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COVID-19 PANDEMIC AND VASCULAR DISEASE

Pattern of vascular disease in Lombardy, Italy, during the first month of the COVID-19 outbreak

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The first confirmed case of COVID-19 infection in Italy was reported in the Lombardy region on February 20, 2020, after the outbreak in Hubei Province, China, where, in just 30 days, it had spread from the city of Wuhan to the entire country. Aggressive policies allowed for containment of the epidemic in China; however, by that time, the World Health Organization had declared a global pandemic.

The first cases in Italy were detected in a few small urban centers of the Lombardy and Veneto regions and, despite the immediate quarantine, the infection rapidly spread to other regions in Italy. However, the largest number of COVID-19 cases was recorded in Lombardy, where the epidemic has been particularly virulent and highly lethal. Lombardy has a high number of elderly citizens. According to the 2019 report of the Italian Institute of Statistics, 13.7% of the citizens are older than 65 years and that for each 100 inhabitants younger than 14 years old, 165.5 inhabitants are older than 65 years—a very high index of an aging population. The life expectancy in Lombardy before the pandemic was 84 years, 3 years greater than the European life expectancy.

Because the virulence and lethality of the COVID-19 epidemic in Italy was unusually grave, both the central and the local authorities rapidly initiated measures of social distancing. On March 22, 2020, a lockdown was ordered for the entire country, with only essential services still functioning. These measures were still active as of April 15, 2020, when the number of new cases had reached a plateau. These measures had initially received skeptical comments from most other countries. However, within a matter of weeks, most western countries had followed in issuing similar drastic measures. From an epidemiologic viewpoint, many of these countries have been reporting a similar pattern of infection curves with a 2- to 3-week delay compared with Italy.

The public health system of Lombardy, where publicly and privately run hospitals coexist, has been struck very hard by the epidemic, especially in municipalities such as Cremona Lodi and Bergamo, where the hospitals were rapidly overwhelmed. The regional healthcare authorities decided to create a hub/spoke system for cardiovascular and surgical emergencies, such that a small number of large centers (hubs: IRCCS Ospedale San Raffaele Milano, Fondazione Poliambulanza Brescia. Centro Cardiologico Monzino Milano, ASST Milanese Ospedale di Legnano) would serve the whole region for nonelective cases and would greatly limit the number of elective cases. (At these centers, patients with respiratory [influenza-like] and nonrespiratory symptoms requiring emergency admission are physically separated and follow different pathways, including dedicated wards, elevators, radiology units, and so forth.) This allowed most other hospitals (spokes) to concentrate their resources for COVID-19-related cases. Moreover, a significant number of dedicated intensive care unit beds were made available within a matter of days at both publicly and privately run centers. Clearly, many further logistical adjustments were required to optimize the resources for this rapidly changing situation. In addition, medical teaching underwent radical changes.

As one of the 4 hubs selected by the local health authorities of Lombardy for vascular surgical emergencies, our institution has been cooperating with eight spokes serving a population of ~2.5 million inhabitants. Several interesting patterns have emerged. During the initial days, the number of nonelective admissions of subjects with vascular disease was lower than usual, possibly owing to a reluctance by the general population to seek assistance at a hospital where they believed they could be in contact with patients with COVID-19.

As we entered the second week, the number of vascular emergencies resumed, and a clear increase occurred in the cases of acute peripheral arterial occlusive disease. The incidence showed a tendency toward older patients (median age, 75 years; range, 50-96 years) with advanced ischemia and below the knee thrombosis (Table). This was unusual for us and clearly differed from our customary patient mix.

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Table

| Age (years) | Number of Patients |
|-------------|--------------------|
| Median      | 75                  |
| Range       | 50-96               |

This was unusual for us and clearly differed from our customary patient mix.
As of the third week, a significant number of patients initially hospitalized for COVID-19-related pneumonia, both requiring and not requiring artificial ventilator use, were presenting with peripheral ischemia of both lower limbs and, occasionally, upper limbs and required treatment. Most of these patients had already been receiving antithrombotic prophylaxis. During duplex ultrasound assessment of these patients, the deep venous circulation was also studied and showed an alarmingly high number of cases of deep venous thrombosis, with few or no additional specific symptoms. We, therefore, screened for deep venous thrombosis in 108 patients with COVID-19. The incidence was 23% for patients requiring a ventilator and 8% for those patients not requiring a ventilator, especially affected were the popliteal and calf veins.

Recent evidence on anomalous coagulation features in patients with severe COVID-19-related pneumonia might explain the higher incidence of arterial and venous thrombosis and has suggested the use of heparin prophylaxis for this subgroup of patients. Given the number of observed arterial and venous thrombosis cases, research studies are being designed to understand the mechanisms underlying COVID-19-associated hypercoagulability and possible virus-mediated endothelial dysfunction. Other research lines include investigating the response of patients with COVID-19 to different anticoagulants and identifying blood-circulating biomarkers as predictors of thrombotic complications.

We are now well into our fifth week of the COVID-19 emergency and have been managing the new challenges in an increasingly efficient manner. The supply chain has posed some issues, not only for personal protective equipment, but also for seemingly trivial devices such as thrombectomy catheters, peripheral vascular grafts, specific drugs, and so forth. Centers treating vascular patients during the COVID-19 pandemic could face similar issues and could be better prepared from our experience.

Finally, adequate protection and wise allocation of human resources, including nurses, doctors, assistant personnel, are of paramount importance, because the infection has not spared healthcare workers. In Italy, 116 physicians have died of COVID-19-related disease since March 10, 2020.

REFERENCES
1. Wu Z, McGoogan JM. Characteristics of and important lessons from COVID-19 outbreak in China. JAMA 2020;323:1239-42.
2. Yin S, Huang M, Li D, Tang N. Difference of coagulation features between severe pneumonia induced by SARS-CoV2 and non-SARS-CoV2 [published online ahead of print April 3, 2020]. J Thromb Thrombolysis doi: 10.1007/s11239-020-02105-8.

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