Received: 30 June 2020 | Revised: 24 August 2020 | Accepted: 6 September 2020

DOI: 10.1111/jocs.15069

REVIEW ARTICLE

JOURNAL OF CARDIAC SURGERY WILEY

Is there a vascular side of the story? Vascular consequences during COVID-19 outbreak in Lombardy, Italy

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Abstract

Background: Lombardy, in the northern Italy, was one of the most affected region in the world by novel coronavirus COVID-19 outbreak. Due to the dramatic amount of confirmed positive cases and deaths, all clinical and surgical hospital departments changed their daily activities to face emergent pandemic situations. In particular, vascular surgery units reorganized their role and priorities for both elective and urgent patients requiring open or endovascular interventions.

Material & Methods: This brief review summarizes organization of vascular Lombardy centers network adopted during pandemic period and clinical evidences published so far by regional referral and nonreferral hospitals in terms of vascular surgery and medicine implications in COVID-19 positive or negative patients managements.

Results: Different patterns of disease were described during phase 1 COVID-19 outbreak in Lombardy region, with major attention in pheriperal artery disease and venous thrombosis.

Conclusion: COVID-19 infection seems to be not only a pulmonary but also a vascular (arterial and venous) disease. Further study are necessary to described mid and long-term outcomes in COVID-19 vascular patients population.

KEYWORDS

acute limb ischemia, aorta and great vessels, COVID-19, vascular emergencies, vascular surgery

1 | INTRODUCTION

Coronavirus disease 2019 (COVID-19) has become a major outbreak spreading worldwide, with more than 7,800,000 confirmed cases and more than 430,000 deaths (as a time of June 16, 2020).[1] In particular, Lombardy—about 10.6 millions of habitants, in northern Italy—was the most affected region in Italy (Figure 1A), with more than 92,000 confirmed cases (about 38% of all cases in Italy) and more than 16,400 confirmed deaths (about 48% of all Italian deaths, Figure 1B).[2] Severity and mortality rate associated with COVID-19 pneumonia have led to an extraordinary effort by all the medical and scientific communities, to provide the best operative support in terms of basic research, rapid diagnosis, and prompt treatments.[3–5] Vascular specialists and vascular surgeons were not spared, treating not only vascular patients but also COVID-19 patients, irrespective of vascular comorbidities or complications.

Therefore, in this dramatic scenario, vascular surgery units and vascular services have modified their daily clinical and surgical activities to face the pandemic situation. In particular, a rapid increase of intensive care unit (ICU) and ward beds were provided for managing patients positive to the virus, with the creation of dedicated pathways for COVID-19 confirmed or suspected cases, for both hospitalized or outpatients.

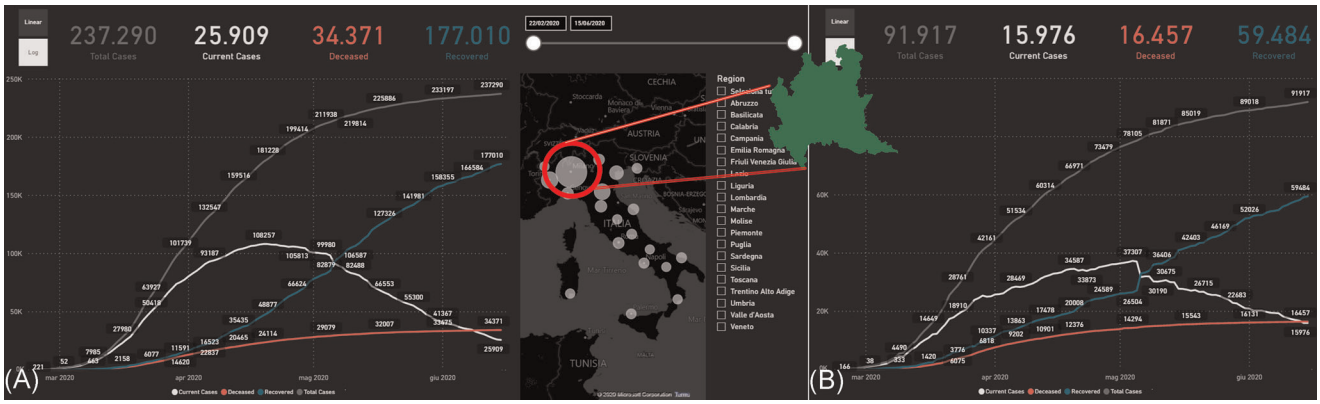

FIGURE 1 Italy (A) and Lombardy (B) report on COVD-19 outbreak (viewed on June 16, 2020)

2 | VASCULAR SURGERY DEPARTMENT ORGANIZATION AND EXPERIENCES

Italy—and Lombardy as one of the first regions—was the first country in the word that restructured its vascular surgery units' network to contrast the COVID-19 outbreak. In fact, on March 8th, 2020, Lombardy Regional Council Ordinance imposes to adopt necessary and special actions due to epidemiological emergency, to provide practical indications for all healthcare operators.[6] Healthcare system reorganization passed through four steps:

- Introduction of a "Hub and Spoke" system.
- Remodulation of outpatient and inpatient services, and priorities.
- Spaces reorganization.
- Practice and clinical research on vascular pathologies and complications increasing in COVID-19 patients.

In the case of Vascular and Cardiovascular Surgery, a taskforce of vascular specialists was created, as described by Bonalumi et al.[7] In this exhaustive report, the institution of Hub hospitals for urgent and emergency patients, supported by satellite Spoke hospitals, was detailed described. In brief, 4 Hub and 15 Spoke hospitals were identified in Lombardy. Hubs guaranteed 24-h emergency service, with the possibility to perform at most three surgical procedures at the same time. Spoke hospitals were invited to transfer urgent cases to their referral Hub center, to potentially concentrate their efforts on COVID patients' treatments only.

Treatment recommendations and criteria for each vascular and cardiac disease that required surgical treatment were described, categorizing patients as presenting with urgent and nonurgent conditions. During the COVID-19 Phase 1, only urgent (class U, as soon as possible, according to Italian priority rank for hospitalization) or high priority (class A, within 30 days from diagnosis) patients were included in the list for planning the treatment. According to this new organization, all elective activities with lower priority (classes B, C, and D) were postponed. The same criteria were used for outpatient diagnostic or clinical evaluations, giving priority to class U patients (to be evaluated within 72 h, according to Italian priority rank for outpatients' services). In anticipation of hospitalization, all patients were screened for COVID-19, through preadmission pharyngeal swab (one or two, between 5 and 2 days before admission). In some hospitals, preoperative chest X-ray and/or computed tomography were also performed as screening tests. In case of an urgent or emergent procedure, patients were treated as COVID-19 positive cases until further perioperative diagnostic evaluation. To minimize contamination among patients, healthcare specialists, and other collaborators, ad hoc COVID-19-free and COVID-19-dedicated areas were established. This subdivision was applied for ICU, wards, operating rooms, elevators, and hospital floors. Furthermore, specific flowcharts were adopted in the case of perioperative complications in COVID-19 patients requiring further diagnostic evaluation or reintervention.

On these bases, in our Hub in Milan, between March 9th and April 18th, 70 cardiac or vascular patients were admitted, of whom 13 urgent and 4 nondeferrable vascular or endovascular surgical procedures. Among these, three urgent patients were COVID-19 positive. No data regarding outcomes are present in this study. The authors concluded that newly designed and shared protocols, including the "Hub and Spoke" network, provide rapid evaluation and management of COVID-19 positive or potential positive patients.

Another Hub hospital reported its experience in Lombardy at this time. Bellosta et al.[8] analyzed the treatment and result of 20 patients affected by COVID-19 pneumonia and acute limb ischemia (ALI). A comparative analysis on patients with ALI between the first trimester of 2019 and the same 2020 period was also performed, confirming an increased number of admissions for ALI during the acute COVID-19 pandemic (1.8% of all vascular treatments during 2019, 16.3% during 2020; $p < .001$). COVID-19 patients presenting with ALI experienced poor outcomes, regardless of the treatment types', with 8 (40%) in-hospital mortalities. The presence of COVID-19 related pneumonia was not significantly associated with successful revascularization, while the use of intravenous heparin was significantly related to postoperative survival (0% vs. 57.1%; $p = .042$). Such a peculiar increase of ALI and/or peripheral arteries lesions was also described by another Milan Hub center.[9] The authors stated as uncommon the number of patients with limb ischemia or acute thrombosis treated during the pandemic period, including

those patients recovered in ICU patients and already receiving antithrombotic prophylaxis. In these three experiences in Lombardy, the incidence of emergent/urgent aortic lesions necessitating intervention was as low as 10%–15%. Such data was then confirmed by a currently unpublished survey conducted among about 90% of vascular centers in Lombardy, which showed a 13% incidence of cumulative thoracic and abdominal aortic diseases in the COVID-19 acute phase 1 (March 8th–May 3rd, 2020).[9] In this time, another important issue was related to vein thrombosis, in particular deep vein thrombosis (DVT)—that was detected as a not-so-rare condition in COVID-19 patients (23% for patients intubated in ICU and 8% for patients breathing spontaneously, on 108 COVID-19 cases).[10] Furthermore, Lodigiani et al.[11] described a 7.7% of arterial and venous thromboembolic events in 362 COVID-19 patients (48 in ICU and 314 in the general ward), admitted to an academic Hospital in Milan (Spoke center for vascular disease). In particular, among these, 57.1% had a venous thromboembolic event (pulmonary embolism and/or DVT).

3 | DISCUSSION

The entity of the COVID-19 pandemic in the Lombardy region was of primary relevance, resulting, as consequence, in a real-word vascular surgery experience, with no unconcreted hypothesis or very preliminary results. The number of patients affected in this area leads to significantly different vascular treatments and results performed in the COVID-19 population, which is associated with increased mortality.[8,9] It is evident that during the pandemic period the number of patients presented at referral hospitals with severe or not-severe ALI or critical limb ischemia (CLI) was increased when compared with the same period in 2019. This was true also in other Italian areas or European and non-European countries, although reported as single cases or limited case series.[12,13] Even though it was stated an increased peripheral artery disease (PAD) rate, no significant mention of ALI or CLI is reported in other large-scale series describing in-hospital or ICU patients with COVID-19.[11,14,15] Only Klok et al.[16] reports two cases of peripheral arterial embolism in 184 ICU patients with confirmed COVID-19 infection. Unfortunately, no details on specific characteristics regarding affected arteries, treatments adopted, and postoperative outcomes are provided.

An important point to be taken into account is that the relative increase of arterial thromboembolism during the pandemic period could be also caused by some biases and confounding factors, like the concentration of all ALI or CLI emergencies in Hub centers, delay in ER presentation attributable to impose lockdown, old patients' age and fear in approaching hospitals because of high contamination risk. In this setting, nonoptimal treatment of patients—particularly outpatients with arterial ulcers, diabetic ulcers, and/or chronic CLI—with other diseases than COVID-19 led to more serious and sometimes irreversible clinical status at the first visit. This statement was also supposed by a brief Italian report that emphasizes not only a quantitative increase in ALI or CLI patients but also an increase of clinical severity in PAD, resulting in an augmented rate of major amputations.[17]

Comparable analysis and hypothesis were found in case of admissions and mortality rate for acute myocardial infarction (AMI) in pandemic-2020 and 2019 same periods.[18] In particular, although the admission rate was significantly reduced during the COVID-19 pandemic across Italy, mortality and complication rates were increased, probably for the same reasons described above. Furthermore, also for a major cardiovascular event such as acute type A aortic dissection, a multicentre observational study conducted in New York, described a significant decrease in the monthly surgical case volume (from 12.8 ± 4.6 cases/month before-COVID to 3.0 ± 1.0 cases/month after-COVID).[19] As the main causes for this observation, authors hypothesized patients fear of contracting COVID-19 if presenting to the hospital, overstretched first responders causing undue delays, or overburdened hospitals causing delayed or missed diagnoses. The same previous reasons have been used by the surgeons of Lombardy for explaining the lower incidence of acute aortic diseases observed in the Lombardy surveys.

In our center, Fondazione Cà Granda Policlinico in Milan, which was included as a spoke center in the Lombardy organization, 21 emergent/urgent patients were treated/observed during the COVID-19 acute phase 1 (from March 8 to May 3, 2020), mostly affected by aortic diseases. Due to the presence of substantial internal hospital resources, in agreement with the coordinator of our Hub, no patients were transferred to the Hub center for interventions. Among others, in this time surgical therapies included open repair of ruptured abdominal aortic aneurysm in inferior vena cava (Figure 2), renovisceral debranching with following thoracic endovascular repair of aorta, and endovascular aneurysm repair for impending rupture of thoracoabdominal aortic aneurysm type 3 (Figure 3), symptomatic juxtarenal penetrating aortic ulcer (Figure 4). All these postoperative hospital courses were uneventful.

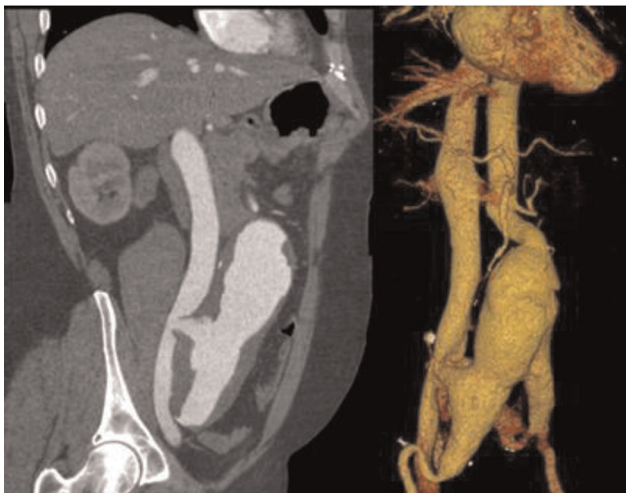

FIGURE 2 Emergency ruptured abdominal aortic aneurysm in a 67-year-old men

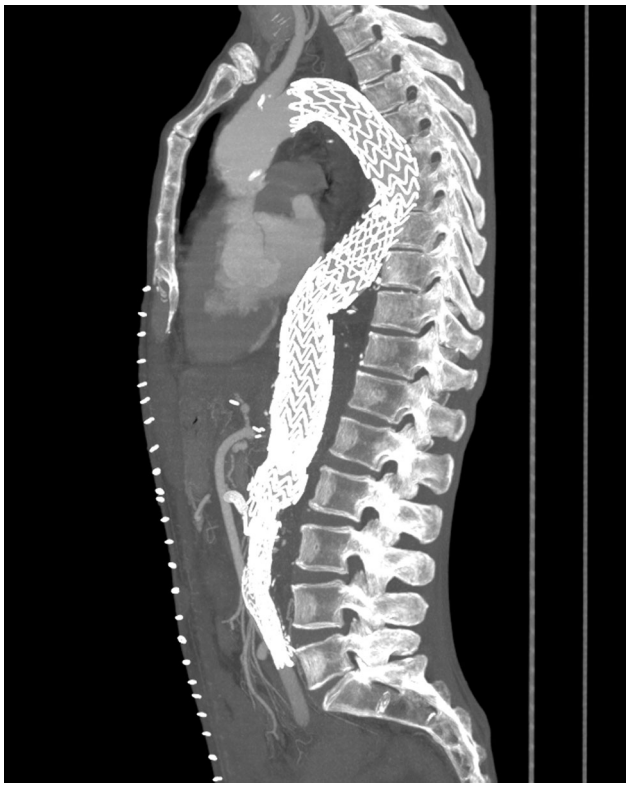

FIGURE 3 Renovisceral debranching with following thoracic endovascular repair of aorta and endovascular aneurysm repair for impending rupture of thoracoabdominal aortic aneurysm type 3

FIGURE 4 Symptomatic juxtarenal penetrating aortic ulcer

However, we noted an increased difficulty in performing operations in those patients for whom there was not enough time for screening about the virus. This peculiar group of patients was managed like a COVID-19 one, which included a surgeon dressing, composed of three sterile gloves, a protective coat, legs protections, proper head and neck coverage, an FFP-2 mask, and, over that, a surgical mask. In the case of endovascular or hybrid intervention, the lead garments were additionally needed, making the surgical act much more complex. These considerations are factual for both types of vascular operations: in the case of endovascular ones, because of a reduced sensibility when using guidewires and catheters, and during open surgery, usually more physically demanding.[20]

Regarding postoperative outcomes, a higher rate of unsuccessful revascularization (29.4%), reintervention (13.0%), and in-hospital mortality rate (40.0%) were reported.[8,21] As the authors claimed, poor outcomes were probably due to the situation of "desert foot" during completion angiography after selective thrombectomy, with scarcity in forefoot microcirculation. The increased PAD severity (Rutherford classes III and IV) may be another risk factor to explain postoperative complications. Although an augmented ALI and reintervention rates were observed in patients with COVID-19, apparently no angiographic and in vivo macroscopic differences were described in thrombus specimens, as mentioned, with a gelatinous consistency.[8]

Despite nonunivocal results and the need for further studies to assess the real incidence of ALI, CLI, and PAD in COVID-19 patients, it is undoubtful that the novel coronavirus infection is associate with hypercoagulability and thrombogenic state with multiple direct and indirect cardiovascular complications.[22–24] In particular, severe endothelial injury, widespread thrombosis with microangiopathy, alveolar-capillary microthrombi, and new vessel growth were found in COVID-19 patients' lung autopsy.[25] These pathological features, if affected also peripheral limb circulation, may aggravate PAD (Figure 5) or may generate thromboembolic disease in non-PAD patients.[11] Furthermore, the chronic infectious state may contribute directly or—more likely—indirectly, to postoperative complications after vascular surgery treatments, as mentioned for other viruses, like during human immunodeficiency virus (HIV) infection.[26,27]

Regarding peripheral venous complications, other studies confirm an augmented DVT rate in patients with COVID-19, particularly in ICU cases.[16,28,29] Despite this, also for venous thromboembolic complications there could be confounding factors that may hide the real incidence of DVT specifically caused by COVID-19 disease: immobility, particular in ICU patients, an infectious state with coagulation disorders due or not to liver impairment, extracorporeal circulation necessary for supporting ventilation, heart pump disorders, disseminated intravascular coagulopathy, multiple organ dysfunction syndromes, dysregulation in corporeal fluid balance with

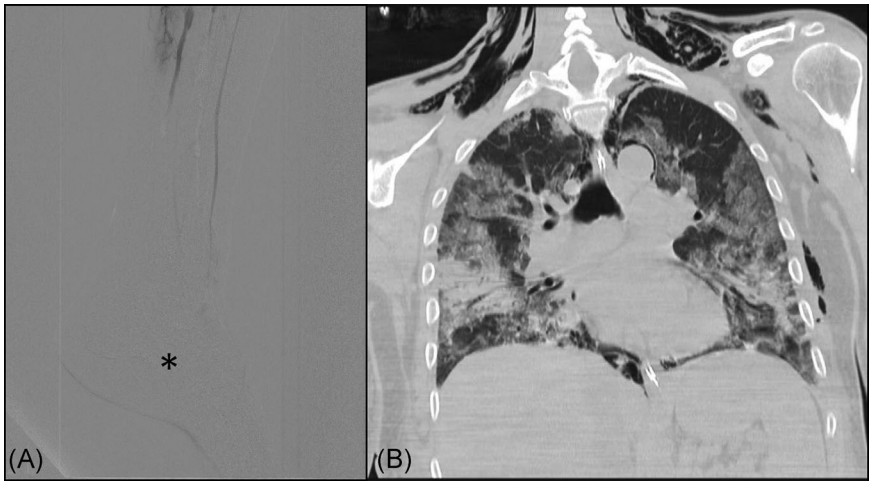

FIGURE 5 Peripheral (A) and pulmonary (B) condition in a patient with COVID-19 pneumonia and acute limb ischemia. Note the "desert foot" (asterisk) condition after thrombectomy, with no atherosclerosis signs in visible vessels

dehydration. These pathological consequences may explain also arterial complications.

4 | CONCLUSION

The vascular side of the COVID-19 hurricane story showed a specific pattern of patients with vascular diseases, characterized by an increased incidence of peripheral arterial diseases and venous thrombosis. Conversely, thoracic and abdominal aortic lesions seem to be reduced, although a definitive sentence cannot be supported because of several biases. Overall, vascular patients with COVID-19 who necessitate urgent/emergent operations show increased mortality.

COVID-19 infection has proper vascular manifestations, evident in pulmonary circulation but still under evaluation in the peripheral circulation. Further studies are required to assess if patients affected by COVID-19 disease, with or without know PAD or risk factor for DVT, are more prone to develop ALI or other thromboembolic venous and arterial complications.

In our region, hospital and daily practice organization had dramatic modifications, with the creations of Hub and Spoke centers for delivering cardiovascular care. However, although this organization was nicely and promptly organized, in some sense appeared undue because the total number of such emergencies was limited, and several other hospitals were able to continue the surgical program because of enough own dedicated resources. Nevertheless, the regional organizing program and the activity effectively performed during the COVID-19 phase 1 represented an important stress test for the entire health system and the cardiac and vascular surgical community in Lombardy.

CONFLICT OF INTERESTS

The authors declare that there are no conflict of interests.

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How to cite this article: Bissacco D, Grassi V, Lomazzi C, et al. Is there a vascular side of the story? Vascular consequences during COVID-19 outbreak in Lombardy, Italy. *J Card Surg*. 2021;36:1677-1682. https://doi.org/10.1111/jocs.15069