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Malignant pleural mesothelioma incidence and survival in the Republic of Ireland 1994–2009

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ABSTRACT

Objective: Malignant pleural mesothelioma (MPM) is a rare malignancy associated with exposure to asbestos. The protracted latent period of MPM means that its incidence has continued to rise across Europe after the introduction of restrictions on asbestos use. In order to obtain a clearer indication of trends in the Republic of Ireland (ROI), incidence and survival were assessed based on all MPM cases reported since the establishment of the National Cancer Registry of Ireland (NCR).
Methods: NCR recorded 337 MPM diagnoses in the ROI during 1994–2009. Survival was assessed for all cases diagnosed with adequate follow-up ($n = 330$). Crude and European age-standardized incidence rates were calculated for all cases and for 4-year periods. A Cox model of observed (all-cause) survival was used to generate hazard ratios for the effect of: gender; age at diagnosis; diagnosis cohort; region of residence; histological type; and tumour stage. Single *P*-values for the variables indicated were calculated using either a stratified log-rank test or stratified trend test.
Results: Over the study period the age-standardized MPM incidence in the ROI rose from 4.98 cases per million (cpm) to 7.24 cpm. The 1-year survival rate for all MPM cases was 29.6% (CI 24.7–34.6%). Excess mortality risk was associated with age at diagnosis (75–89 yrs vs. 55–64 yrs, HR 1.88, 95% CI 1.35–2.63, $P < 0.001$) and tumour stage (III vs. I HR 1.57, 95% CI 1.00–2.48, $P < 0.05$; IV vs. I HR 1.55, 95% CI 1.08–2.21, $P < 0.05$). Age showed a significant survival trend ($P < 0.001$) but tumour stage did not ($P = 0.150$). There was significant heterogeneity between the survival of patients resident in different regions ($P = 0.027$).
Conclusion: MPM incidence and mortality continued to rise in the ROI after the restrictions on asbestos use and the predictors of survival detected in this study are broadly consistent with those identified for other countries.

1. Introduction

Exposure to the asbestos group of silicate minerals is the greatest risk factor for the development of malignant pleural mesothelioma (MPM) [1]. The six minerals categorised as 'asbestos' are divided into two structural types: amphibole and serpentine, with amphibole minerals having the greatest carcinogenicity. Legislation enacted since the mid 1980s has progressively limited the use of asbestos in the Republic of Ireland (ROI), and the importation and use of all asbestos was banned in 2000 following the introduction of legislation by the European Union. Despite the widespread use of asbestos over past decades and its continued presence in existing buildings, few studies have been carried out on MPM incidence or survival in the ROI.

Most cases of MPM diagnosed in the ROI between 1994 and 1998 were in individuals involved in construction-related trades [2]. That study showed an annual increase of 14.4% in MPM incidence ($P = 0.08$) and predicted a large increase in incidence over coming decades. A geographical comparison study on the incidence of MPM and other mesotheliomas in patients diagnosed between 1978 and 2002, across five European regions, grouped the UK and ROI together as one region [3]. That study concluded that the European age-standardized incidence of pleural and pericardial mesothelioma was highest in the UK and ROI, at 18.2 cases per million (cpm) per year, compared with 10 in Northern Europe, 12.1 in Central Europe, 3.3 in Eastern Europe and 11.4 in Southern Europe. Patients diagnosed with MPM in the UK and ROI also had a lower 1-year survival (31%) compared with patients in other regions (34–48%) [3]. Gender differences in MPM survival have been observed in multiple studies from various parts of the World [4,5]. The gender dichotomy has variously been attributed to the greater burden of asbestos fibres in the lungs of male patients

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Table 1
Case numbers, and influence of gender and other factors on observed survival of pleural mesothelioma patients diagnosed 1994–2009 (based on follow-up to 31/12/2010.

	n (%)	HR[b]	95% CI	*P*[c]	Age-adjusted (and crude) rate per million[a]	*n* (for survival analysis)
Diagnosis cohort				0.184		
1994–1997	59 (16.3)	–	–		4.98 (4.08)	58
1998–2001	64 (17.7)	–	–		5.04 (4.24)	63
2002–2005	97 (26.8)	–	–		6.85 (6.03)	95
2006–2009	117 (32.3)	–	–		7.24 (6.70)	114
1994–2009	337 (100)	–	–		6.02 (5.34)	330
HSE region of residence				0.027		
Dublin/Mid-Leinster	105 (31.8)	1.00	–			
Dublin/North–East	60 (18.2)	0.77	0.54–1.10			
South	87 (26.4)	0.98	0.70–1.35			
West	78 (23.6)	1.24	0.90–1.72			
Age (years) at diagnosis				<0.001		
18–54	43 (13.0)	0.78	0.53–1.16			
55–64	113 (34.2)	1.00	–			
65–74	107 (32.4)	1.18	0.87–1.58			
75–89	67 (20.3)	1.88***	1.35–2.63			
Gender				0.778		
Male	289 (87.6)	1.00	–			
Female	41 (12.4)	0.80	0.55–1.16			
Histology type	*n* (*% of 81 known*)			0.762		
Epithelioid	63 (77.8)	–	–			
Biphasic	14 (17.3)	–	–			
Sarcomatoid	4 (4.9)	–	–			
Unspecified	249	–	–			
Tumour stage	*n* (*% of 153 known*)			0.150		
I	48 (31.4)	1.00	–			
II	3 (2.0)	1.26	0.37–4.22			
III	46 (30.0)	1.58*	1.00–2.48			
IV	56 (36.6)	1.67*	1.09–2.55			
Unknown	177	1.08	–			

[a] Age-standardized rates per million per year using the European standard population (crude rates in parentheses)). Age-standardized rate is calculated as the mean (or midpoint) of the age-standardized rates for males and females separately, crude rate as sum of male and female cases/sum of male and female populations. The age-standardized (and crude) rates for mesothelioma of all sites combined (not just pleura) were 5.39 (4.49) cpm for 1994–1997, 5.14 (4.51) 1998–2001, 7.78 (7.15) 2002–2005, 7.83 (7.22) 2006–2009 and 6.62 (5.93) 1994–2009.

[b] Cox model of observed survival, stratified by subtype and diagnosis cohort to allow for non-proportional hazards, also adjusted for gender, age, region, and stage. In an equivalent but less optimal model, adjusted for but not stratified by subtype and diagnosis cohort, the HR for female gender was 0.68 (95% CI 0.47–0.98, $P=0.036$); HRs for subtype, relative to unspecified subtype, were 0.59 (0.20–1.72, $P=0.332$) for epithelioid, 0.79 (0.58–1.06, $P=0.118$) for sarcomatoid and 1.31 (0.75–2.28, $P=0.347$) for biphasic; HR for 1998–2001 relative to 1994–1997 cohort was 1.73 (1.18–2.55, $P=0.005$), otherwise no significant variation by cohort; HRs for age and stage showed little change.

[c] *P*-value from log-rank test for equality of survivor functions or (for age and stages I–IV) from trend test, all adjusted for (stratified by) the other variables listed.

* $P<0.05$.

*** $P<0.001$.

compared to females [5] or the tumour suppressive actions of oestrogen receptor beta activation by circulating oestrogens, so attenuating tumour cell growth and MPM progression [6,7].

We performed analysis on all MPM cases diagnosed in the ROI between 1994 and 2009, to provide more comprehensive figures on MPM incidence here and to assess factors influencing survival.

2. Methods

The data source for this study was the National Cancer Registry, Ireland (NCR). The NCR was established in 1991 and has recorded all cancer diagnoses made in the ROI for the years 1994 onwards. The data collated by the NCR have been used in many epidemiological studies and include age at diagnosis, gender, post-diagnosis survival, histological type, tumour stage, occupation and geographical region of residence. Data were analysed for all cases of MPM recorded by the NCR between 1994 and 2009. The age-standardized incidence rates were calculated for the time periods shown and for the whole study period using the European standard population distribution [8]. Observed (all-cause) and relative survival estimates to five years after diagnosis were calculated actuarially using STATA-11 software (StataCorp LP, TX). Follow-up intervals used were three months in the first year after diagnosis, six months in the second and third years, and annually thereafter. Follow-up was based on linkage of cases to national death certificate data held by the Central Statistics Office, Ireland, covering deaths up to the end of 2010, supplemented by clinical information for some patients. Deaths after 31st December 2010 were excluded.

A total of 337 MPM cases were diagnosed over the study period (1994–2009) (Table 1). Of 16 patients without a recorded death up to the end of 2010, 6 were known to have died after 2010 and, along with 3 patients diagnosed in 2008 or 2009, were assumed to be still alive at the end of 2010. For the seven remaining patients (diagnosed 1995–2003) without recorded death data, follow-up was censored on the most recently available treatment or hospital in-patient date. Adequate follow-up ($\geq$1 day) was available for 330 patients (Table 1). A Cox model of observed (all-cause) survival, adjusted for age, gender, region and stage, and stratified for histological subtype (epithelioid, sarcomatoid, biphasic and undetermined) and diagnosis period to allow for non-proportional hazards shown by these variables, was used to generate hazard ratios for the effect of patient and tumour factors (Table 1). For comparison, a less optimal model was also applied, adjusted but