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The impact of COVID-19 on new mesothelioma diagnoses in Italy

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Abstract

Background: The aim of this work was to evaluate the impact of the restrictions put in place to control the COVID-19 pandemic on new diagnoses of malignant mesothelioma (MM) in Italy.

Methods: Twelve of the 21 Italian malignant mesothelioma CORs (regional operating centres) participated. The study included all cases of MM with microscopic confirmation; cases without microscopic confirmation and death certificate only (DCO) were excluded. For each case, information on sex, date of birth, tumor site, morphology, and date of diagnosis was retrieved. We compared the number of incident cases in 2020 with 2019, looking at the overall picture and for four periods: pre-pandemic (January–February), first wave (March–May), low incidence (June–September), and second wave (October–December).

Results: A total of 604 cases were registered: 307 in 2019 and 297 in 2020. In the 2020 pre-pandemic period, the incidence was higher than in the same months in 2019

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(+45%); there was no significant change during the first wave (+1%) or in the low-incidence period (−3%), while a decrease was observed during the second wave (−32%). However, the data were not homogeneous across the country: the increase in the pre-pandemic period concerned mostly the regions of northern (+61.5%) and central Italy (+43.5%); during the first wave, MM diagnoses increased in the northern (+38.5%) and central (+11.4%) regions but decreased in the southern regions (−52.9%). All these differences are compatible with random fluctuations.

Conclusion: The COVID-19 pandemic had little or no impact on new MM diagnoses, and variations were not homogeneous throughout the country.

KEYWORDS
COVID-19, incidence, mesothelioma

INTRODUCTION

Malignant mesothelioma (MM) is a rare disease of great interest to the scientific community and to public health due to its high lethality and its association with asbestos exposure.[1]

The timely diagnosis of MM, although not able to modify the prognosis of the disease, can certainly help in reconstructing the medical history (occupational and non-occupational) as recounted by the patient in order to document previous exposure to asbestos and to contribute to any request for compensation.[2]

During the COVID-19 pandemic, there was a delay in the diagnosis of oncological diseases both because many departments were converted into COVID wards and because many outpatient activities were suspended.[3]

A recent study showed a 39% decline in cancer diagnoses at secondary care hospitals in Italy. Bladder cancer, colorectal cancer, and prostate cancer diagnoses decreased by 66%, 62%, and 75%, respectively.[4] The most probable hypothesis is that this decrease in the number of diagnoses reflects a delay in access to testing and assessment related to the COVID-19 pandemic and to infection-control measures.[4] How much this delay caused a shift to more advanced disease at diagnosis, and therefore with a potentially worse prognosis, probably depended on the cancer site and on how the regional health systems reacted to the pandemic; this is an important public health question to be answered over the next few years.[5]

The aim of this work was to evaluate the impact of the COVID-19 pandemic on the number of new MM diagnoses in relation to the phase of the pandemic and geographical area.

METHODS

The study involved the CORs (regional operating centres) present throughout Italy, whose task is to systematically collect information on MM and to reconstruct the occupational, environmental, and family history of patients to ascertain any exposure to asbestos.

Twelve of the 21 Italian CORs participated in the study: 7/9 in the north, 2/4 in the centre, and 3/8 in the south of Italy. At least one reference anatomical pathology laboratory for each COR provided information pertinent to this study's aim, 11 registries contributed with only one pathology laboratory, and one contributed with all the laboratories in that region. To be included, pathology laboratories had to have

TABLE 1 Characteristics of the patients with malignant mesothelioma included in the study

	2019–2020	2019	2020	% Variation
All	604	307	297	−3.3
Sex				
Male	473	238	235	−1.3
Female	131	69	62	−10.1
Age (years)				
45–54	16	8	8	0.0
55–64	80	45	35	−22.2
65–74	189	93	96	3.2
75–84	269	133	136	2.3
85+	50	28	22	−21.4
Tumor subsite				
Pleura	567	287	280	−2.4
Peritoneum	37	20	17	−10.5
Geographical area				
North	339	163	176	8.0
South-Tyrol	15	7	8	14.3
Friuli Venezia Giulia	96	50	46	−8.0
Liguria	54	27	27	0.0
Lombardy	39	16	23	43.8
Piedmont	52	21	31	47.6
Reggio Emilia	33	13	20	53.8
Veneto	50	29	21	−27.6
Centre	192	103	89	−13.6
Marche	32	19	13	−31.6
Tuscany	160	84	76	−9.5
South	73	41	32	−22.0
Calabria	10	4	6	50.0
Puglia	30	13	17	30.8
Sicily	33	24	9	−62.5

completed registration of all cases that had initiated their pathological assessment before 31 December 2020.

The study included only *certain* MM (histology present with characteristic morphological report, characteristic/suggestive/absent immuno-histochemistry + diagnostic confirmation by images/clinical diagnosis of discharge) or *probable* MM (histology present with doubtful morphological report or cytology with characteristic report + confirmation by diagnostic imaging/clinical diagnosis of discharge). *Possible* MM (absent histology/cytology, clinical and radiological diagnosis) corresponding to 6% of the total registered cases and death certificate only (DCO), less than 1% of the total registered cases, were excluded.[6]

The CORs, coordinated by the Italian National Mesothelioma Registry (ReNaM), are responsible for regional activities, including supporting the network and standardizing case collection and registration procedures.[7]

All the diagnoses of sites affected by MM (pleura, pericardium, peritoneum, tunica vaginalis of testis) in the periods January–December 2019 and January–December 2020 were included.

For each case, information on sex, age, tumor site, morphology, and month of diagnosis was collected. The analyses were conducted by the Reggio Emilia Cancer Registry and the Emilia-Romagna COR and include distribution by sex, age (45–54, 55–64, 65–74, 75–84, and 85+), and residence (regions of northern, central, and southern Italy). The incidence periods are defined according to the pandemic phases in Italy in 2020 and the same months in 2019 were used for comparison: pre-pandemic (January–February), first wave (March–May), low incidence (June–September), and second wave (October–December). The percentage differences between 2020 and 2019 in the four periods were calculated, with relative 95% confidence intervals (95% CI) estimated with binomial distribution assuming equal denominator.

As the reporting of MM to a registry is compulsory by law (Italian Decrees 277/1991, 308/2002, and 81/2008), ethics approval was not required.

RESULTS

In the period 2019–2020, 604 cases were recorded (473 in men and 131 in women), mostly in the 75–84 age group (Table 1). Most of the cases (567) involved the pleura, with 37 in the peritoneum; 339 cases were registered in the

TABLE 2 Distribution by age group and period of diagnosis of patients with malignant mesothelioma

	2019					2020				
	Age group					Age group				
Period	**45–54**	**55–64**	**65–74**	**75–84**	**85+**	**45–54**	**55–64**	**65–74**	**75–84**	**85+**
January–February	0	7	11	21	3	1	7	17	32	4
March–May	2	13	22	32	5	4	11	33	23	4
June–September	5	13	29	44	16	3	9	32	52	8
October–December	1	12	31	36	4	0	8	14	29	6
Total	**8**	**45**	**93**	**133**	**28**	**8**	**35**	**96**	**136**	**22**

Note: Comparison 2019 versus 2020.

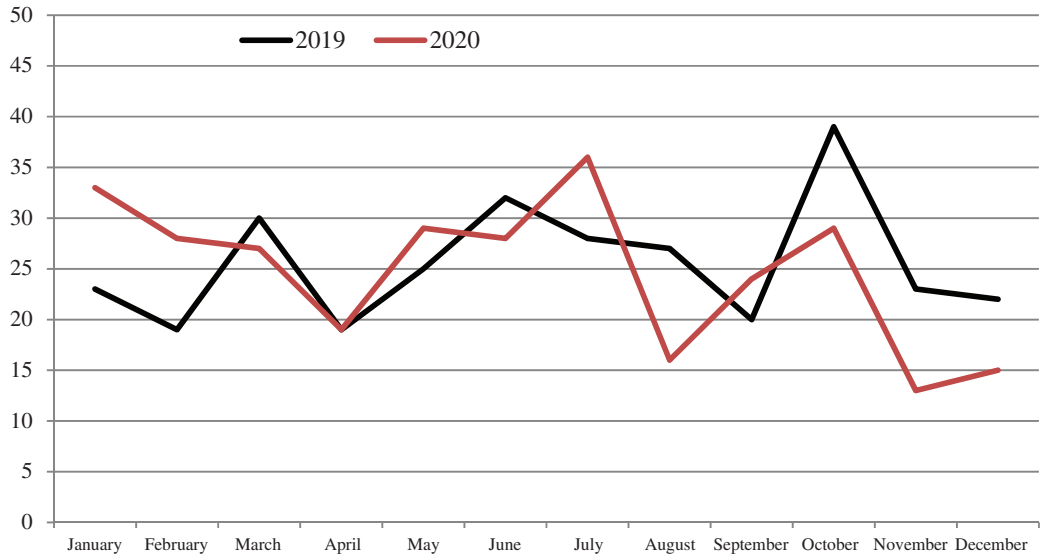

FIGURE 1 Trend of malignant mesothelioma in Italy by month of diagnosis. Comparison 2019 versus 2020

TABLE 3 Distribution by geographic area and period of diagnosis of patients with malignant mesothelioma

	2019				2020				% Variation				
	North	Centre	South	Italy	North	Centre	South	Italy	North	Centre	South	Italy (%; 95% CI)	
January–February	13	23	6	42	21	33	7	61	61.5	43.5	16.7	45	−4 to +121
March–May	13	44	17	74	18	49	8	75	38.5	11.4	−52.9	1	−27 to +42
June–September	45	51	11	107	31	63	10	104	−31.1	23.5	−9.1	−3	−27 to +29
October–December	32	45	7	84	19	31	7	57	−40.6	−31.1	0	−32	−52 to −4

Note: Comparison 2019 versus 2020.

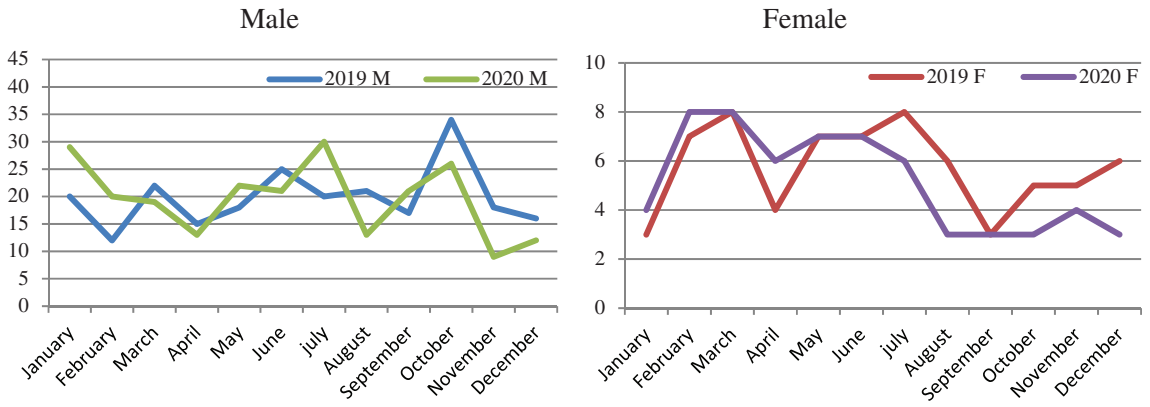

FIGURE 2 Trend of malignant mesothelioma in Italy by month of diagnosis and sex. Comparison 2019 versus 2020

northern regions, 192 in the centre, and 73 in the south. In 2020, 297 cases were diagnosed, 10 fewer (−3.3%, 95% CI −18% to +14%) than in 2019. The decrease mainly concerned the 55–64 and 85+ age groups and more the peritoneum than the pleura, especially in the central-southern regions. In relation to age and period, during the first wave the number of cases in the 55–64 (−10 cases) and 85+ (−6 cases) age groups decreased: the most evident decline started in June, which coincided in Italy with the reopening of activities following the restrictions during the first wave (Table 2).

When comparing 2020 versus 2019 by month of diagnosis, a decline is appreciable only in the last 3 months of 2020, that is, during the second wave (Figure 1). On the contrary, incidence was higher during the 2020 pre-pandemic period than in the same months in 2019 (+45%, 95% CI −4% to +121%) (Table 3). There were very few cases in women, with no particular observable patterns, while the pattern in men resembled the overall pattern (Figure 2).

The data are not homogeneous across the country: the increase in diagnoses recorded in the months of January–February mainly concerned the regions of northern Italy (+61.5%) and central Italy (+43.5%). During the first wave, MM diagnoses increased in the northern regions (+38.5%), were stable in the central regions (+11.4%), and dropped in the southern regions (−52.9%). It is worth noting that all the observed differences are compatible with random fluctuations (Table 3).

DISCUSSION

There are only a few published studies on COVID-19 and MM diagnoses, and none that uses population data specifically on the impact of the pandemic on new diagnoses. We observed 307 cases in 2019 and only 10 fewer in 2020. Thus, in both years, the pathology laboratories involved in the study provided about one fifth of the 1400 cases expected to be reported yearly to the ReNaM in recent periods.[8]

In January and February 2020, there were more diagnoses of MM than in the previous year (+45%). However, no significant differences were observed during the first wave (+1%) or in the low-incidence period (−3%), while a reduction was observed during the second wave (−32% in October–December). The increase in the pre-pandemic period could be linked to early diagnosis of MM in people presenting respiratory symptoms in a silent phase of the pandemic. Nevertheless, detailed epidemiological and virology[9] investigations conducted on data from the beginning of the early phases of the pandemic in Italy showed that only a few hundred COVID-19 patients sought care before 20 February 2020,[10] and the seasonal influenza virus was predominant until the end of February 2020.[9]

However, the data show some geographical differences. The patterns of increase and decrease in the number of diagnoses during the different phases of the pandemic do not show any association with regional COVID-19 incidence nor with the physical distancing measures. In fact, no overall change was observed during the first wave compared to the

same period in the previous year, and in the northern regions, where there had been a very high incidence of COVID-19 during the first wave of the pandemic,[11] there was even an increase in diagnoses. The only change that was consistent with a change due to the pandemic was the decrease in incidence during the second wave, which occurred in Italy in October–December and involved all regions.[11] Nevertheless, we cannot rule out that some cases diagnosed in the final days of December 2020 were still waiting to be confirmed when the data were collected, thus this could partially explain the decrease in cases reported in this month.

It is interesting to note that, with reference to the data from two previous studies, there was a sharp decline in all malignant tumors during the first wave in Italy (−44.9% Ferrara and −37% Kumara-Mangone compared to 2019), but the decrease was smaller for the diagnosis of lung cancer (−27.5% Ferrara and −22% Kumara-Mangone).[4,12]

There was also a progressive decline in lung cancer diagnoses in the United StatesA during the first 4 months of 2020 (4%, −8%, −24%, and −47%, respectively)[13]; the authors stated that the decline was expected for cancers such as breast, colorectal, and prostate cancer but less so for lung cancer, as the initial symptoms are similar to those of COVID-19. The Netherlands also saw a decrease in new cancer diagnoses, which was also appreciable for lung cancer.[14]

An interesting point of view is the perception between mesothelioma and COVID-19 cases,[15] described as two diseases that, despite the obvious differences in terms of their respective fatality rate, etiology, and lag time, present some less obvious similarities: they may have similar respiratory symptoms at onset and cause a kind of "guilt" in affected patients for not having been careful or protected enough or for having put their families at risk.[16,17]

The management of patients with lung cancer and of those with mesothelioma have also changed during the COVID-19 pandemic: the guidance to healthcare organizations was to reduce the time patients spent in hospital and their contact with healthcare workers, whilst maintaining quality of care. There is no doubt that patients with lung cancer and mesothelioma, who are often elderly and with respiratory diseases, have a more unfavorable outcome if they also contract COVID-19.[17,18] For this reason, the approach to these patients in clinical practice must also be modified, limiting hospital access and promoting telemedicine as much as possible.[19]

Another study that investigated the association between COVID, lung cancer, and MM was the Thoracic Cancers International COVID-19 Collaboration (TERAVOLT) study. This observational study, which included lung cancers, mesothelioma, thymic epithelial tumors, and pulmonary neuroendocrine neoplasms, confirmed that although age, smoking, and recent computed tomography are risk factors for cancer in these sites, the multivariate analysis confirmed that only smoking history was associated with an increased risk of death in cancer patients who acquired the SARS-CoV-2 infection (odds ratio [OR] 3.18, 95% CI 1.11–9.06).[20]

Our study has some limitations, the first being the representativeness of the CORs: only 12 of the 21 present in Italy participated in the study, contributing with only a part of their cases. While mainly the central Italy CORs are absent, those regions most affected in terms of MM incidence and the COVID-19 pandemic are all present.[21]

For each participating region, information was retrieved from at least one anatomical pathology laboratory to promptly retrieve the 2020 information. We therefore assumed that this one centre was a proxy for the entire region both in terms of MM incidence and the recent COVID-19 pandemic.

In addition, no cases of MM were retrieved from other sources (hospital discharge records, death certificates, etc.). All this means that our sample is not necessarily representative of all Italian MM, but this should not affect the validity of the comparison between the 2019 and 2020 data. Furthermore, even if the collection of MM data in Italy is uniform, trying to accelerate the data collection for all of 2020 could have introduced some problems in the correct attribution of the incidence data for cases occurring at the very end of the study period, for which the diagnostic process may not have been completed. Finally, during the different phases of the pandemic, the reorganization of hospital services introduced several changes in the diagnostic pathways. Therefore, in our study we cannot distinguish if changes in the occurrence of mesothelioma cases between 2019 and 2020 were due to early or delayed diagnosis or to a change in the diagnostic procedures that made the case not detectable to our methods, for example fewer histological diagnoses or changes in the reference hospitals.

In conclusion, the COVID-19 pandemic had little or no impact on new MM diagnoses. The observed changes in incidence in 2020 compared to 2019 in different periods and geographical areas did not show any association with the spread of the infection nor with its control measures.

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