosa (Lagergren et al., 1999; Cheng et al., 2000; Conio et al., 2001; La Vecchia et al, 2002; Nyren and Adami, 2002).

Contemporaneous increases in adenocarcinoma of the gastric cardia also have been observed in some populations,

with several researchers suggesting these cancers and oesophageal adenocarcinomas to be manifestations of the same disease (Wijnhoven et al., 1999; Suleiman et al., 2000; Powell et al., 2002). Others have questioned this suggestion, pointing to differences in temporal trends and other epidemiological characteristics (Corley and Buffler, 2001; El-Serag et al., 2002).

A previous study showed an increase in age-adjusted oesophageal cancer incidence of approximately 30% in South Australia between 1977 and 1999, with increases of a similar magnitude occurring in each sex, but histological trends were not investigated (SACR, 2001; ACF, 2001). Meanwhile, a reduction in gastric cancer incidence of about 33% was found, similarly affecting males and females (SACR, 2001; ACF, 2001). While reductions affected both

¹Epidemiologist, Epidemiology Branch, Department of Human Services, Adelaide, South Australia; ²Senior Medical Consultant, Epidemiology Branch, Department of Human Services, Adelaide, South Australia; ³Consultant Epidemiologist, The Cancer Council South Australia, Adelaide, South Australia

Corresponding Author: Colin Luke, Senior Medical Consultant, Epidemiology Branch, Department of Human Services, PO Box 6, Rundle Mall, Adelaide, South Australia Telephone: (08) 8226 6360 FAX: (08) 8226 6291 E-mail: Colin.Luke@dhs.sa.gov.au

Anh-Minh Nguyen et al

the cardia and other gastric sub-sites, the reduction was relatively small for cardia lesions in males.

Secular trends in age-adjusted oesophageal cancer incidence have been investigated in this study by histological type and sex for 1977-2000. The epidemiological characteristics of oesophageal adenocarcinomas were compared with corresponding characteristics of oesophageal squamous cell carcinomas and adenocarcinomas of the cardia. Implications of results for cancer prevention are discussed.

Materials and Methods

Data Collection

The South Australian Cancer Registry has received statutory notifications of cancers since 1977 (SACR, 2001). The Registry is population-based and covers all regions of the State. Its procedures have been described previously (SACR, 2000; SACR, 2001). Underreporting has been monitored through electronic searching of hospital, laboratory and death records, and found to be minimal (SACR, 2000).

This study included 1,581 oesophageal cancers (ICD-O-3: C15), diagnosed in 1977-2000 and notified to the Registry (Fritz et al., 2000). They comprised two main histological types, plus a "remainder" category for unknown and rare types (Parkin et al., 1998). The respective ICD-O codes were:

- squamous cell carcinomas ICD-O: 80503-80763.
- adenocarcinomas ICD-O: 81403-81413, 81903-82313, 82603-82633, 83103, 84803-84903, 85603, and 85703-85723.
- remainder ICD-O: 80003 and other.

Data items included in this study were age at diagnosis; sex; place of residence (i.e., 4 sub-divisions of the State capital and 17 country sub-divisions, as used by the Australian Bureau of Statistics); place of birth, expressed as Australia, United Kingdom/Ireland, Southern Europe (mostly Italy, Malta, Greece, and former Yugoslav states), other Europe, Asia, and other countries; race, classified as Caucasian, Aboriginal, Asian or other; and year of diagnosis, as defined in previous reports (SACR, 2000) (SACR, 2001). Place of residence also was sub-classified into four categories by socio-economic status of postcode, using the SEIFA index (Australian Bureau of Statistics, 1998).

Statistical Analysis

A de-identified registry file was extracted and analysed in-house, under legal authority of Section 42a of the Public and Environmental Health Act, using STATA 7.0 software (StataCorp, 2001).

Directly age-standardised (World Population) annual incidence rates (95% confidence limits) were calculated by sex for the three histological types by diagnostic period (1977-81, 1982-86, 1987-91, 1992-96, and 1997-2000)

(Armitage and Berry, 1987; StataCorp, 2001; Parkin, 2002). This was undertaken separately for all ages combined, 15-49 year olds, 50-69 olds, and the age range of 70 years or more. The likelihood of non-random secular trends was assessed from the 95% confidence intervals of annual means. In addition, differences by diagnostic period were tested using Poisson regression (four dummy variables), after adjusting for five-year age categories, with an open-ended category from age 80 years (StataCorp, 2001). Negative binomial regression was substituted, where indicated, to improve model fit. Over-dispersion was checked and not found to be present, using the likelihood ratio test (StataCorp, 2001).

In addition, epidemiological characteristics of oesophageal adenocarcinomas were compared with corresponding characteristics of oesophageal squamous cell carcinomas and cardia adenocarcinomas, respectively, using the Mann-Whitney U test for age at diagnosis, socioeconomic status, and diagnostic year, and the Pearson chisquare test for place of residence, place of birth, and race (Armitage and Berry, 1987; StataCorp, 2001). In addition, two multiple logistic regression analyses were undertaken to identify predictors of adenocarcinomas when compared with: (1) squamous cell carcinomas of the oesophagus; and (2) adenocarcinomas of the cardia (Armitage and Berry, 1987; StataCorp, 2001). All socio-demographic variables were entered into these models, with backwards elimination when this did not reduce model fit (p>0.050 for change in chi-square goodness-of-fit). Model assumptions, including colinearity assumptions, were checked and found to be met in both models (Armitage and Berry, 1987; StataCorp, 2001).

Results

Age-standardised Incidence by Diagnostic Period Males

The annual age-standardised incidence of squamous cell carcinomas did not vary significantly by diagnostic period for all ages collectively (p=0.195) or by age (p>=0.146) (Table 1). By comparison, a 169% increase applied for adenocarcinomas for all ages combined between 1977-81 and 1997-2000 (p<0.001), with a corresponding 233% increase for ages 70 years and over, and a 136% increase for 50-69 year olds. A statistically significant difference in adenocarcinoma incidence was not evident by diagnostic period in the age range under 50 years, although with only 31 cancers available for analysis, statistical power was limited (Table 1). Statistically significant differences in incidence of tumours of other and unknown histological type were not evident across the study period (p=0.083) and differences were relative small in absolute terms when compared with the scale of increase for adenocarcinomas.

Females

An increase in annual age-standardised incidence of approximately 40% applied for squamous cell carcinomas

				Year of diagnosis			
Histological type	Age at diagnosis (yrs.)	1977-81	1982-86	1987-91	1992-96	1997-2000	P value*
Squamous	15-49 (n=25)	0.4 (0.1, 0.8)	0.4 (0.0, 0.7)	0.3 (0.0, 0.5)	0.2 (0.0, 0.4)	0.2 (0.0, 0.5)	0.870
cell carc.	50-69 (n=244)	8.4 (6.0, 10.7)	9.1 (6.8, 11.5)	8.7 (6.5, 10.9)	6.3 (4.4, 8.2)	5.9 (3.9, 8.0)	0.146
	70+ (n=194)	18.0 (11.4, 24.6)	15.4 (9.7, 21.0)	19.6 (13.8, 25.4)	17.6 (12.6, 22.7)	14.9 (10.2, 19.6)	0.778
	Total (n=463)	2.3 (1.8, 2.8)	2.2 (1.8, 2.7)	2.3 (1.9, 2.7)	1.8 (1.5, 2.2)	1.7 (1.3, 2.0)	0.195
Adenocar-	15-49 (n=31)	0.2 (0.0, 0.5)	0.4 (0.1, 0.7)	0.2 (0.0, 0.4)	0.3 (0.1, 0.6)	0.6 (0.2, 0.9)	0.460
cinoma	50-69 (n=210)	5.0 (3.2, 6.8)	3.8 (2.3, 5.3)	5.0 (3.3, 6.6)	7.7 (5.6, 9.8)	11.8 (9.0, 14.7)	< 0.001
	70+ (n=243)	9.9 (5.0, 14.8)	15.2 (9.6, 20.9)	17.0 (11.5, 22.4)	26.4 (20.3, 32.6)	33.0 (25.9, 40.2)	< 0.001
	Total (n=484)	1.3 (0.9, 1.7)	1.4 (1.1, 1.8)	1.6 (1.2, 1.9)	2.4 (2.0, 2.9)	3.5 (2.9, 4.0)	< 0.001
Other &	15-49 (n=6)	0.1 (0.0, 0.2)	0.0	0.1 (0.0, 0.3)	0.1 (0.0, 0.2)	0.1 (0.0, 0.2)	NA
unknown	50-69 (n=29)	1.7 (0.6, 2.7)	1.3 (0.4, 2.2)	0.4 (0.0, 0.9)	0.4 (0.0, 1.0)	0.8 (0.1, 1.6)	0.121
	70+ (n=47)	6.1 (2.0, 10.2)	2.2 (0.0, 4.5)	7.2 (3.6, 10.9)	2.8 (0.7, 5.0)	4.1 (1.6, 6.6)	0.076
	Total (n=82)	0.5 (0.3, 0.8)	0.3 (0.1, 0.5)	0.4 (0.2, 0.6)	0.2 (0.1, 0.4)	0.3 (0.2, 0.5)	0.083

Table 1. MeanAnnual Age-standardised (World Population) Incidence (95% confidence limits) of Oesophageal Cancerper 100,000 South Australian Males by Histological Type and Age; Diagnostic Period 1977-2000*

* Data source: South Australian Cancer Registry.

P values derived by Poisson regression (see text). NA: not assessed due to small numbers.

for all ages collectively between 1977-81 and 1997-2000, although differences by diagnostic period were not statistically significant (p=0.087) (Table 2). By comparison, differences were significant for adenocarcinomas (p=0.015), with an increase of approximately 150% applying between 1977-81 and 1997-2000. Differences in adenocarcinoma incidence also were significant by diagnostic period for the age range of 70 years and over (p=0.033). Statistically significant variations in incidence of tumours of other and unknown histological type did not present by diagnostic period.

Comparisons of Epidemiological Features of Adenocarcinomas and Squamous Cell Carcinomas of the Oesophagus

Univariate analyses showed that the three histological types (including those of other or unknown histology) were heterogeneous by age at diagnosis, sex, place of birth, and year of diagnosis (p <= 0.007). The ratio of adenocarcinomas to squamous cell carcinomas was higher for patients born in the United Kingdom/Ireland, and patients diagnosed in the 1990s (Table 3). By comparison, adenocarcinomas and squamous cell lesions were not heterogeneous by age

Table 2. Mean Annual Age-standardised (World Population) Incidence (95% confidence limits) of OesophagealCancer per 100,000 South Australian females by Histological Type and Age; Diagnostic Period 1977-2000.*

		Year of diagnosis					
Histological type	Age at diagnosis (yrs.)	1977-81	1982-86	1987-91	1992-96	1997-2000	P value*
Squamous	15-49 (n=11)	0.2 (0.0, 0.5)	0.1 (0.0, 0.2)	0.2 (0.0, 0.4)	0.1 (0.0, 0.3)	0.1 (0.0, 0.2)	NA
cell carc.	50-69 (n=152)	3.4 (2.0, 4.8)	3.8 (2.4, 5.3)	5.5 (3.8, 7.2)	4.6 (3.1, 6.1)	4.6 (2.8, 6.3)	0.393
	70+ (n=228)	7.7 (4.2, 11.2)	13.8 (9.5, 18.1)	13.8 (9.8, 17.9)	14.1 (10.5, 17.7)	15.0 (10.8, 19.1)	0.130
	Total (n=391)	1.0 (0.7, 1.3)	1.2 (0.9, 1.5)	1.5 (1.2, 1.8)	1.4 (1.1, 1.7)	1.4 (1.0, 1.7)	0.087
Adenocar-	15-49 (n=3)	0.0	0.0	0.0	0.0 (0.0, 0.1)	0.1 (0.0, 0.3)	NA
cinoma	50-69 (n=26)	0.4 (0.0, 0.9)	0.6 (0.0, 1.1)	1.0 (0.3, 1.7)	0.7 (0.1, 1.3)	1.2 (0.3, 2.1)	0.617
	70+ (n=73)	2.2 (0.4, 4.0)	3.1 (1.2, 5.1)	2.1 (0.7, 3.5)	5.9 (3.5, 8.4)	5.6 (3.2, 8.0)	0.033
	Total (n=102)	0.2 (0.1, 0.3)	0.2 (0.1, 0.3)	0.2 (0.1, 0.4)	0.4 (0.2, 0.5)	0.5 (0.3, 0.7)	0.015
Other &	15-49 (n=0)	0.0	0.0	0.0	0.0	0.0	NA
unknown	50-69 (n=16)	0.6 (0.0, 1.3)	0.3(0.0, 0.7)	0.6(0.1, 1.2)	0.3 (0.0, 0.7)	0.5(0.0, 1.1)	0.726
	70+ (n=43)	3.6 (1.5, 5.8)	1.1 (0.0, 2.2)	2.5 (0.9, 4.1)	2.4 (0.8, 3.9)	1.7 (0.5, 2.8)	0.512
	Total (n=59)	0.2 (0.1, 0.4)	0.1 (0.0, 0.2)	0.2 (0.1, 0.3)	0.1 (0.1, 0.2)	0.2 (0.0, 0.3)	0.293

* Data source: South Australian Cancer Registry.

P values derived from Poisson regression (see text). NA: not assessed due to small numbers.

Anh-Minh Nguyen et al

	Histological type				
Characteristic	Squamous cell carcinoma	Adenocarcinoma	Other & unknown	P value*	
Age at diagnosis (yrs.):	(n=854)	(n=586)	(n=141)		
Under 50 (n=76)	4.2	5.8	4.3		
50-59 (n=215)	14.5	13.5	8.5		
60-69 (n=462)	31.9	27.0	22.7	KW p<0.001	
70-79 (n=523)	33.7	33.4	27.7	(MW p=0.125)	
80+ (n=305)	15.7	20.3	36.9		
Total (n=1,581)	100	100	100		
Sex:	(n=854)	(n=587)	(n=140)		
Male (n=1,029)	54.2	82.6	57.9	$c_{(2)}^2 p < 0.001$	
Female (n=552)	45.8	17.4	42.1	$(c^{2}_{(1)}p < 0.001)$	
Total (n=1,581)	100	100	100	(1)	
Place of birth:	(n=845)	(n=584)	(n=139)		
Australia (n=1,110)	70.1	70.5	76.3		
United Kingdom/Ireland (n=3)	16) 18.6	23.3	16.5		
Southern Europe (n=42)	3.9	0.9	2.9	$c_{(8)}^2 p=0.007$	
Other Europe (n=83)	6.2	4.5	3.6	$(c_{(4)}^{2}p=0.001)$	
Other (n=17)	1.3	0.9	0.7	()	
Total (n=1,568)	100	100	100		
Year of diagnosis:	(n=854)	(n=586)	(n=141)		
1977-81 (n=222)	15.1	9.9	24.8		
1982-86 (n=254)	19.0	12.6	12.8		
1987-91 (n=332)	23.7	16.0	25.5	KW p<0.001	
1992-96 (n=388)	23.3	28.0	17.7	(MW p<0.001)	
1997-2000 (n=385)	19.0	33.4	19.1	- '	
Total (n=1,581)	100	100	100		

 Table 3. Distribution of Oesophageal Cancers by Socio-demographic Characteristic and Histological Type; South Australia, 1977-2000*

* Data source: South Australia cancer registry. KW = Kruskal-Wallis ANOVA. MW = Mann-Whitney U test.

c²_{(db}=Pearson chi-square test. Bracketed values are for comparisons of squamous cell carcinomas with adenocarcinomas only.

(p=0.125), race (p=0.964) or place of residence classified by socio-economic status (p=0.159), statistical sub-division (p=0.161), or as State capital or a country area (p=0.522).

The multiple logistic regression analysis confirmed that ratios of adenocarcinomas to squamous cell carcinomas were higher in:

- Older patients aged 80 years or more than younger patients.
- Males than females.
- Patients residing in high than low or mid-low socioeconomic areas.
- Patients diagnosed in 1992-96 or 1997-2000 than 1977-91.
- Patients born in the United Kingdom/Ireland than Australia (Conversely, relatively low ratios presented for patients born in Southern Europe or other parts of Europe than Australia) (Table 4).

International comparisons of ratios of age-standardised (World Population) incidence rates circa 1993-97 provided similar results, in that there was a relatively high ratio of adenocarcinomas to squamous cell lesions for the United Kingdom/Ireland, and relatively low ratios for Southern Europe and other parts of Europe, when compared with South Australia (Table 5) (Parkin et al., 2002).While ratios for South Australia and the United Kingdom/Ireland had overlapping 95% confidence ranges, this was not so for ratios for South Australia and Southern Europe and other parts of Europe.

When the multiple logistic analysis (Table 4) was re-run for males and females separately, similar temporal trends were evident by sex, although females tended to present smaller elevations in relative odds (95% confidence limits) for 1992-96 and 1997-2000 of 1.57 (0.92, 2.69) and 1.97 (1.15, 3.39) respectively, when compared with the relative odds among males of 2.06 (1.48, 2.86) for 1992-96 and 3.33 (2.37, 4.67) for 1997-2000. When the analysis for both sexes combined was repeated, substituting place of residence by statistical sub-division instead of socio-economic status of postcode, the relative odds of an adenocarcinoma, as opposed to squamous cell carcinoma, was higher for the Onkaparinga Table 4. Relative Odds of Adenocarcinoma as Opposed to Squamous Cell Carcinoma of the Oesophagus by Socio-demographic Characteristic and Diagnostic Period; South Australia, 1977-2000*

- Multiple logistic regression -			
Characteristic	Relative odds (95% confidence limits)		
Age at diagnosis (yrs.): Under 80 (reference (n=1,181) 80+ (n=248)	1.00 1.62 (1.19, 2.21)		
Sex: Male (n=941) Female (n=488)	1.00 0.19 (0.15, 0.25)		
Place of birth: Australia (reference) (n=1,004) United Kingdom/Ireland (n=293 Southern Europe (n=38) Other Europe (n=78) Other (n=16)	1.00 1.39 (1.04, 1.85) 0.18 (0.07, 0.47) 0.54 (0.32, 0.90) 0.52 (0.17, 1.61)		
Socio-economic status: Low/mid-low (reference) (n=846 Mid-high (n=254) High (n=329)	5) 1.00 1.37 (1.00, 1.86) 1.58 (1.18, 2.11)		
Year of diagnosis: 1977-91 (reference) (n=714) 1992-96 (n=361) 1997-2000 (n=354)	1.00 1.92 (1.45, 2.54) 2.91 (2.19, 3.86)		

* Data source: South Australian Cancer Registry. Includes cases with complete data on these characteristics (n=1,429). Sub-division at 3.25 (1.02, 10.41), and lower for the Western Metropolitan Sub-division at 0.67 (0.49, 0.91) and the Riverland Sub-division at 0.48 (0.24, 0.98), than for the rest of South Australia.

Comparison of Epidemiological Features of Adenocarcinomas of the Oesophagus and Cardia

Univariate analyses showed that ratios of oesophageal adenocarcinomas to cardia adenocarcinomas increased during the 1990s (p<0.001), and varied by country of birth (p<0.001), with lower ratios presenting among patients born in Southern or other parts of Europe than Australia. These ratios did not vary by age at diagnosis (p=0.395), race (p=0.447), or place of residence, irrespective of whether classified by socio-economic status (p=0.250), as the State capital or a country area (p=0.454), or by statistical subdivision (p=0.376).

Multiple logistic regression analysis confirmed that the ratio of oesophageal adenocarcinomas to cardia adenocarcinomas increased in the 1990s and was lower in residents born in Southern and other parts of Europe than Australia (Table 6). Separate models by sex showed similar odds ratios by diagnostic period. In males, the relative odds increased to 1.40 (1.04, 1.88) for 1992-96 and 2.22 (1.65, 3.00) for 1997-2000, when compared with 1977-91, whereas in females, the corresponding relative odds were 1.93 (1.03, 3.65) and 2.30 (1.21, 4.40) respectively.

International comparisons for diagnostic periods circa 1993-97 confirmed ratios of oesophageal to cardia adenocarcinomas to be relatively low for Southern Europe and other parts of Europe (Parkin et al., 2002). The ratio for males was 0.35 (0.29, 0.41) for Southern Europe and 0.42 (0.40, 0.45) for other parts of Europe, compared with 0.96 (0.72, 1.19) for South Australia. Corresponding ratios for females were 0.22 (0.12, 0.32) for Southern Europe and 0.26

 Table 5. Ratio (95% confidence limits) of Age-standardised (World Population) Incidence of Adenocarcinoma and

 Squamous Cell Carcinoma of the Oesophagus by Region of the World; Circa 1993-97*

	Se		
Region	Male	Females	Total**
South Australia	1.95 (1.54, 2.36)	0.33 (0.05, 0.60)	1.21 (0.96, 1.47)
Australia	1.13 (1.04, 1.21)	0.25 (0.18, 0.32)	0.77 (0.71, 0.82)
New Zealand	1.38 (1.16, 1.59)	0.36 (0.16, 0.55)	0.99 (0.84, 1.14)
North America	1.05 (1.00, 1.09)	0.31 (0.26, 0.36)	0.82 (0.78, 0.86)
United Kingdom/Ireland	2.01 (1.96, 2.07)	0.51 (0.47, 0.54)	1.33 (1.29, 1.36)
Northern Europe	0.54 (0.51, 0.57)	0.30 (0.26, 0.35)	0.48 (0.46, 0.51)
Eastern Europe	0.19 (0.15, 0.22)	0.23 (0.13, 0.33)	0.19 (0.16, 0.22)
Southern Europe	0.18 (0.14, 0.22)	0.20 (0.10, 0.30)	0.18 (0.15, 0.22)
Central & South America	0.18 (0.10, 0.25)	0.11 (0.00, 0.25)	0.16 (0.09, 0.23)
Asia	0.08 (0.07, 0.10)	0.08 (0.05, 0.11)	0.08 (0.07, 0.10)
Africa	0.08 (0.00, 0.21)	0.07 (0.00, 0.30)	0.08 (0.03, 0.19)

* Adenocarcinoma incidence divided by squamous cell carcinoma incidence.

** Age-sex standardised (World Population).21

Data source: Cancer Incidence in Five Continents.²¹

Table 6. Relative Odds of Oesophageal Adenocarcinoma as Opposed to Gastric Cardia Adenocarcinoma by Sociodemographic Characteristic and Diagnostic Period; South Australia, 1977-2000*

Characteristic	Relative odds (95% confidence limits)
Place of birth:	
Australia (reference) (n=859)	1.00
United Kingdom/Ireland (n=305	5) 0.88 (0.67, 1.15)
Southern Europe (n=47)	0.12 (0.05, 0.30)
Other Europe (n=77)	0.52 (0.32, 0.86)
Other (n=19)	0.35 (0.12, 1.00)
Year of diagnosis:	
1977-91 (reference) (n=607)	1.00
1992-96 (n=352)	1.49 (1.14, 1.95)
1997-2000 (n=348)	2.25 (1.71, 2.96)

* Includes cases with complete data on these characteristics (n=1,307).

Data source: South Australian Cancer Registry.

(0.22, 0.30) for other parts of Europe, compared with 0.82 (0.31, 1.33) for South Australia.

Discussion

South Australian males have experienced the increase in oesophageal adenocarcinoma incidence that has been reported for other western populations. (Lord et al., 1998; La Vecchia et al., 2002; Nyren and Adami, 2002; Wijnhoven et al., 2002) While increases for some other populations applied to periods since the 1970s (La Vecchia et al., 2002; Nyren and Adami, 2002), the increase in South Australia was not evident until the 1990s, when it was approximately two-fold. This finding is consistent with results of an earlier Australian study for 1982-93, which found statistically significant increases among males in all states except South Australia (Lord et al., 1998).

Females had a much lower incidence of oesophageal adenocarcinoma than males, as seen in other populations (La Vecchia et al, 2002; Nyren and Adami, 2002; Wijnhoven et al., 2002). This was less evident for squamous cell lesions, such that the male to female ratio of adenocarcinomas to squamous cell carcinomas was 5 to 1, after adjusting for age, place of birth, socio-economic status, and period of diagnosis.

Despite the lower incidence of adenocarcinoma in females, this incidence also increased approximately twofold in the 1990s. This contrasts with results for some other populations where increases were largely restricted to males (Lord et al., 1998; La Vecchia et al., 2002; Wijnhoven et al., 2002).

Adenocarcinomas first exceeded squamous cell carcinomas of the oesophagus numerically in South Australia

in 1997-2000, when they comprised 55% of these lesions. This compared with a corresponding 31% for 1977-81. Accordingly, the epidemiological features of oesophageal cancers are increasingly reflecting those of adenocarcinomas.

The present results indicate that the ratio of adenocarcinomas to squamous cell lesions was higher among patients who were aged 80 years or more, males, residents of higher socio-economic areas, and born in the United Kingdom/Ireland, and (less so) Australia, than elsewhere. International data also showed relatively high ratios of adenocarcinomas to squamous cell carcinomas in the United Kingdom/Ireland and South Australia, when compared with other regions of the world (except New Zealand) (Parkin et al., 2002). This suggests that migrants from these regions to Australia have persisted with the patterns of disease of their parent countries.

A number of researchers have proposed that adenocarcinomas of the oesophagus and gastric cardia be treated as one disease entity (Wijnhoven et al., 1999; Suleiman et al., 2000; Powell et al., 2002), whereas others have found these to be different diseases with different epidemiological characteristics (Corley and Buffler, 2001; EL-Serag et al., 2002). While the results of our study show similar profiles by age, sex, and socio-economic status, differences present by diagnostic period and country of birth. In particular, the ratio of oesophageal to cardia adenocarcinomas increased during the 1990s, and the ratio was lower in residents born in Southern and other parts of Europe than in Australia. International data showed lower ratios for these European regions than Australia, again suggesting that migrants to Australia from these regions have persisted with the disease profiles of their parent countries (Parkin et al., 2002).

With the upward trend in ratio of adenocarcinomas to oesophageal cancers in South Australia, it is evident that preventive endeavours will need to focus more on the sociodemographic groups at increased risk of these cancers, plus adenocarcinoma risk factors. Alcohol consumption, an established risk factor for oesophageal squamous cell carcinomas, appears not to be important in the aetiology of adenocarcinomas (Lagergren et al., 2000). While tobacco smoking may increase the risk of adenocarcinoma, its effect appears to be smaller for this disease than for squamous cell carcinoma (Nyren and Adami, 2002).

Associations between obesity and oesophageal adenocarcinoma have been demonstrated in a number of studies (Lagergren et al., 1999; Cheng et al., 2000; La Vecchia et al., 2002; Nyren and Adami, 2002), indicating its potential importance as a risk factor. It has been hypothesised that obesity may pose a greater risk for males, because excess weight in this sex is more likely to be centred on the abdomen (La Vecchia et al., 2002). Obesity, more sedentary lifestyles, and possibly trends in male fashion towards the wearing of tight belts, may predispose to gastrooesophageal reflux and consequently, to oesophageal metaplasia, dysplasia and adenocarcinoma (La Vecchia et al., 2002).

Comparative Epidemiology of Esophageal Adenocarcinomas and SCCs

More research is required to determine aetiological factors for oesophageal adenocarcinoma (Nyren and Adami., 2002). In the meantime, reductions in obesity levels should be pursued as a preventive measure, particularly in patients with Barrett's oesophagus. Obesity is becoming more common in western societies and is a well-established risk factor for a range of major public health problems, such as diabetes mellitus, heart disease, and other cancers (Cameron et al., 2003). Efforts to reduce its prevalence are of paramount importance to improve public health in general, as well as to reduce the incidence of oesophageal adenocarcinoma.

Some researchers have raised the prospect of achieving better surgical outcomes and higher survivals from oesophageal adenocarcinoma through early detection from endoscopic surveillance of patients with oesophageal metaplasia or dysplasia (van Sandick et al., 2001; Todd and de Caestecker, 2002), whereas others have questioned the effectiveness and cost-effectiveness of this strategy (Nilsson et al., 2000; Rana and Johnston, 2000). Further research is indicated to determine the merits of this surveillance, both in a clinical and broader public health context.

Acknowledgement

The authors wish to acknowledge the staff of the South Australian Cancer Registry for their attention to detail in the collection of these data over the 24-year study period.

References

- Anti-Cancer Foundation of South Australia (ACF) (2001). South Australian Cancer Statistics Monograph No. 1. Cancers of the digestive system. Anti-Cancer Foundation, Adelaide pp 3-6.
- Armitage P, Berry G (1987). Statistical methods in medical research. Blackwell Scientific Publications, Oxford.
- Australian Bureau of Statistics (1998). 1996 census of population and housing. Socio-economic indexes for areas. Catalogue no. 2039.0. Australian Bureau of Statistics, Canberra.
- Cameron AJ, Welborn TA, Zimmet PZ, et al (2003). Overweight and obesity in Australia: the 1999-2000 Australian Diabetes, Obesity and Lifestyle Study (AusDiab). *Med J Aust*, **178**, 427-32.
- Cheng KK, Sharp L, McKinney PA, et al (2000). A case-control study of oesophageal adenocarcinoma in women: a preventable disease. *Br J Cancer*, **83**, 127-32.
- Conio M, Filiberti R, Blanchi S, Giacosa A (2001). Carditis, intestinal metaplasia and adenocarcinoma of the oesophogastric junction. *Eur J Cancer Prevention*, **10**, 483-7.
- Corley DA, Buffler PA (2001). Oesophageal and gastric cardia adenocarcinomas: analysis of regional variation using the Cancer Incidence in Five Continents database. *Int J Epidemiol*, **30**, 1415-25.
- EI-Serag HB, Mason AC, Petersen N, Key CR (2002). Epidemiological differences between adenocarcinoma of the oesophagus and adenocarcinoma of the gastric cardia in the USA. *Gut*, **50**, 368-72.
- Fritz A, Percy C, Jack A, et al (eds) (2000). International Classification of Diseases for Oncology. Third Edition. World Health Organization, Geneva.

- La Vecchia C, Negri E, Lagiou P, Trichopoulos D (2002). Oesophageal adenocarcinoma: a paradigm of mechanical carcinogenesis? *Int J Cancer*, **102**, 269-70.
- Lagergren J, Bergstrom R, Lindgren A, Nyren O (1999). Symptomatic gastroesophageal reflux as a risk factor for esophageal adenocarcinoma. *New Engl J Med*, **340**, 825-31.
- Lagergren J, Bergstrom R, Lindgren A, Nyren O (2000). The role of tobacco, snuff and alcohol use in the aetiology of cancer of the oesophagus and gastric cardia. *Int J Cancer*, **85**, 340-6.
- Lord RW, Law MG, Ward RL, et al (1998). Rising incidence of oesophageal adenocarcinoma in men in Australia. J Gastroenterol Hepatol, 4, 356-62.
- Nilsson J, Skobe V, Johansson J, Willen R, Johnsson F (2000). Screening for oesophageal adenocarcinoma: an evaluation of a surveillance program for columnar metaplasia of the oesophagus. *Scand J Gastroenterol*, **35**, 10-6.
- Nyren O, Adami H-O (2002). Esophageal cancer. In Adami H-O, Hunter D, Trichopoulos D. Textbook of cancer epidemiology. Oxford University Press, Oxford pp 137-61.
- Parkin DM, Shanmugaratnam K, Sobin L, Ferlay J, Whelan SL (1998). Histological groups for comparative studies. International Agency for Research on Cancer/International Association of Cancer Registries, Lyon pp 12, 29.
- Parkin DM, Whelan SL, Ferlay J, Teppo L, Thomas DB (eds.) (2002). Cancer Incidence in Five Continents. Vol. VIII. IARC Scientific Publications no. 155. International Agency for Research on Cancer, Lyon.
- Powell J, McConkey CC, Gillison EW, Spychal RT (2002). Continuing rising trend in oesophageal adenocarcinoma. *Int J Cancer*, **102**, 422-7.
- Rana PS, Johnston DA (2000). Incidence of adenocarcinoma and mortality in patients with Barrett's oesophagus diagnosed between 1976 and 1986: implications for endoscopic surveillance. *Dis Esophagus*, **13**, 28-31.
- South Australian Cancer Registry (SACR) (2000). Epidemiology of cancer in South Australia. Incidence, mortality and survival, 1977 to 1999. Incidence and mortality, 1999. Openbook Publishers, Adelaide.
- South Australian Cancer Registry (SACR) (2001). Epidemiology of cancer in South Australia. Incidence, mortality and survival, 1977 to 2000. Incidence and mortality, 2000. Openbook Publishers, Adelaide pp 15-81.
- Stata Corp (2001). STATA statistical software. Release 7.0. STATA Corporation, College Station, Texas.
- Suleiman UL, Harrison M, Britton A, McPherson K, Bates T (2000). H2-receptor antagonists may increase the risk of cardiooesophageal adenocarcinoma: a case-control study. *Eur J Cancer Prev*, **3**, 185-91.
- Todd JA, de Caestecker J (2002). Surgery or endotherapy for highgrade dysplasia/early adenocarcinoma in Barrett's oesophagus? *Eur J Gastroenterol Hepatol*, **14**, 1049-51.
- van Sandick JW, van Lanschot JJ, Tytgat GN, et al (2001). Barrett oesophagus and adenocarcinoma: an overview of epidemiologic, conceptual and clinical issues. *Scand J Gastroenterol (Suppl.)*, 51-60.
- Wijnhoven BP, Siersema PD, Hop WC, van Dekken H, Tilanus HW (1999). Adenocarcinomas of the distal oesophagus and gastric cardia are one clinical entity. Rotterdam Oesophageal Tumour Study Group. Br J Surg, 86, 529-35.
- Wijnhoven BP, Louwman MW, Tilanus HW, Coebergh JW (2002). Increased incidence of adenocarcinomas of the gastrooesophageal junction in Dutch males since the 1990s. Eur J Gastroenterol Hepatol, 14, 115-22.