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Reduced Vascular Practice and Increased Cardiovascular Mortality for COVID-19–Negative Patients



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ABSTRACT

Background: The aim of our study was to compare COVID-19– and not-COVID-19–related mortality rates in two Italian regions during the pandemic period when the same isolation rules and therapeutic approaches were introduced for all hospitals in Italy. Risk factors for not-COVID-19–related deaths during the pandemic were analyzed; we tried to assess a possible correlation between reducing hospital visits and “deferrable” vascular operations and the increased cardiovascular mortality not related to COVID-19 infection.

Methods: We analyzed COVID-19– and not-COVID-19–related mortality rates in two Italian regions in the period January 2020–January 2021. We compared mortality rates during the pandemic period with those of the previous five years. We tried to determine the factors involved in increased mortality rates during the pandemic period.

Results: Despite the same isolation rules for people and the same therapeutic approaches for hospitals, mortality rates did not increase in the region Lazio, where the pandemic was not severe. In the region Lombardy, the mortality rate was doubled in comparison with the previous years, and 50% of the increase was related to not-COVID-19 deaths.

Conclusions: The increase in mortality rates for not-COVID-19–related deaths in the region Lombardy was connected to the generalized turmoil in the acute phase of an overwhelming pandemic, including diffuse stress, inadequate communications, reluctance to ask for medical help unless symptoms were severe, and unexpected inadequate number of health workers, hospital beds, and intensive care unit beds. Reduced hospital visits may have had a fundamental role.

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Introduction

In Italy, more than 106,000 deaths from COVID-19 have been reported up to March 30th, 2021; 250 health workers died from COVID-19 infection, and 110,266 health workers were

diagnosed positive for COVID-19.^{1–4} The pandemic has brought unexpected consequences, including shortage of medical personnel and reluctance from patients to ask for medical help unless their symptoms were severe.^{3–5} Isolation rules were introduced for all hospitals in Italy including

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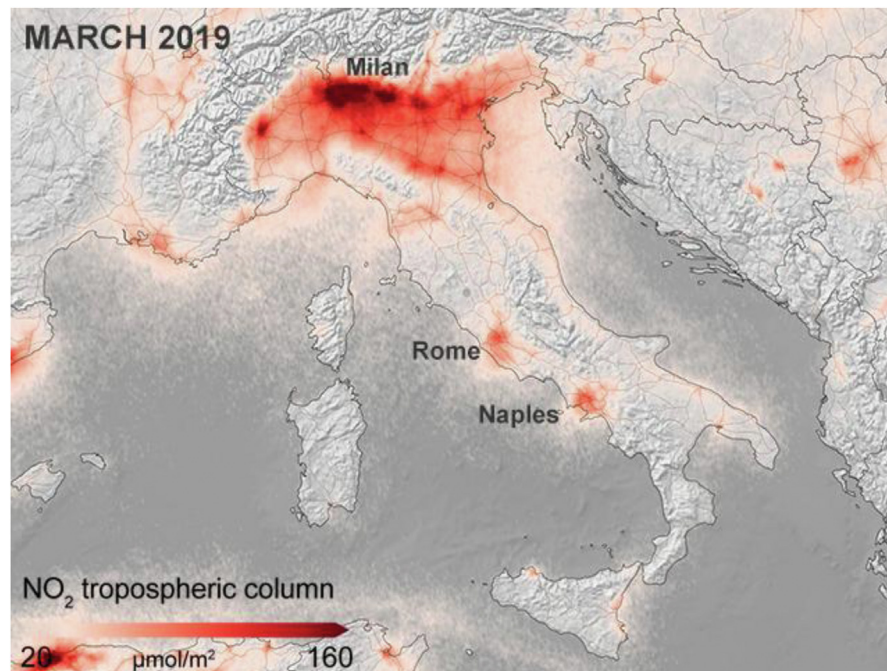


Fig. 1 – Nitrogen dioxide tropospheric columns in Italy. Nitrogen dioxide production is an index of “pollution” related to CO₂ production. COVID-19 pandemic in Italy was more severe in regions with high pollution. In the region Lombardy (Milan-Pavia), with high industrialization, the pandemic was more severe. (Color version of the figure is available online.)^{8,9}

separate sections for COVID-19 patients, diffuse testing, and specific measures for health workers and patients. Admissions to hospitals were reduced, avoiding visits for not-urgent conditions and deferrable elective surgeries.^{6,7} Often, it is difficult to determine the difference between deferrable and not-deferrable procedures and urgent or not-urgent examinations in patients suffering from vascular diseases.

The objective of our analysis was to identify the potential risk factors for increased cardiovascular mortality not related to COVID-19 infection during the pandemic. We tried to determine the influence of deferring not-urgent visits and operations for patients with vascular disease; we analyzed mortality rates in two Italian regions with different levels of severity of the pandemic (high in Lombardy and low in Lazio) (Fig. 1). In both regions, the same isolation rules for the general population and the same therapeutic attitudes in hospitals were introduced during the acute phases of the pandemic, when the differences were not clear in regional levels of the pandemic.

Material and methods

Mortality analysis

The mortality data in Italy during the pandemic period March 2020–March 2021 were reviewed. The analysis was based on the data reported by the national health institute (Istituto Superiore Sanità–ISS) and the national statistics institute (ISTAT), which are national not-for-profit institutions supported by public funds. Mortality data are based on a real-time report of deaths in each single town, including more than 95% of the registered resident Italian population (Italian and non-Italian citizens).¹⁻⁴ All causes of death are reported to ISS and ISTAT as per the International Classification of Diseases and Related Deaths (ICD 10) as recommended by the World Health Organization. The classification is based on rigid rules. A person is considered dying from COVID-19 infection according to the World Health Organization definition: a patient

Table 1 – Mortality in Italy in the year 2020 (population 60 million) compared with the mean of the previous five years (2015-2019).

Region	Overall mortality	Increase in mortality [*]	COVID-19–related mortality (% total deaths)	Number of COVID-19 deaths/100,000 inhabitants
Lombardy	136,249	+36.56	25,120 (18.4%)	208.6
Lazio	62,161	+5.5	3717 (5.9%)	56.5
All Italy (20 regions)	746,146	+15.6	75,891 [†] (10.2%)	103.9

^{*} Percentage in comparison with the mean of the previous five years.

[†] The overall number of COVID-19–related deaths has increased to 106779 including the period January 1–March 30, 2021.

Table 2 – Total deaths and percentage of COVID-19–related deaths in Lombardy and Lazio during the first two acute phases of the pandemic (March-May 2020; October-November-December 2020).

Region	March-May 2020			October-November-December 2020		
	Overall mortality	Increase in mortality (%)	COVID-19–related mortality (% total deaths)	Overall mortality	Increase in mortality (%)	COVID-19–related deaths (% total deaths)
Lombardy	51,902	+111.8	16,223 (31.3)	34,572	+37.1	8243 (23.8%)
Lazio	15,009	+2.5	833 (5.5)	17,996	+22.5	2753 (15.3%)

Comparison with the same periods of the previous five years (2015-2019).

dying with clinical and laboratory evidence of COVID-19 infection, without an alternative cause of death clearly not referable to the COVID-19 infection even if present (e.g., a trauma-related death).^{10,11} All laboratory tests to determine a probable COVID-19 infection were performed in specialized regional referral centers with a real time polymerase chain reaction of the oropharyngeal swab.

Comparison of mortality rates during and before the pandemic period

The number of patients who died during the period January 2020–December 2020 was compared with the mean number of patients who died in the previous five years (2015-2019).

Reduced medical and surgical activity during the acute phases of the pandemic

The isolation rules imposed by the Central Government for the general population and the restrictions for hospitals to perform only urgent visits or operations were the same all over Italy, independently from the level of the pandemic. Deferrable, elective operations were not performed. Outpatient visits were performed only for patients with severe symptoms and emergency conditions. There was a spontaneous tendency in the general population to avoid medical facilities. As a result, even the number of not-COVID-19 patients seen and admitted through the emergency rooms of hospitals was significantly reduced. We analyzed the number of vascular outpatient visits and vascular interventions during the acute phases of the pandemic in the University Hospital San Matteo of Pavia. The hospital is a university tertiary center where almost all patients with cardiovascular problems are

referred from the city of Pavia (Lombardy) and the surrounding area (population, 545,000 inhabitants; density, 184 inhabitants/km²). The number of vascular operations and outpatient visits performed during the year 2020 was compared with the numbers of the previous years for the Hospital San Matteo. The same data were collected from four tertiary referral hospitals in Rome (Lazio). The study was approved by the Ethical Committee of the Hospital San Matteo and of the Sapienza University.

Clinical data were tabulated in Microsoft Excel 1 (Microsoft Corp, Redmond, Wash) database: statistical analysis was performed with SPSS, release 25.0 for Windows (IBM SPSS Inc.; Chicago–ILL; USA). Categorical variables were analyzed using a chi-square test or Fisher's exact test where appropriate.

Results

Overall mortality in Italy during the COVID-19 pandemic

During the pandemic, 106,779 COVID-19 infection–related deaths were reported in Italy. The mean age was 81 years (female 44% and male 56%). Of the total number, 30,341 deaths were registered in the region Lombardy (28.4%) and 6,501 in the region Lazio (6.1%) (Table 1).

Increased mortality rates in Lombardy and Pavia (January-December 2020)

Table 1 shows the difference in overall mortality in the regions Lombardy and Lazio during the pandemic. People older than 50 years of age had higher mortality rates in comparison with the previous years (Tables 2-4). This increase was related to

Table 3 – Total deaths and percentage of COVID-19–related deaths in Italy as per age in the year 2020 and in the previous five years (2015-2019).

Age	Mean previous five years (2015-2019)	2020	Difference (%)	% COVID-19–related deaths/total deaths
0-49	19,442	17,788	–1654 (–8.6)	4.6
50-64	52,032	57,395	+5363 (+10.3)	9.2
65-79	164,598	184,708	+20,110 (+12.2)	12.4
80+	409,547	486,255	+76,708 (+18.7)	9.6
Total	645,620	746,146	+100,526 (15.6)	10.2

Table 4 – Increase (%) of deaths in Lombardy and Lazio as per age during the first acute phase of the pandemic (March-April 2020) in comparison with the previous 5 years (2015-2019).

Age	January-February	March	April	May
Italian regions with high diffusion (including Lombardy)				
50-64	-5.2%	+89.0%	+50.1%	+1.9%
65-80	-10.9%	+144.6%	+67.4%	-3.9%
>80	-5.8%	+121.1%	+100.3%	+8.2%
Italian regions with low diffusion (including Lazio)				
50-64	-4.3	-1.3	-4.9	-9.3
65-80	-8.2	+1.2	-0.9	-11.4
>80	-5.4	+4.5	+2.6	-5.2
Italy (all 20 regions)				
50-64	-4.8	+3.5	+15.5	-3.5
65-80	-9.3	+54.7	+27.2	-7.1
>80	-5.3	+51.6	+45.4	+0.9

people dying from COVID-19 infection for its 50%. The remaining 50% of the increase in mortality was related to people not dying from COVID-19 infection (70% of these deaths were defined as a consequence of cardiovascular events). During the overwhelming outbreaks, the collection of data was inevitably inaccurate. The cause of deaths was based on the certificate of death written by family practitioners or by hospital staff physicians without an autopsy. Not-COVID-19 cardiovascular mortality was defined in the absence of COVID-19 infection, and it was hypothesized on the past medical history of patients (Fig. 2).

Surgical and medical activity in Pavia

During the pandemic period, surgical and outpatient visits for not-COVID-19 patients in the University Hospital of Pavia

were not performed. Admissions to the emergency room of not-COVID19 patients were reduced by 90%, testifying at the fear in the general population of getting infected in medical facilities. In the Hospital San Matteo, 90% of admissions in the first acute phase of the pandemic (March-April 2020) were for patients with COVID-19 infection (942 patients). The number of elective arterial operations during the year 2020 was reduced in comparison with the previous year (483 versus 694 $P < 0.001$). We canceled operations for asymptomatic carotid occlusive disease, endovascular operations for claudication, and surgery for small abdominal aortic aneurysms. This decision was based on a frank and open discussion with patients. Sometimes patients preferred to defer operations which we thought indispensable. The number of admissions for emergency operations was slightly reduced (142 versus 167). There was an increased number of operations for acute ischemia of the lower limbs secondary to distal embolization (60% of the emboli were in patients with atrial fibrillation) and an increase in patients with frank rupture of an abdominal aortic aneurysm (Table 5). Mortality and complication rates were similar over the two years.

Overall mortality in Lazio and in Rome (January-December 2020)

The mortality rates related or not with COVID-19 infection were lower in the region Lazio than those in the region Lombardy (Table 2).

Surgical and medical activity in Rome (January-December 2020)

In the four major hospitals in Rome, surgical and elective outpatient visits were reduced at a rate similar to Pavia. The number of emergency room visits was almost doubled in the Hospital San Matteo, whereas they were reduced in the four hospitals of Rome ($P < 0.001$). Excluding patients with COVID-19 infection, the number of patients seen in the four hospitals

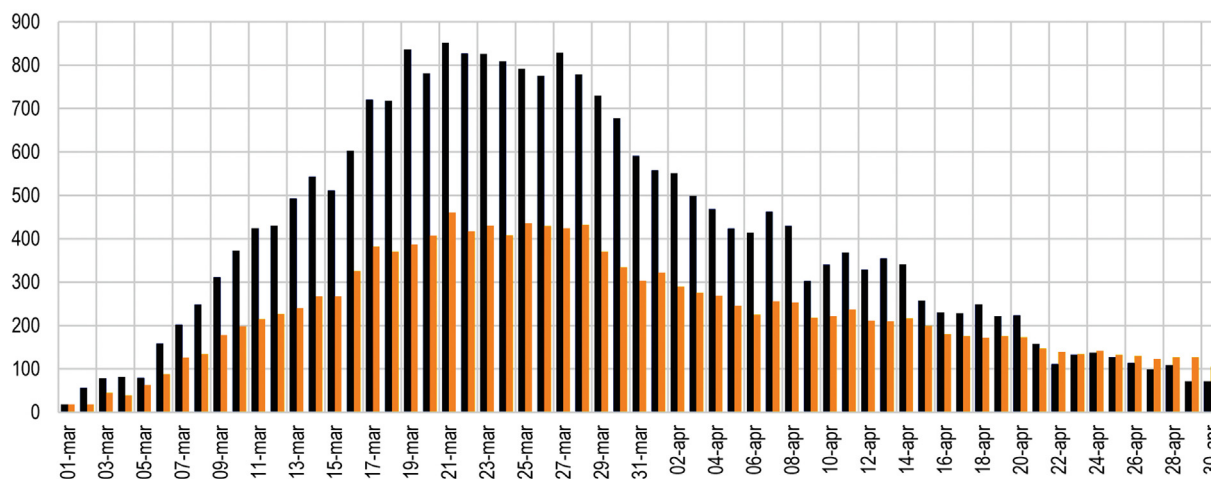


Fig. 2 – Increase in daily mortality for people 50 years of age or more in the acute phase of the pandemic (March-April 2020) in comparison with the average of the mean number of deaths in the same days during the previous five years (2015-2019) in the region Lombardy. Each line indicates the daily increase of deaths in March-April 2020 in comparison with the previous five years. Black represents the overall number of increased deaths. Yellow represents the number of deaths diagnosed as related to COVID-19 infection. (Color version of the figure is available online.)

Table 5 – Arterial surgery 2019 (960 patients—excluding hemodialysis access).

Emergency-not deferrable (N° Patients 166/960; 17.4%)

	N°	
1	Abdominal aortic aneurysms	17
	Rupture	5
	Symptoms	12
2	Iliac artery aneurysms	5
	Rupture	2
	Symptoms	3
3	Pararenal abdominal aneurysms	9
	Rupture	5
	Symptoms	4
4	Femoral pseudo-aneurysms	10
5	Carotid occlusive disease (symptoms and stenosis greater than 90%)	13
6	Severe occlusive disease lower-limb arteries with limb at risk	80
	Embolitic origin	29
	Acute thrombosis on pre-existing plaque	21
	Chronic limb ischemia (limb at risk)	30
7	Arterial trauma	9
8	Amputation (gangrene)	24
	Total	166

Arterial surgery 2020 (624 patients excluding hemodialysis access)

Emergency-not deferrable (N° Patients 141/624; 22.7%)

Type	N°	
1	Abdominal aortic aneurysms	13
	Rupture	11
	Symptoms	2
2	Iliac artery aneurysms	2
	Rupture	2
	Symptoms	0
3	Pararenal abdominal aneurysms	5
	Rupture	5
	Symptoms	0
4	Femoral pseudoaneurysm	4
5	Carotid occlusive disease (symptoms and stenosis greater than 90%)	10
6	Severe occlusive disease lower-limb arteries with limb at risk	78
	Embolitic origin	37
	Acute thrombosis on pre-existing plaque	14
	Chronic limb ischemia (limb at risk)	27
7	Arterial trauma	10
8	Amputation gangrene	20
	Total	141

in Rome and in Pavia was reduced in comparison with the previous years in a similar percentage (reduction of 90%). The number of elective vascular operations decreased by 50%.

The number of emergency operations for ruptured abdominal aortic aneurysm and for acute ischemia of the lower limbs was similar to the previous years.

Shortage of ICU beds and health workers

In the Hospital San Matteo, there was a significantly high number of admissions for COVID-19 patients with inevitable continuous need and shortage for COVID-19 beds in the wards and in the semi-intensive and intensive care unit (ICU). In the region Lombardy, the number of available ICU beds at the time of the acute phase of the pandemic was 861 (8.5/100,000 residents). The admissions for COVID-19 patients were less common in the four hospitals in Rome, without an overwhelming shortage of ward and ICU beds for COVID-19–positive and –negative patients. In the region Lazio, the number of available ICU beds was 571 at the time of the first acute phase of the pandemic (9.5/100,000 residents).

Discussion

The COVID-19 pandemic has changed perspectives and attitudes in medicine.¹²⁻¹⁴ During the pandemic, there has been a general tendency to cancel and to defer elective surgeries, reserving hospital admission only for patients with problems that could pose a threat to survival. This situation is the consequence of a general attitude to prevent contamination, involving all levels of the society, from legislators to the general population. In the acute phases of the pandemic, only patients with severe symptoms asked for medical advice. The general attitude of surgeons, not rarely forced by the patient's desire to avoid operations in this period, has been to eliminate low-value treatments and to modify therapeutic schema.¹⁵⁻¹⁷ It is not easy to decide which operation is deferrable or not in a significant proportion of patients with cardiovascular pathology. Therapies considered to have a marginal effect are often delayed or even canceled, but this decision is difficult for patients with vascular disease. In the four major hospitals in Rome, surgical and elective outpatient visits were reduced at a rate similar to Pavia. The number of emergency room visits was almost doubled in the Hospital San Matteo, whereas it was reduced in the four hospitals of Rome ($P < 0.001$). In the Hospital San Matteo, the overall number of arterial procedures was reduced in the year 2020 in comparison with the previous years (625 versus 961). We canceled operations for asymptomatic carotid occlusive disease, endovascular operations for claudication, and surgery for small abdominal aortic aneurysms. This decision was based on a frank and open discussion with patients. Sometimes patients preferred to defer operations that we thought indispensable. Despite the reduced number of elective operations, the number of emergency operations was not increased, as one might expect analyzing the high number of people dying during the pandemic period. There was an increase in operations for acute ischemia of the lower limbs secondary to emboli and an increase in surgeries for ruptured abdominal aortic aneurysm.

Despite the high number of COVID-19–negative patients dying from cardiovascular events in the pandemic period, the number of emergency admissions for acute cardiovascular events did not increase in Pavia. Several factors may explain

this discrepancy: high stress level in general population,¹⁸ reluctance of patients to ask for medical help unless symptoms are unbearable, and difficult communication between patients and the medical system. The possibility that the reduced number of clinic visits imposed in the pandemic periods may have contributed to the increased number of cardiovascular mortality in patients negative for COVID-19 infection should be considered.¹⁹⁻²¹

Despite the inevitable problems related to the overwhelming number of COVID-19–positive patients, the overall results of arterial vascular procedures in the Hospital San Matteo were similar to those of the previous year, either for COVID-19–positive or COVID-19–negative patients. This accomplishment has been the consequence of adapting surgical therapy to the specific levels of the pandemic, often giving preference to endovascular treatments in patients in whom usually an open surgery was preferred.

Patients with cardiovascular pathology, who are older than 65 years, and with pulmonary problems are at a higher risk for COVID-19 infection and mortality.^{22,23} General anesthesia with endotracheal intubation, postoperative pain, and ICU permanence are some of the most common risk factors for postoperative pulmonary infection and pulmonary major complications. Minimally invasive operative procedures like endovascular surgery generally require shorter operative time, no general anesthesia and tracheal intubation, and less organizational effort. Hospital stay is shorter.

There were no significant differences in therapeutic attitude and hospital isolation rules between the two examined Italian regions (Lombardy and Lazio). The only major difference was the level of the pandemic severity. In Rome, the pandemic had a low intensity, and the medical system was adequate without major deficits of hospital beds and equipment. In Pavia, the pandemic was severe, and in the acute phase, the workforce had limited capacity, and the health care system was overwhelmed with COVID-19 cases with problems concerning hospital and intensive care beds and equipment. The tendency to limit outpatient visits and to defer elective surgery may have played a major role for the increased mortality of not-COVID-19–related deaths, even if this matter is difficult to analyze and to quantify.²⁴ In Pavia, the number of admissions for ruptured abdominal aortic aneurysm and for acute ischemia of the lower limbs was higher in the year 2020 than that in the previous year. This problem was not evident in the region Lazio where the pandemic was less severe.^{25,26}

Despite optimistic reports from local governments and the media, the communication between patients, hospitals, and organizational centers was less than appropriate in the acute phases of the pandemic. This observation does not want to be a negative criticism, but rather a constructive thought. The pandemic and its consequences were unpredictable.^{14,27}

COVID-19 has forced widespread adoption of remote encounters by video applications, patient portals, or phone calls. Patients, hospitals, and physicians are rapidly adapting to this new way of communicating, but there are many problems to solve. Inevitably, this new form of communication resulted inadequate in the acute phases of the pandemic. Efforts should be made to improve it, and this enterprise may be more

difficult than expected considering that most patients requiring help and information are old and often without a continuous-efficient help.

Our study presents inevitable limits: the retrospective nature of the analysis and possibility of inaccurate data, which were collected in the difficult acute phase of the pandemic.

The increased contamination and mortality rates in Northern Italian regions may be related to several factors, including higher air pollution and lower temperatures and higher number of elderly people, international exchanges, and contacts.

Surgeons should adapt indications and therapeutic approaches considering the level of the pandemic.²⁸⁻³⁰ Analysis of the factors influencing increased not-COVID19–related mortality rates during the acute phases of the pandemic is of paramount importance for the present and for the future organization of the medical system.^{31,32} In the Hospital San Matteo, we have a close and valid collaboration with the administration staff, and as soon as the pandemic level reduced, a regular surgical activity was resumed.

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Disclosure

The authors have no conflicts of interest to declare.

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