Mortality from Pleural Mesothelioma in Rio de Janeiro, Brazil, 1979–2000:

Estimation from Death Certificates, Hospital Records, and Histopathologic Assessments

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To obtain information about the occurrence of pleural mesothelioma on a population basis in Brazil, mortality related to pleural tumors in the State of Rio de Janeiro during 1979–2000 was examined. Death certificates with pleural tumors as the main cause of death and hospital records were analyzed, together with histopathologic material, which was reevaluated. Of 217 death certificates coded as pleural tumors, 34.1% were considered wrongly coded. Results after reclassification were: definite mesothelioma = 45 cases; probable = 7; possible = 31; inconclusive = 65; other tumors = 11. Thus, the number of mesotheliomas in Rio de Janeiro in 1979–2000 is estimated to have been 83. The analysis also suggests a problem with mortality codification in the State. *Key words*: pleural mesothelioma; death certificates; mortality; epidemiology; Brazil, Rio de Janeiro; asbestos; pleural tumors.

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Primary pleural tumors have been recognized since 1870, but the definitive causal link between mesothelioma and asbestos was discovered only in 1960 by Wagner, in South Africa crocidolite miners.[1] Since then, many epidemiologic studies have been performed worldwide. The annual incidence of this tumor in the United States is about 10 cases/million/year for males and 1.8 for females.[2] An increase in mortality is expected to occur in many countries, with peak incidences around 2020–2030.[3-5] Nowadays, exposure to asbestos is known to be the most important cause of malignant mesothelioma.[6]

In Brazil, more than 20,000 workers are directly exposed to chrysotile.[7] Mining activities are carried out in the central part of the country, in one of the world's largest open pit mines. The annual production of chrysotile is about 200,000 to 250,000 tons.[8] In the State of Rio de Janeiro, the most important activity is the fiber-cement industry, but the number of exposed workers is unknown.

According to the International Agency for Research on Cancer (IARC),[9] mesothelioma is not considered an occupational cancer in Brazil, because of the lack of local studies and information about this tumor in the medical literature. There is just one paper, reporting three cases of mesothelioma in the country.[10]

A preliminary report shows that death certificates can underestimate mesothelioma mortality.[11] In our hypothesis, this tumor is underreported and underdiagnosed in Brazil.

The objective of this study was to estimate the mortality related to pleural malignant mesothelioma in the State of Rio de Janeiro, in the period 1979–2000, and to assess the reliability of the diagnoses reported by death certificates.

METHODS

Death certificates from the period in 1979–1994 were the primary targets of the study. Cases of pleural tumors registered in the State of Rio de Janeiro were located with the CD-ROM of the Brazilian DATASUS mortality system.[12] For this purpose, category 163 (163.0, 163.1, 163.8, and 163.9) of the International Classification of Diseases–9th revision (ICD-9) was used.[13] Subsequently, the certificates were revised manually by two of the investigators, and according to the main or contributing causes of death, were reclassified into five categories: pleural mesothelioma, nonspecified pleural tumor, malignant pleural effusion, metastatic pleural effusion, and non-pleural neoplasms or other diseases. Cases from the two last categories were excluded from the

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analysis, because they represented misclassifications, since a clear indication of a non-pleural primary tumor or other disorder was present in each.

Additional data, such as name, gender, date of birth, profession, address, method of diagnosis, and place of death were extracted from the death certificates as well.

Further cases up to the year 2000 were obtained through personal contact with pathologists from the entire state. The professionals, including those from cancer reference centers and from universities, were asked to provide histopathologic material from cases of pleural tumors.

When available, medical records of the patients were assessed to obtain additional information about cause of death, diagnostic methods, exposure to asbestos, clinical course, and prognosis. Data were collected with the use of standardized forms.

Letters were sent by mail to the families of all deceased persons included in the study, inviting relatives to be interviewed, either in person or by telephone, in order to provide further information about the disease and exposure to asbestos.

Histopathologic material (slides and paraffin blocks) from transcutaneous pleural biopsies, open biopsies, or autopsies of the cases was gathered from various hospitals. This material was processed for immunohistochemical analysis, using CEA, Leu-M1, calretinin, thrombomodulin, p53, and Ki-67, to make the differential diagnosis among mesothelioma, adenocarcinoma, and sarcomas.[14] Two pathologists, experienced in pleural pathology and blinded for the initial diagnosis, analyzed the histologic patterns and immunohistochemical reactions independently, and stated the final diagnoses, according to the World Health Organization guidelines.[15]

The accuracy of death certificate coding and medical record information was evaluated by calculation of confirmation rates and detection rates according to the method proposed by Percy et al.[16] For this purpose, the cause of death coded on each death certificate was compared with the diagnosis reported on medical records and each of these results was further compared with the histopathologic confirmation by the pathologists.

After the evaluation of all the information above, the cases were classified into five groups, according to the following scheme:

	Diagnosis	*Definition*
Group 1	Mesothelioma	a
Group 2	Probable mesothelioma	b + (c or d)
Group 3	Possible mesothelioma	c or d
Group 4	Undetermined	e
Group 5	Not mesothelioma	f

a = Histopathologic evidence of mesothelioma after review by pathologists
b = Description of histopathologic pattern or necropsy on medical records
c = Clinical history and radiologic aspect suggestive of mesothelioma
d = Diagnosis of "mesothelioma" written on death certificate
e = Diagnosis of "pleural tumor" without other primary site, written on death certificate or medical record
f = Histopathologic or written evidence of other tumor, in the absence of the above

Data were managed with the software EPI-INFO 6.04d (CDC, Atlanta, GA, USA).

RESULTS

The analysis of CD-ROM data yielded 224 cases coded as pleural tumors in the period 1979–1994. The original codings, according to the ICD-9, by year, are listed in Table 1, showing that the majority of cases were classified into the 163.9 code, whereas codes 163.0 and 163.1 had, respectively, two and eight cases. No case was classified as 163.8.

A total of 217 death certificates were recovered from the Vital Records Branch of Rio de Janeiro State Office for Health. After the initial reclassification, 45 cases of mesothelioma were found, and 74 cases (34.1%) were considered wrongly coded (Table 2). The most common causes of death erroneously classified as primary pleural tumors were metastatic pleural effusion without specified primary site (ICD = 199.1) and lung cancer (ICD = 162.9). Other inaccurate causes included pneumonia and neoplasms of ovary, prostate, and stomach (Table 3).

The pathologists provided material from 16 additional patients with mesothelioma. None of them had been reported among the death certificates previously collected.

TABLE 1. ICD-9 Coding of Pleural Tumors in 1979–1994

	ICD-9*				
	163.0	163.1	163.8	163.9	Total
1979	—	—	—	6	6
1980	—	—	—	12	12
1981	—	—	—	13	13
1982	1	1	—	5	7
1983	—	—	—	13	13
1984	—	1	—	8	9
1985	—	—	—	9	9
1986	—	2	—	19	21
1987	—	—	—	16	16
1988	—	2	—	9	11
1989	—	—	—	12	12
1990	—	—	—	17	17
1991	—	—	—	19	19
1992	—	2	—	15	17
1993	1	—	—	20	21
1994	—	—	—	21	21
TOTAL	2	8	—	214	224

*163.0 = malignant neoplasm of pleura—parietal portion
163.1 = malignant neoplasm of pleura—visceral portion
163.8 = malignant neoplasm of pleura—other site
163.9 = malignant neoplasm of pleura—unspecified

TABLE 2. Initial Reclassification of Cases, According to Information Contained in Death Certificates

Classification	No.	%
Pleural mesothelioma	45	20.7
Pleural neoplasm	90	41.5
Malignant pleural effusion	8	3.7
Metastatic pleural effusion*	45	20.7
Non pleural neoplasms or other diseases*	29	13.4

*Wrongly coded.

Only 73 hospital records were located. Thirty-three of them mentioned the diagnosis of mesothelioma. In 21 cases, a histopathologic description of the tumor was present, whereas in 23 the descriptions referred to other tumors. Clinical histories and radiologic exams were suggestive of mesothelioma in 36 cases. Only eight medical records stated that the patient had been exposed to asbestos.

Although letters were sent to 139 families with reliable addresses, only five people answered the invitation to be interviewed and provide further information about the patients.

Histopathologic material was reevaluated in 51 cases. Paraffin blocks were available from 34 individuals, and the remaining 17 had one or two slides of the tumor. In 45 cases a typical histopathologic pattern for mesothelioma was seen, and was confirmed by immunohistochemistry. Five cases presenting unusual patterns required differential diagnosis with poorly differentiated carcinoma/adenocarcinoma. One case of lung cancer was also identified. The most common histopathologic pattern was epithelioid mesothelioma in 27 (60%); biphasic mesothelioma was seen in 8 (17.8%). Five cases exhibited the spindle-cell type and five the desmoplasic pattern. Peripheral adenocarcinoma of the lung infiltrating the pleura (5/51) was further diagnosed by immunohistochemistry.

After this examination, we selected only the cases in which there were data from death certificates, medical records, and histopathologic analyses together, to calculate the detection and confirmation rates. In relation to death certificates, 20 cases (58.8%) confirmed histopathologically as mesotheliomas had been previously reported as other pleural tumors. When medical records were compared with histopathologic diagnoses, 14 cases (41,2%) proved to have been misdiagnosed (Table 4).

Both death certificates and medical records were available in 64 cases. Underreporting was evident in 17.2% of these. The detection and confirmation rates for this group are shown in Table 5.

After the reclassification, 45 cases (28.3%) were diagnosed as definite mesotheliomas, seven were considered probable, 31 were regarded as possible. Sixty-five remained undetermined, and 11 were diagnosed as other tumors. The distribution of reclassified cases, according to gender and age group, is shown in Table 6.

DISCUSSION

This is the first population-based study of mesothelioma in Brazil. In our country, there is an impressive lack of studies of this tumor, and for this reason it is difficult to make public health decisions.

According to the ICD-9,[13] pleural neoplasms must be coded into category 163. After the review of all death certificates, a serious problem in the Mortality Codification System in Rio de Janeiro State was found: 74 death certificates (31.4%) were wrongly coded. Most of the wrongly coded tumors were metastatic pleural effusion with a known primary site (20.7%) and other nonpleural neoplasms (13.4%). In the latter, the most common errors were the inclusion of malignant neoplasm without specification of site (199.1) and malignant neoplasm of the lungs (162.2).

TABLE 3. ICD-9 Codes for the Causes of Death Incorrectly Coded as Pleural Tumors (163.0, 163.1, 163.8 or 163.9)

ICD-9 Code	Description	No.	%
149.0	Malignant neoplasm of pharynx, unspecified	1	1.35
151.9	Malignant neoplasm of stomach, unspecified	1	1.35
162.3	Malignant neoplasm of upper lobe, bronchus, or lung	1	1.35
162.9	Malignant neoplasm of bronchus and lung, unspecified	12	16.22
164.9	Malignant neoplasm of mediastinum, unspecified site	2	2.70
174.9	Malignant neoplasm of female breast, unspecified	2	2.70
183.0	Malignant neoplasm of ovary	1	1.35
185	Malignant neoplasm of prostate	2	2.70
186	Malignant neoplasm of testis	1	1.35
199.1	Malignant neoplasm, without specific site, other	45	60.81
202.8	Other malignant neoplasms of lymphoid and histiocytic tissue, other lymphoma	1	1.35
486	Pneumonia, organism unspecified	2	2.70
511.9	Pleural effusion	1	1.35
799.9	Other ill-defined causes of morbidity and mortality	2	2.70
TOTAL		74	

TABLE 4. Detection Rates and Confirmation Rates of Death Certificates and Medical Records Compared with Histopathologic Diagnosis of Mesothelioma

	Histopathology				Detection Rate	Confirmation Rate
		+	–			
Death certificate	+	11	0	11	35.5%	100%
	–	20	3	23		
		31	3	34		
		+	–			
Medical record	+	17	0	17	54.8%	100%
	–	14	3	17		
		31	3	34		

TABLE 5. Detection Rates and Confirmation Rates of Death Certificates Compared with the Diagnosis of Mesothelioma on Medical Records

	Medical Record				Detection Rate	Confirmation Rate
		+	–			
Death certificate	+	16	4	20	59.3%	80%
	–	11	33	44		
		27	37	64		

Codification problems related to mesothelioma have been described in many studies,[17] but the implementation of a specific code for mesothelioma in ICD-10 will possibly reduce coding errors in the future.

In a study of the "missing" cases of pleural malignant mesothelioma in Minnesota, Lilienfeld and Gunderson reported that these tumors were coded as 162.2–162.9 (malignant neoplasm of bronchus and lung), 195.1 (malignant neoplasm of other and ill-defined sites of thorax), or 199.1 (malignant neoplasm without specification of site), rather than 163.0 through 163.9.[18] In our hypothesis, these errors also occur in Brazil, because the most common mistakenly coded pleural tumors were 199.1 and 162.9. Conversely, some cases of mesothelioma might have been misclassified under these codes. In the small number of cases provided by pathologists, it was possible to confirm the theory of misclassification, because none of these cases were coded as pleural tumors on death certificates.

Data from the Massachusetts Cancer Registry and death certificates were matched for mesothelioma from 1982 to 1987. Only 12% of the people whose death certificates reported mesothelioma were detected using underlying cause-of-death codes for cancers of peritoneum and pleura.[19] However, other studies suggest that estimates of numbers of mesothelioma cases from death certificates may overestimate their incidence.[17]

The assessment of hospital records was important for a better comprehension of the cases. We were able to analyze clinical histories and diagnostic methods, and to find information about histopathologic material, such as the location of paraffin blocks and slides, because sometimes they were kept in other institutions. Although the Brazilian laws state that medical records must be stored for at least 20 years, in many hospitals, histopathologic material or records were not found, causing a loss of precious information.

Only eight records had information about exposures to asbestos, showing that occupational history is not well explored, because asbestos is responsible for the majority of cases of mesothelioma.[6]

TABLE 6. Pleural Tumors in Rio de Janeiro State (1979–2000), after Reclassification, Aaccording to Gender and Age Group

		Gender (*n*)		Age Group (*n*)			
	Diagnosis	Male	Female	< 60 Years	> 60 Years	Total	%
Group 1	Mesothelioma	31	14	15	30	45	28.3
Group 2	Probable mesothelioma	3	4	5	2	7	4.4
Group 3	Possible mesothelioma	20	11	12	19	31	19.5
Group 4	Undetermined	32	33	23	42	65	40.9
Group 5	Not mesothelioma	7	4	4	7	11	6.9

Interviews with relatives could complement data about exposures to asbestos, but only five relatives agreed to cooperate. Many factors may have contributed to this disappointing response, such as low levels of education, changes of address, and the fact that this kind of procedure is not common in Brazil. In other countries, high response rates to both mail questionnaires and telephone interviews are reported.[20,21]

One important aspect of this study was the attempt to confirm the diagnosis of mesothelioma by reevaluating histopathologic material with modern techniques of immunohistochemistry and experienced pathologists. The differential diagnosis among mesothelioma and adenocarcinomas/sarcomas is difficult,[22] but the use of large pieces of tissue, as well as the experience of the pathologist, can improve the accuracy of diagnosis, especially for the biphasic subtype.[23]

Forty-five cases were confirmed as mesotheliomas. As in other studies, epithelial was the most common histopathologic pattern, followed by biphasic and sarcomatous types.[24]

To increase the reliability of the study, the authors decided to calculate the detection and confirmation rates for the cases with histopathologic confirmation, but only if both medical record and death certificate data were available. This resulted in a smaller sample, but we could see that almost 60% of the cases had been underreported when compared with death certificates and that 41% had been misdiagnosed when medical records were considered.

The detection rate reflected in the death certificates in this study was 35.5%. Selikoff and Seidman[25] found a similar detection rate of 34.1%, studying a cohort of insulation workers. Ducic in 1971 and Delendi in 1991, cited by Iwatsubo et al.,[17] obtained detection rates of 11% and 51%, respectively, examining cases of mesothelioma confirmed by autopsies.

High confirmation rates of the information in death certificates, as in our study, also have been reported by Delendi et al., who found a rate of 85.6% in men in the Province of Trieste.[26]

The accuracies of the diagnoses written on medical records of these patients were also evaluated, and a detection rate of 54.8% and a confirmation rate of 100% were found. We are not aware of similar studies, but this finding can raise the concern of misdiagnosis as an important cause of the underreporting of mesothelioma in Brazil.

When medical records were compared with the death certificates, the results also show that mesothelioma was underreported, according to the classification proposed by Percy et al.[16] because the confirmation rates are greater than the detection rates.

Considering the confirmed, probable and possible mesotheliomas together, the number of cases in the State of Rio de Janeiro in the period 1979–2000 is estimated to have been 83. Most of the cases occurred after the age of 60. Among the confirmed cases, there was a 2:1 male/female ratio. This finding shows a greater occurrence in females, compared with reports in the literature, where the rates are usually five to ten times higher in men.[27]

Despite all efforts to find reliable information, the diagnoses in 40% of the cases were still undetermined. This fact poses a challenge for professionals involved in diagnosing, reporting, and coding malignant and nonmalignant diseases.

Future studies would be facilitated by a national commission formed by epidemiologists, clinicians, and pathologists to define public health policies, clarify doubtful cases, and propose a standardized diagnostic protocol. In addition, a national mesothelioma registry would help to identify case clusters and their geographic locations.

Finally, the estimated number of mesotheliomas found in the period of 1979–2000 in the State of Rio de Janeiro is 83. However, because of problems in the codification system, this number may be an underestimate.

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