Epidemiology of malignant pleural mesothelioma in the province of Sassari (Sardinia, Italy)
A population-based report.

Ann. Ital. Chir., 2014 85: 244-248
pii: S0003469X13021192

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Epidemiology of malignant pleural mesothelioma in the province of Sassari(Sardinia, Italy). A population based report

The aim of this population-based study was to analyze and describe the epidemiological characteristics and trends of malignant pleural mesothelioma in the province of Sassari (Sardinia, Italy), in the period 1992–2010. Data were obtained from the local tumor registry which makes part of a wider registry web, coordinated today by the Italian Association for Tumor Registries. The overall number of malignant pleural mesothelioma cases registered was 70. The male-to-female ratio was 4:1 and the mean age 65.1 years for males and 63.4 years for females. The standardized incidence rates were 1.2/100,000 and 0.3/100,000 and the standardized mortality rates 0.6/100,000 and 0.2/100,000 for males and females respectively. A trend to increase in incidence in recent years was evidenced. This trend seems to follow the general national tendency and it depends on a large diffusion of asbestos usage in the past, delayed legislative interventions and probably a cleaning strategy of residual contamination fonts to intensify. The relative 5 years survival was low, suggesting the necessity to further intensify research and cure methods for the treatment of this extremely aggressive disease.

KEY WORDS: Asbestos exposure, Mesothelioma, Pleura, Sassari

Introduction

Malignant pleural mesothelioma (MPM) is the most common type of mesothelioma, arising in the pleura from mesothelial cells and showing a diffuse growth pattern over the pleural surfaces. MPM is an extremely aggressive neoplasia characterized by a high local diffusion rate, with early involvement of the pericardium, the diaphragm and the anatomical structures of the thoracic wall [1]. Without treatment the median survival from diagnosis ranges from 4 to 12 months [2]. Extrapleural pneumonectomy represents the surgical approach used with curative intent, but it has a great impact on patient's quality of life and poor survival outcomes when used alone[3]. To date, multimodality approach combining surgery, radiotherapy and chemotherapy is considered the most effective treatment strategy [1]. Nevertheless prognosis remains poor because of the attitude of the tumor to recur and patients often need palliation, especially for the management of recurrent pleural effusions [1,4-6].

Pervenuto in Redazione Gennaio 20113. Accettato per la pubblicazione Marzo 2013
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Macroscopically local forms have been described (Localized Malignant Pleural Mesothelioma LMPM); these forms are rarer and less aggressive in comparison to the common diffuse forms (DMPM) [7]. There are three different histological types of DMPM: epithelial, accounting for approximately 50% of all cases, sarcomatoid (35%) and mixed or biphasic (15%), with the epithelial form having a better prognosis [1,4,8].

In most industrialized countries, more than 90% of MPMs in men are linked, principally for occupational reasons, to asbestos exposure (especially amosite and crocidolite fibre types). This leaded to a progressive banning of asbestos in these countries, but it still remains widely used especially in emerging countries [9]. The incidence of the disease in western countries remains high because of the extensive use of asbestos in industrial activities between the 1950s and the 1980s and the extremely variable latency, ranging from 20 to 50 years from exposure [10].

The aim of this population-based study was to analyze and describe the epidemiological characteristics and trends of MPM in the province of Sassari (Sardinia, Italy), in the period 1992–2010.

Materials and Methods

The epidemiological data presented in this article were obtained from the "Registry of the tumors of the province of Sassari". This registry was created in 1992 by the local health agency for the epidemiological surveillance of tumors in the province. In 1999 it became part of a wider web of tumor registries, coordinated today by the Italian Association for Tumor Registries. The association coordinates 34 registries in the country, collects and publishes data, and collaborates with international organizations in the field.

Every registry collects data on tumoral diseases affecting inhabitants in the territory of jurisdiction through the local hospitals and health care services, as with other registries (e.g., death registries). Demographic, clinical, pathological and prognostic data are collected for each case of cancer and are registered in a digital database. This database was the data source for the present population-based report.

The demographic characteristics of the patients affected by MPM were collected. Crude incidence and mortality rates per 100,000 inhabitants per year were calculated, as were standardized rates for European population standards. A comparison between incidence and mortality in the province of Sassari and those in other Italian provinces was performed. Additionally, the cumulative risk of developing the disease and of dying between zero and 74 years of age was estimated. The age class distribution and time trends of incidence, mortality, and mean age of disease onset were also evaluated. Finally, relative 5-year survival was calculated.

Results

The overall number of MPMs registered was 70. Among them 56 were males and 14 females, with a male-to-female ratio of 4:1. The mean age was 65.1 years for males and 63.4 years for females. The cumulative risk of developing the disease was 0.12% for males and, considerably lower, 0.03% for females.

The crude incidence of MPM in the period under investigation was 1.4/100,000 for men and 0.3/100,000 for women. Standardized incidence rates were 1.2/100,000 for males and 0.3/100,000 for females.

Table I shows the distribution of incidence in relation to age in percentages, while the Table II shows the distribution of incidence rates in relation to age. Peak incidence occurred between 70 – 74 years for both sexes. Incidence rates were also calculated for the following three time periods: 1992 – 2000, 2001 – 2005 and 2006

TABLE I - *Age-class incidence distribution.*

Age (years)	Incidence (%)	
	Males	Females
0-14	0	0
15-29	0	0
30-44	5.36	7.14
45-59	17.8	21.4
60-74	62.5	57.1
75+	14.3	14.3

TABLE II - *Age-class incidence and mortality rates*

Age (years)	Incidence (/100.000 per year)		Mortality (/100.000 per year)	
	Males	Females	Males	Females
0-4	0	0	0	0
5-9	0	0	0	0
10-14	0	0	0	0
15-19	0	0	0	0
20-24	0	0	0	0
25-29	0	0	0	0
30-34	0.3	0	0	0
35-39	0.3	0	0	0
40-44	0.3	0.3	0	0
45-49	0	0.3	0	0
50-54	1.1	0.7	0.4	0.4
55-59	2.8	0	0.4	0.4
60-64	5.8	1.2	4.5	0
65-69	6.2	0.9	2.6	1.4
70-74	6.5	1.6	3.9	1
75-79	3.7	0.7	2.8	0
80-84	2.9	0.9	2.9	0.9
85+	4	0	4	1.1
Total	**1.4**	**0.3**	**0.7**	**0.2**

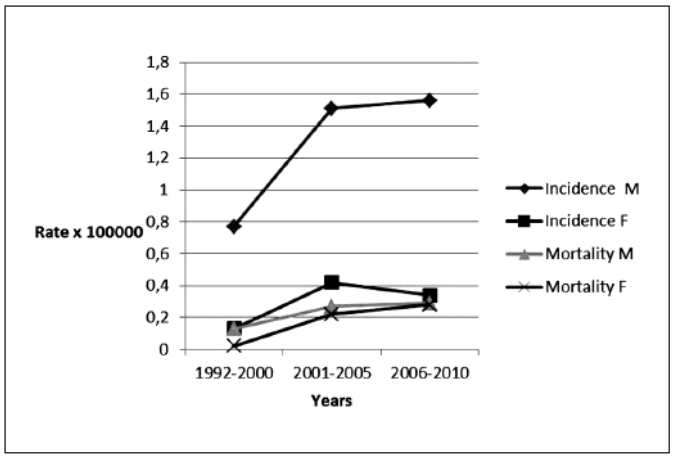

Fig. 1: Incidence and mortality rates trends.

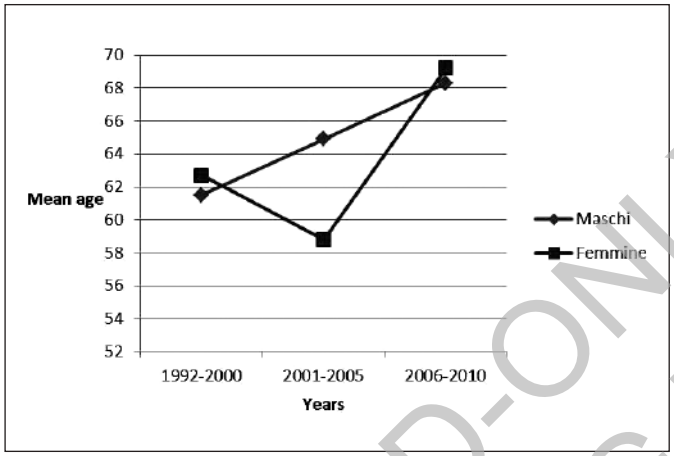

Fig. 2: Trends of mean age at disease onset.

TABLE III - *Comparison with incidence rates in other Italian* provinces

Province	Males	Females
Alto Adige	1.3	0.3
Biella	1.3	0.9
Ferrara	3.3	0.8
Firenze	1.5	0.4
Friuli V.G.	6.5	1.1
Genova	9.1	1.8
Macerata	1.2	0
Modena	1.5	0.5
Napoli	2.6	1.2
Parma	1.8	0.9
Ragusa	0.8	0.2
Reggio Emilia	3	0.7
Romagna	1.8	0.7
Salerno	0.9	0.1
Sassari	**1.1**	**0.3**
Torino	2.4	1.6
Trento	1.8	0.2
Umbria	1.2	0.5
Varese	2.1	0.5
Veneto	2.4	0.6
POOL	**2.6**	**0.7**

TABLE IV - *Relative survival one to five years from diagnosis.*

Years from diagnosis	Overall (%)
1	52.7
2	28.4
3	20.7
4	17.4
5	13.6

– 2010 (Fig. 1). There was a progressive increase in incidence rate for males, from 0.77/100.000 in the first period, to 1.51/100,000 in the second and 1.56/100,000 in the last period. A two-fold increase in incidence occurred between 1992 and 2010. The corresponding figures for females were: 0.13/100,000, 0.42/100,000 and 0.34/100,000 respectively. Analysis of the trend of mean age at disease onset for the same periods of time revealed a certain increase in recent times (Fig. 2).

Table III shows the comparison of the incidence in the province of Sassari with those in other Italian provinces. There were 40 cases of death in the period under investigation (30 males and 10 females). Crude overall mortality was 0.7/100,000 for males and 0.2/100,000 for females. Mean age at death was 57 and 50 years respectively. Standardized mortality rates were respectively 0.6/100,000 for males and 0.2/100,000 for females. The cumulative risk of death was low (0.06% for males and 0.02% for females). Table II shows the age-class distribution of mortality rates, with peaks occurring between 60 and 64 years for males and 80-84 years for females. Figure 1 shows the time trend of mortality between 1992 and 2010: a steady and relevant increase in mortality was evidenced. Finally, relative 1 year survival was approximately 52.7%. Relative survival at 5 years from diagnosis was 13.6 (Table IV).

Discussion

Malignant pleural mesothelioma is the most common type of mesothelioma, arising in pleural mesothelial cells and showing a diffuse growth pattern over the pleural surfaces. It accounts for approximately 93% of mesotheliomas, followed by other forms: peritoneal, pericardial and tunica vaginalis of the testis mesothelioma [11].

Although considered as a rare tumor in the past, it became a relevant public health problem in the last decades, especially in industrialized countries. The cause is the etiological relationship with exposure to asbestos,

particularly in amosite and crocidolite fibres. Asbestos is a natural fibrous mineral, characterized by flexibility, plasticity and resistance to high temperatures, acids, alkalis and other chemical substances. These properties rendered it useful in a wide spectrum of industrial applications, especially for fire, water and sound insulation. The industrial sectors most frequently implicated were: building constructions, heavy metal industry and metallurgy, shipbuilding, asbestos-cement industry, textiles, railways and military activities.

Asbestos production and industry was extremely diffuse in Italy, up to the end of the 1980s. Indeed, at that time Italy was the first country in asbestos production in the European Community and the second in Europe, after the Sovietic Union. It was calculated that from the end of the Second World Word until 1992 approximately 3,750,000 tons of raw asbestos were produced in the country [11]. The most productive period was between the 1970s and 1980s, with peaks of approximately 160,000 tons/year in the late 70s. Furthermore, a relevant quantity of asbestos was imported, amounting in about 50,000 tones since 1991 [11]. It was estimated that approximately 3.5 millions of workers have been occupied in asbestos related professional activities. Finally, in 1992 asbestos was banned in Italy. Considering that the median latency of onset on MPM is about 40 years from exposure, it is probable that the peak of incidence in Italy will be observed in the present decade.

Given the dimensions of asbestos production and diffusion in the territory in the past and the progressive increasing of incidence of mesotheliomas, particularly in areas with intense industrial and shipyard activities, it was created on 1991 the National Mesothelioma Register (ReNaM). ReNaM is a dynamic instrument useful for epidemiological surveillance of mesotheliomas, medico – legal purposes and the identification of any remaining asbestos contaminations sources[12]. In the last ReNaM report published, containing data for the period 1993 - 2008, the standardized incidence rate of ascertained, probable or possible MPM in Italy was 3.55/100,000 for males and 1.35/100,000 for females[13]. Sardinia entered in the ReNaM web and provides data from 2000, but the entire regional territory it is not yet completely covered. Actually Sardinia results as one of the Italian regions with lower MPM incidence and mortality rates, particularly in comparison with more industrialized areas.

Focusing on the province of Sassari, the crude incidence and the cumulative risk of developing the disease were significantly lower than national values and similar to those reported for the entire region. This probably depends on the relatively low industrial activity in the area, as the most important economic sources are agriculture, farming, fishing and tourism. There are two relevant industrial and shipyard poles in the province (Porto Torres and Olbia – La Maddalena) [14]; indeed, the most cases occurred in these areas.

Comparison of incidence rates with those of other Italian provinces, placed our province near to those with lower incidences, like Macerata, Salerno, Ragusa e Trento. Provinces with consistently higher incidence rates were Genoa, Turin and Naples, characterized by a long tradition in shipyard and industrial activities.

Considering the distribution of the disease in relation to age, less than 10% of the cases occurred in individuals younger than 45 years. This reflects the modalities of exposure to asbestos, occurring generally for professional reasons, and the relatively long latency, as we mentioned before. More than half of the cases were observed after the sixth decade of life in both sexes. The mean age at disease onset was 65.1 years for men and 63.4 years for women; these values are slightly lower to those reported for the entire nation (68.8 for males and 70.1 for females) [13]. There were no significant differences regarding the mean age at disease onset between males and females. Peak incidence occurred between 70 and 74 years of age in both sexes.

The time trends analysis showed a stable increase in incidence in the province of Sassari. This trend is common to numerous national and international geographical areas and depends principally on delayed legislative interventions. In countries where asbestos was banned earlier, like most European countries and the USA, it seems that the peak of incidence was overcame[9]. Furthermore, it is of paramount importance the accurate cleaning of residual contamination fonts, especially in countries with a previous wide consumption and territorial diffusion of asbestos like Italy.

Concerning mortality, 40 deaths occurred in the 18 years we studied. Crude overall mortality was 0.7/100,000 for men and 0.2/100,000 for women. Mean age at death was approximately 69 years in both sexes and the cumulative risk of death relatively low, 0.06% for males and 0.02% for females.

Considering the age-class mortality trend a natural increase linked to aging was observed in both sexes, with peaks after the seventh decade of life and with a significant increase for males between 2001 and 2010. The relative 5 years survival was low (13.6%) because of the intrinsic biological characteristics of mesotheliomas and the lacking of effective treatment strategies.

Conclusions

Our data evidenced low incidence rates of MPM in the province of Sassari, as well as a trend to increase in incidence in recent years. This trend seems to follow the general national tendency and it depends on delayed legislative interventions and probably a cleaning strategy of residual contamination fonts to intensify. The relative 5 years survival in patients with MPM remains low, suggesting the necessity to further intensify research and cure methods for the treatment of this extremely aggressive disease.

Riassunto

Lo scopo di questo studio era quello di analizzare e descrivere le caratteristiche epidemiologiche del mesotelioma pleurico maligno nella provincia di Sassari negli anni 1992 - 2010. I dati epidemiologici sono stati ottenuti dal registro locale dei tumori che fa parte di una rete più ampia di registri, coordinata attualmente dall'Associazione Italiana Registri Tumori (AIRTUM). Il numero complessivo di casi di mesotelioma pleurico registrati nel periodo sotto esame era 70. Il rapporto maschi - femmine era 4:1 e l'età media 65.1 e 63.4 anni rispettivamente. I tassi standardizzati di incidenza erano 1.2/100.000 per i maschi e 0.3/100.000 per le femmine, mentre i rispettivi tassi standardizzati di mortalità erano 0.6/100.000 e 0.2/100.000. Una tendenza all'aumento dell'incidenza è stata evidenziata, presumibilmente in relazione con la vasta diffusione dell'asbesto in passato e con il ritardo nell'adozione di strategie legislative di soppressione e bonifica di questo materiale nel territorio. La sopravvivenza relativa a 5 anni è stata estremamente bassa e questo impone l'intensificazione degli sforzi per il miglioramento dei metodi di cura della malattia.

Acknowledgements

The authors wish to thank Prof. Fabrizio Scognamillo and Dr. Alessia Azzu for their useful suggestions.

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