

Cumulative COVID-19 incidence, mortality and prognosis in cancer survivors: A population-based study in Reggio Emilia, Northern Italy

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Abstract

The aim of this population-based study was to evaluate the impact of being a cancer survivor (CS) on COVID-19 risk and prognosis during the first wave of the pandemic (27 February 2020 to 13 May 2020) in Reggio Emilia Province. Prevalent cancer cases diagnosed between 1996 and 2019 were linked with the provincial COVID-19 surveillance system. We compared CS' cumulative incidence of being tested, testing positive for severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), being hospitalized and dying of COVID-19 with that of the general population; we compared COVID-19 prognosis in CS and in patients without cancer. During the study period, 15 391 people (1527 CS) underwent real-time polymerase chain reaction for SARS-CoV-2, of whom 4541 (447 CS) tested positive; 541 (113 CS) died of COVID-19. CS had higher age- and sex-adjusted incidence rate ratios (IRR) of testing (1.28 [95% confidence interval, CI = 1.21-1.35]), of positive test (IRR 1.06 [95% CI = 0.96-1.18]) and of hospitalization and death (IRR 1.27 [95% CI = 1.09-1.48] and 1.39 [95%CI = 1.12-1.71], respectively). CS had worse prognosis when diagnosed with COVID-19, particularly those below age 70 (adjusted odds ratio [OR] of death 5.03; [95% CI = 2.59-9.75]), while the OR decreased after age 70. The OR of death was higher for CS with a recent diagnosis, that is, <2 years (OR = 2.92; 95% CI = 1.64-5.21), or metastases (OR = 2.09; 95% CI = 0.88-4.93). CS showed the same probability of being infected, despite a slightly higher probability of being tested than the general population. Nevertheless, CS were at higher risk of death once infected.

KEYWORDS

cancer prevalence, COVID-19, prognostic factors, risk factors

1 | INTRODUCTION

After China, Italy was one of the first countries to experience a tragic increase in the incidence of and mortality from COVID-19, with more

than 232 000 cases and over 33 000 deaths by the end of May 2020.¹

The first Chinese study, on a group of only 18 patients, showed that cancer patients presented a higher risk of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection and a higher risk of requiring mechanical ventilation or intensive care unit admission compared to the general population.²

Further studies have found that COVID-19 patients with cancer tend to have much more severe symptoms and a nearly 3-fold higher

Abbreviations: CI, confidence interval; COVID-19, coronavirus disease 19; CS, cancer survivors; IRR, incidence rate ratios; OR, odds ratio; RE-CR, Reggio Emilia Cancer Registry; RT-PCR, real-time polymerase chain reaction; SARS-CoV-2, severe acute respiratory syndrome coronavirus 2.

death rate than do COVID-19 patients without cancer.³ In particular, hematologic, lung and metastatic cancer patients demonstrated higher rates of severe events compared with patients without cancer.³ In addition, patients who underwent cancer surgery and later contracted SARS-CoV-2 showed higher death rates and higher chances of having critical symptoms.^{4,5} Thus, several authors have suggested that immunosuppressed status (whether caused by the disease itself or by treatment) of some cancer patients increases their risk of SARS-CoV-2 infection and of worse outcomes compared to the general population.^{6,7}

In Italy, over 377 000 new cases of cancer are estimated to have occurred in 2020, with an estimate of about 3.6 million cancer survivors (CS); this prevalence is estimated to increase markedly in the next few years.⁸

The aim of this work was to evaluate the impact of being a CS on COVID-19 risk and prognosis in an Italian province with a high incidence rate of tumors that saw a high cumulative incidence of COVID-19 between late February and early May 2020. To achieve this aim, we compared the risk of undergoing a SARS-CoV-2 test, testing positive, being hospitalized and dying of COVID-19 for people diagnosed with cancer in the previous 25 years with the same risks for the general population. Considering all COVID-19 patients, we also compared cancer survivors' risk of dying of COVID-19 with that of other COVID-19 patients.

2 | METHODS

2.1 | Study design

This was a population-based cohort study using registry data of the Reggio Emilia Province. The resident population was classified as having had a cancer or not as of 31 December 2019, entered the cohort on 1 January 2020 and was followed up to 13 May to identify those individuals who had undergone a SARS-CoV-2 test and whether the test was positive. SARS-CoV-2-positive cases (COVID-19 cases, according to Italian Ministry of Health's definition) were followed up for 45 days from symptom onset or a positive test result, whichever occurred first, to observe COVID-19-related hospitalization and/or death.

2.2 | Setting

Reggio Emilia Province, in northern Italy, has a population of about 532 000 inhabitants. The Local Health Authority, the local public entity of the Italian National Health Service, provides hospital, outpatient, primary and preventive care to the entire population residing in the province.

The following measures were adopted throughout northern Italy to contain the spread of the SARS-CoV-2 virus: on 22 February, schools were closed, and social restrictions were imposed; on 8 March, mobility and travel restrictions were imposed and on 11 March, only essential services were permitted to remain open. During this phase, all cases with suspicious symptoms (fever, cough, dyspnea) were

What's new

Immunosuppressed status caused by cancer or cancer treatment has been suggested to increase the risk of SARS-CoV-2 infection and worse outcomes in cancer patients compared to the general population. This study in an Italian province with a high tumour incidence rate that saw a high cumulative COVID-19 incidence found that, during the first wave, the cumulative incidence of COVID-19 in cancer survivors was similar to that in the general population, despite their slightly higher probability of being tested. Cancer survivors had a greater risk of hospitalisation and death once infected, especially if aged <70 years or recently diagnosed with cancer.

tested. The first case of SARS-CoV-2 disease (COVID-19) in the Reggio Emilia Province was diagnosed on 27 February 2020. As of 13 May, the end of the study recruitment period, there were more than 4500 confirmed cases in the province; the epidemic was still spreading at that point, but at a slower rate, and cumulative incidence reached about 9 per 1000.

2.3 | Participants

This study included all the residents in Reggio Emilia Province on 31 December 2019. Information on SARS-CoV-2 tests, COVID-19 patients and prevalent cancer patients was linked. A COVID-19 patient was diagnosed based on real-time reverse transcription polymerase chain reaction (RT-PCR) of nasopharyngeal specimens according to World Health Organization (WHO) indications; a CS, excluding non-melanoma skin cancer and brain (nonmalignant) cancer, was defined as such if present in the Reggio Emilia Cancer Registry (RE-CR) with a malignant cancer.

2.4 | Data sources

The Reggio Emilia Cancer Registry, set up 2000, registers all new cancer diagnoses occurring in people residing in the Reggio Emilia Province. The main information sources of the RE-CR are the anatomic pathology reports, the hospital discharge records and mortality data. The RE-CR has registered all incident cases from 1996 to 2019, with active follow-up for deaths and residence of all prevalent cases updated to 31 December 2019. It collects information on site, morphology, partial staging (presence of metastases), mode of diagnosis and survival.⁹

All RT-PCR SARS-CoV-2 tests performed in Italy must be recorded in the national case-based integrated COVID-19 surveillance system.¹⁰ This surveillance system contains data on all COVID-19 patients, collected by the Public Health Department of the Local Health Authority

during epidemiologic investigations through: (a) daily reports from COVID-19 labs for all positive RT-PCR tests; (b) an initial epidemiologic investigation conducted through phone interviews with all cases, followed by daily phone calls to patients cared for in outpatient settings, both conducted by the Public Health Department of each Local Health Authority; (c) daily reports extracted from electronic medical records for hospitalized patients; (d) check of death records to assess mortality, particularly in outpatient settings.

The whole resident population registered on 1 January 2020 was classified as CS or not having had a cancer through a linkage with cancer registry. This cohort was then linked with the list of cases tested for SARS-CoV-2 (positive and negative) from late February up to 13 May 2020.

2.5 | Outcome measures

From the COVID-19 surveillance system data, we report the cumulative incidence up to 13 May 2020 of being tested for SARS-CoV-2, testing positive for SARS-CoV-2 (according to the COVID-19 definition adopted by the Italian Ministry of Health, these are all COVID-19 cases), hospitalizations of COVID-19 patients and deaths among COVID-19 patients. For testing and infection, the follow-up period was from 1 January 2020 to 13 May 2020. All COVID-19 cases were followed up for 45 days from the first positive test for hospitalization or death. Furthermore, hospital admissions occurring in the 8 days before SARS-CoV-2 positivity were considered as COVID-19 hospitalizations. Hospitalization and mortality follow-up for the last SARS-CoV-2-positive patients was closed on 28 June 2020.

Based on the data collected by the RE-CR, all the tested subjects were grouped according to their oncological history: patients who had never been diagnosed with a malignancy vs patients with a clinical history of malignancy at any time since 1996. Cancer survivors were then categorized according to the time since cancer diagnosis (<2 years, 2-5 years and >5 years), cancer site and presence of metastases at diagnosis. Age was calculated on 31 December 2019.

2.6 | Statistical analysis

Pearson's chi-square test was used to examine differences in the proportions of subjects with and without cancer and tested/not tested for SARS-CoV-2. We report age- and sex-adjusted incidence rate ratios (IRR), with relative 95% confidence intervals (95% CIs) using Poisson regression, for cumulative incidences. The outcomes of interest for this analysis were cancer survivors' being tested for SARS-CoV-2, having a positive test, being hospitalized and dying of COVID-19, compared with the same outcomes of those who had never had a cancer diagnosis. Multivariable analysis was performed using a logistic regression model to measure the odd ratios, with relative 95% CI, of hospitalization and death for COVID-19 patients with cancer, adjusting for age and sex. STATA v. 13.0 (StataCorp LP, College Station, TX) was used for all analyses.

TABLE 1 Distribution of 15 391 patients who tested for SARS-CoV-2, were positive for SARS-CoV-2, COVID-19 hospitalization, and death, by sex, age and cancer history

	Tested for SARS-CoV-2		Positive for SARS-CoV-2		Hospitalization		Death			
	N (% test rate)		N (% positive rate)		N (% hospitalization rate)		N (% case fatality rate)			
	Population with cancer	Population without cancer	Population with cancer	Population without cancer	Population with cancer	Population without cancer	Population with cancer	Population without cancer		
All cases	27 386 (5.1)	512 050 (94.9)	1527 (5.6)	13 864 (2.7)	447 (29.3)	4094 (29.5)	201 (45.0)	1093 (26.7)	113 (25.3)	428 (10.5)
Sex										
Males	12 431 (4.7)	253 417 (95.3)	769 (6.2)	5972 (2.4)	205 (26.7)	1784 (29.9)	115 (56.1)	625 (35.0)	62 (30.2)	217 (12.2)
Females	14 955 (5.5)	258 633 (94.5)	758 (5.1)	7892 (3.1)	242 (31.9)	2310 (29.3)	86 (35.5)	468 (20.3)	51 (21.1)	211 (9.1)
Age (years)										
<50	3034 (1.0)	303 882 (99.0)	125 (4.1)	6051 (2.0)	32 (25.6)	1366 (22.6)	4 (12.5)	140 (10.2)	1 (3.1)	5 (0.4)
50-59	3955 (4.8)	79 085 (95.2)	181 (4.6)	2465 (3.1)	44 (24.3)	792 (32.1)	9 (20.5)	144 (18.2)	2 (4.5)	9 (1.1)
60-69	5782 (9.4)	55 894 (90.6)	271 (4.7)	1594 (2.9)	71 (26.2)	544 (34.1)	37 (52.1)	208 (38.2)	9 (12.7)	39 (7.2)
70-79	7819 (15.8)	41 821 (84.2)	407 (5.2)	1354 (3.2)	100 (24.6)	461 (34.0)	63 (63.0)	246 (53.4)	26 (26.0)	78 (16.9)
>79	6796 (17.8)	31 368 (82.2)	543 (8.0)	2400 (7.7)	200 (36.8)	931 (38.8)	88 (44.0)	355 (38.1)	75 (37.5)	297 (31.9)

Abbreviation: SARS-CoV-2, severe acute respiratory syndrome coronavirus 2.

TABLE 2 Incidence rate ratio (IRR) of being tested, having a positive test, being hospitalized and dying within 45 days from COVID-19 diagnosis for people with previous diagnosis of cancer compared with the general population without cancer

	Test SARS-CoV-2			Test positive			Hospitalization			Death		
	IRR	95% CI		IRR	95% CI		IRR	95% CI		IRR	95% CI	
All cancer	1.28	1.21	1.35	1.06	0.96	1.18	1.27	1.09	1.48	1.39	1.12	1.71
Cancer diagnosis												
<2 y	1.67	1.49	1.86	1.03	0.82	1.30	1.73	1.28	2.34	2.13	1.41	3.21
2-5 y	1.36	1.24	1.51	1.03	0.85	1.25	1.19	0.88	1.60	0.94	0.58	1.53
>5 y	1.13	1.05	1.21	1.09	0.96	1.23	1.18	0.97	1.44	1.38	1.07	1.77

Abbreviations: 95% CI, 95% confidence interval; SARS-CoV-2, severe acute respiratory syndrome coronavirus 2; y, years.

3 | RESULTS

On 31 December 2019, there were 27 386 residents in the Reggio Emilia Province still alive after a cancer diagnosis, for a prevalence of 5.1%.

Between 27 February 2020 and 13 May 2020, 15 391 residents in the Reggio Emilia Province underwent molecular testing for SARS-CoV-2 (2.9% of the resident population). Testing was more frequent among the elderly and among females; 1527 cancer survivors underwent testing (5.6% of all cancer survivors) (Table 1). The age- and sex-adjusted cumulative incidence rate ratio of being tested was 1.28 (95% CI = 1.21-1.35) (Table 2).

Of the 15 391 tests performed, 4541 (29.5%) were positive for SARS-CoV-2, that is, were COVID-19 cases, with no differences between those with a cancer diagnosis (29.3%) and those without (29.5%) (Table 1). The cumulative incidence of SARS-CoV-2-positive tests was 0.8% in the general population and 1.6% in cancer survivors (Table 1). The age- and sex-adjusted COVID-19 incidence rate ratio was 1.06 (95% CI = 0.96-1.18) (Table 2).

The overall cumulative incidence of hospitalizations was 0.24%, higher in males and in older people; in cancer survivors, it was 0.7% (201 hospitalized cases) (Table 1), corresponding to an age- and sex-adjusted hospitalization incidence rate ratio of 1.27 (95% CI = 1.09-1.48) (Table 2). The overall cumulative mortality was 0.1% in the general population, reaching 1.0% in people over age 80. Crude cumulative mortality was higher in cancer survivors (113 deaths, 0.41%), while the age- and sex-standardized mortality incidence rate ratio was 1.39 (95% CI = 1.12-1.71) (Table 2).

The multivariable logistic analysis (Table 3) of COVID-19-positive patients showed that females had a lower risk of being hospitalized and of dying (odds ratio [OR] 0.43; 95% CI = 0.37-0.49 and OR 0.48; 95% CI = 0.39-0.59, respectively). People ages 70 to 80 had the highest probability of being hospitalized, while those age < 70 had a lower probability than people age > 80. The probability of death increased with age, with ORs for those below age 70 compared to those over 80 of 0.04 (95% CI = 0.03-0.05) and for age 70 to 80 vs over 80 of 0.37 (95% CI = 0.29-0.48). We observed a strong interaction between age and cancer in the effect on fatality rate and, to a lesser degree, also on hospitalization. The OR of being hospitalized for COVID-19 among for patients with cancers vs those without cancer

TABLE 3 Multivariable logistic regression of positive cases by age and sex, and age-stratified multivariable logistic regression for cancer history

	Hospitalization			Death		
	OR	95% CI		OR	95% CI	
Sex						
Male	1			1		
Female	0.43	0.37	0.49	0.48	0.39	0.59
Age (years)						
<70	0.33	0.28	0.38	0.04	0.03	0.05
70-80	1.62	1.32	1.98	0.37	0.29	0.48
>80	1			1		
Cancer and age (years)						
Age < 70						
Without cancer	1			1		
With cancer	2.58	1.79	3.72	5.03	2.59	9.75
Age 70-80						
Without cancer	1			1		
With cancer	1.37	0.92	2.06	1.90	1.20	3.01
Age > 80						
Without cancer	1			1		
With cancer	1.15	0.82	1.61	1.13	0.80	1.58

Abbreviations: 95% CI, 95% confidence interval; OR, odds ratio.

below age 70 was 2.6 (95% CI = 1.8-3.7), which decreased with age (among those over age 80, OR 1.2 [95% CI = 0.8-1.6]). The OR of dying was 5.0 (95% CI = 2.6-9.8) for patients below age 70, which decreased with age (OR 1.1; 95% CI = 0.8-1.6 for patients over age 80).

Excess mortality in cancer survivors was higher in the presence of metastases, but differences could be due to chance (OR 2.1; 95% CI = 0.9-4.9) (Table 4). Concerning timing, the strongest mortality excess was for cancers diagnosed less than 2 years before the onset of COVID-19 symptoms (OR 2.9; 95% CI = 1.6-5.2). The patterns were similar for hospitalization, except for 2 to 5 years from cancer diagnosis. We also analyzed the distribution by cancer site: among the 447 SARS-CoV-2-positive cancer survivors, the sites most

TABLE 4 Multivariable logistic regression of positive cases related to clinical outcomes, adjusted for age and sex

	n	Hospitalization			Death		
		OR	95% CI		OR	95% CI	
Cancer							
None	4094	1			1		
Yes	447	1.55	1.25	1.93	1.54	1.18	2.00
Metastasis							
None	419	1			1		
Yes	28	1.28	0.58	2.83	2.09	0.88	4.93
Cancer diagnosis							
None	4094	1			1		
<2 y	72	2.93	1.74	4.91	2.92	1.64	5.21
2-5 y	106	1.52	1.00	2.33	0.96	0.54	1.71
>5 y	269	1.32	1.01	1.73	1.51	1.10	2.07
Cancer site							
Without cancer		1			1		
Breast	101	1.27	0.81	2.00	1.02	0.56	1.83
Gastrointestinal tract	87	1.55	0.99	2.45	1.14	0.68	1.93
Male genital organs	58	1.04	0.60	1.80	0.89	0.46	1.74
Urinary tract	54	1.08	0.61	1.93	1.92	1.01	3.64
Other hematological	28	4.64	1.97	10.95	4.58	1.89	11.10
Thyroid	24	1.88	0.74	4.77	1.91	0.44	8.18
Female genital organs	23	1.73	0.70	4.23	3.27	1.19	9.00
Respiratory organs	21	2.10	0.83	5.29	2.35	0.84	6.61
Melanoma	19	1.98	0.75	5.24	6.25	1.75	22.31
Lymphoma	18	3.23	1.20	8.70	1.56	0.42	5.75
Head-neck	8	0.68	0.13	3.45	0.59	0.06	5.43
Other site	6	2.22	0.42	11.71	6.60	0.90	48.64

Abbreviations: 95% CI, 95% confidence interval; OR, odds ratio; y, years.

frequently involved were breast (101 cases), digestive organs (87 cases, of which 46 colon, 22 rectum, 13 stomach, 3 pancreas, 2 liver, 1 biliary tract), urinary tract (54 cases, of which 38 bladder, 14 kidney, 2 upper urinary tract) and male genital organs (58 cases, of which 53 prostate, 3 testis, 1 penis and 1 undefined male genital organs). COVID-19 patients with cancer of the gastrointestinal tract, lymphoma or other hematological neoplasms showed the greatest excess in hospitalizations; cancer of the urinary tract, other hematological neoplasms, melanoma and female genital organs showed the strongest excess mortality.

4 | DISCUSSION

Although cancer survivors had a slightly higher probability of being tested for SARS-CoV-2 than did the general population, their risk of infection was comparable. On the other hand, the risk of COVID-19-related hospitalization and death was higher among CS than in the general population. The higher probability of being tested, but not of

infection, was also observed in CS with a recent cancer diagnosis, despite their having more frequent access to health services and a much higher probability of being tested.

Once having COVID-19, the probabilities of being hospitalized and of dying were much higher for CS that were below the age of 70; excess mortality was appreciable only up to the age of 80, while after 80 the excess was compatible with random fluctuation. The excess in hospitalization also decreased with age.

Higher fatality and hospitalization rates for COVID-19 patients with a previous diagnosis of cancer have been observed in several studies,¹¹⁻¹⁷ including a recent large registry-based Italian study.¹¹ Instead, we did not find any studies comparing the risk of SARS-CoV-2 infection and COVID-19 death in CS with that in the general population. Only a few case series have tried to infer the risk of infection, comparing the prevalence of SARS-CoV-2 infection in CS with that in health care workers¹² or with that in the general population,¹³⁻¹⁵ or comparing the prevalence of cancer among COVID-19 patients with that in the general population.¹⁶ These studies have provided inconsistent results.^{12,17}

In our cohort of COVID-19 patients, being a cancer survivor increased the risk of death up to the age of 80, after which the impact of having had cancer was modest or null; the small impact on prognosis in this group could be partially due to a higher proportion of cured cancer survivors, for whom we would expect a small or null impact. In fact, the proportion of CS who received their diagnosis more than 5 years earlier was 70.4% and 51.7% in patients over 80 and below 70, respectively (Supplementary Table). A systematic review including about 50 000 COVID-19 patients observed the same phenomenon: the impact of previous cancer on survival was important before the age of 65 but was almost null over that age.¹⁸ This has also been observed for the impact of all comorbidities on COVID-19 survival, which decreases as age increases.¹⁰

It is worth noting that the excess risks in COVID-19-related death and hospitalization were stronger in CS with a recent diagnosis of cancer and in those with metastases at diagnosis. This is consistent with the findings of Liang et al,² who found an excess only in cancer patients who had recently received treatment, and with the results of Dai et al, who reported an excess in cancer patients who had had a diagnosis of Stage IV cancer.³ Data from a large cohort of patients with active cancer and COVID-19 in the United Kingdom did not confirm an excess risk in cancer patients recently undergoing chemotherapy or radiotherapy compared to the cancer patients that did not. The excess risk in patients with metastases, however, was confirmed.¹⁹

Thus, it remains unclear whether the increased risk of death was due to the direct effects of cancer or to treatment (surgery and chemotherapy). However, our data, plus insights from other studies, suggest that the magnitude of the effect on COVID-19 prognosis is greater during the active phase of cancer treatment, after which the effect decreases.

The strongest excess mortality was observed in patients with cancer of the female genital organs, urinary tract, other hematologic neoplasms and melanoma, while for lymphomas and gastrointestinal tract (borderline), we observed a considerable excess in hospitalizations but just a small excess in deaths. It is not easy to compare our results with those of other studies because most included only hospitalized COVID-19 patients; if the risk of hospitalization does not reflect that of death, relative risk among hospitalized patients is affected by a collider bias. Nevertheless, our data are not consistent with those of the large UK cohort, where small excess risk was observed for lymphoma and respiratory cancers.¹⁸

These results make it difficult to put together a profile of those cancer survivors at higher risk of dying of COVID-19 based on cancer site and phase of care, for whom particular measures, including delaying treatments, could be taken to reduce the risk of infection, as suggested by some authors.^{20,21} The only features that clearly emerged from our findings were recent diagnosis and the presence of metastases.

Our data suggest that the SARS-CoV-2 control measures adopted in the oncology and diagnostic departments, together with public awareness and the specific measures implemented by the Italian Government to protect people with chronic diseases (eg, exemption from any work involving social contact), allowed cancer survivors to control

their risk of infection even when they were in an active phase of care or in follow-up. This is an important message for the policy makers, physicians and patients who are trying to better manage cancer during this public health emergency.²²

The main strength of this study is its population-based design, which eliminates any selection bias occurring in case series. Furthermore, the assessment of exposure, that is, a previous diagnosis of cancer, was conducted through the linkage with a cancer registry with 25 years of prevalence data and timely registration of incident cases (to 31 December 2019). It is worth noting that this information was acquired before the onset of the pandemic and is thus completely independent of outcome occurrence. The main limitation of our study is that we do not have any information on treatment or on comorbidities, which could have influenced outcomes. Furthermore, because we could not include cancer patients with a diagnosis occurring in 2020, we could not observe the phase of diagnosis and disease assessment, which for many cancer sites involves intensive access to health care facilities.

5 | CONCLUSION

Our population-based study showed that during the peak of the COVID-19 epidemic in northern Italy, the cumulative incidence of COVID-19 in cancer survivors was similar to that in the general population, despite the former's having a slightly higher probability of being tested. On the other hand, cancer survivors had a greater risk of hospitalization and of death once infected, especially in the age group <70 years or in those with a recent diagnosis.

CONFLICT OF INTEREST

The authors declare no potential conflict of interest.

DATA AVAILABILITY STATEMENT

Researchers who would like to access individual data should present their request, together with a study protocol, to the Area Vasta Emilia Nord Ethics Committee for approval (cereggioemilia@ausl.re.it).

ETHICS STATEMENT

The study was approved by the Area Vasta Emilia Nord Ethics Committee (no. 2020/0045199). The Ethics Committee authorized the use of patient data, even in the absence of consent, if all reasonable efforts had been made to contact that patient.

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SUPPORTING INFORMATION

Additional supporting information may be found online in the Supporting Information section at the end of this article.

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