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## COVID-19 General Review

# Aortic Pathology During COVID - 19 Pandemics. Clinical Reports in Literature and Open Questions on the two Co-Occurring Conditions

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**Abstract: Background:** Cardiovascular involvement in SARS-CoV-2 infection has emerged as one of viral major clinical features during actual pandemic; limb arterial ischemic events, venous thrombosis, acute myocardial infection and stroke have occurred in patients.

Acute aortic conditions have also been described, followed by interesting observations on cases, hypothesis, raised since the emergence of the pandemics.

**Methods:** a review of cases in literature of aortic pathology in patients with clinically suspected/microbiologically confirmed COVID-19 infection has been carried out to analyze anagraphic data, clinical presentation, treatment options and outcome.

**Results:** Seventeen cases have been included. Mean age of patients was  $58.6 \pm 15.2$  years, with a male to female ratio of 12:15 (70.5% vs. 29.5%). Comorbidities were reported in 11 cases (64.7%), but in 5 cases (29.4%) no previous pathology was signaled in history. Hypertension was the most frequently reported comorbidity, in 8 cases, (47%), followed by renal pathology (17.6%), coronary artery disease (17.6%), previous aortic surgery (11.7%) and arrhythmia (11.7%); but also cerebrovascular disease, diabetes, autoimmune conditions, previous neoplasia and arrhythmia were reported once each. Fever and thoracic pain were the most frequently reported findings at presentation (8 cases, 47% each), followed by respiratory symptoms (6, 35.2%), low lymphocyte count (17.6%), features related to aneurysm rupture, ischemic stroke, abdominal pain and acute renal insufficiency. Reported aortic pathology included: type A aortic dissection (11 cases; 64.7%); new pathology of previous aortic graft (2 cases, 11.7%); 2 aortitis, 1 associated with type A aortic dissection; 1 thoraco-abdominal aortic aneurysm, 1 ruptured aortic aneurysm and 1 aortic embolizing thrombosis. Open surgery was carried out in 10 cases (58.8%), endovascular treatment in 3 (17.6%). Three patients (17.6%) died before surgery. Exitus was reported in 4 cases, with a total mortality of 23.5%.

**Conclusions:** Acute aortic events have occurred during pandemic in patients with clinically suspected/microbiologically confirmed COVID-19 infection. Confounding clinical features at presentation, the importance of anamnestic details (as previous vascular graft implant), the observed surgical and postoperative challenges may suggest the need to consider the implications of the possible link between acute aortic events and SARS-CoV-2 infection, in order to promptly correctly diagnose the patient and respond to specific needs.

Conflict of interest: None to be declared by the authors.

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## INTRODUCTION

Many different clinical cardiovascular manifestations in COVID-19 patients have been described since the start of the pandemics, including acute myocardial infarction, acute heart failure,<sup>1</sup> ischemic cerebrovascular disease,<sup>2</sup> acute upper<sup>3</sup> and lower limb ischemia, associated with acquired hypercoagulability and poorer surgical outcome.<sup>4</sup>

Angiotensin converting enzyme 2 (ACE-2) has been observed to have a role as a host receptor for SARS-CoV-2, and a prominent overall role in physiopathology of the infection. Present in lungs, gut, kidneys, central nervous system, adipose tissue, ACE-2 is known to be widely expressed in cardiovascular system (cardiomyocytes, cardiac fibroblasts, epicardial adipose tissue, and coronary vascular endothelium).<sup>5</sup>

From a physiopathology point of view, endothelium damage that mimics vasculitis has been observed in patients and pathological autoimmune responses involved in the antiviral immunity are worth to be emphasized.<sup>6</sup> Severe endothelial injury has been described in COVID-19 patients, associated with intracellular SARS-CoV-2 virus; direct viral effects as well as perivascular inflammation may contribute to it. Additionally, a widespread vascular thrombosis with microangiopathy, occlusion of alveolar capillaries and a significant new vessel growth through a mechanism of intussusceptive angiogenesis have been described in histopathology assessment.<sup>7</sup>

According to the above reported findings of increased inflammatory burden in patients with a severe clinical presentation, the first vascular sign in early CT scan imaging has been referred to as "vascular thickening," "vascular enlargement," or "vascular congestion."<sup>8</sup>

Many infectious diseases are known to potentially induce lesions involving the aorta, leading to aneurysms (eventually causing its rupture) or dissections.<sup>9-11</sup> Even though it is early to drive conclusions about aortic pathology and SARS-CoV-2 infection, interesting observations on cases, hypothesis, questions raised since the emergence of the pandemics, are worth to be summarized, which could inspire future investigations.

## MATERIALS AND METHODS

Aim of our report is to describe aortic pathology occurring in patients with reported positivity to SARS-CoV-2, through the analysis of case reports and case series published in literature since the start of the pandemic.

Literature was reviewed using as key words for research COVID-19 OR SARS-CoV-2 AND aortic aneurysm OR aortic dissection OR aortic pathology. The following databases were searched for relevant studies: MEDLINE (PubMed) and EMBASE (Embase.com). A filter for language was applied and only papers written in English were included.

Anagraphic data and details regarding comorbidities, clinical presentation (including fever, respiratory symptoms or pain or signs of ischemia), kind of aortic involvement (extension of lesion, presence of rupture), treatment (conservative, open surgery or endovascular) and patient's outcome were extrapolated from text and registered in an electronic record. Descriptive analysis was carried out. The low number of patients and heterogeneity of reports was not suitable for analytic comparison.

## RESULTS

A total of 13 papers and 17 cases were finally included (Table 1). Mean age of patients was  $58.6 \pm 15.2$  years; the majority were male (12 males, 5 females, respectively 70.5% and 29.5 % of the total number of patients).

Among anamnestic comorbidities, hypertension was the most frequently reported (7 cases, 58.3%), followed by renal pathology (3 cases, 25%), coronary artery disease (2 cases, 16.7%), and previous aortic surgery (2 cases, 16.7%). Furthermore, previous cerebrovascular disease, diabetes, autoimmune conditions, specifically Crohn disease, COPD, previous neoplastic condition and arrhythmia were also reported once each. In 4 patients (33.3%) no comorbidity was reported in previous clinical history.

COVID diagnosis was suspected after clinical assessment in 4 cases (23.5%), carried out by laboratory investigations at hospitalization in 9 cases (52.5%) and during the hospital stay in the remaining 4 patients.

Fever was the most frequent symptom (8 cases, 47%), followed by thoracic pain (8 cases, 47%), respiratory symptoms (6 cases 35.2%) and low lymphocyte count (3 cases, 17.6%). Thoracic pain was the most frequent vascular related symptom; in other cases, clinical presentation was characterized by ruptured aneurysm (2 cases; 11.7%), ischemic stroke and abdominal pain (2 cases each). Acute renal insufficiency was present in 1 case.

Aorta was found to be involved by the following acute aortic conditions: Type A aortic dissection (11 cases; 64.7%); aortitis in 2 cases, 1 associated

**Table 1.** Summary of case reports of aortic pathology in patients with clinically suspected or microbiologically confirmed covid-19 infection

Author	Age	Sex	Comorbidities	Clinical presentation	Aortic involvement	Surgical management	Outcome	COVID +
Fukuhara [29]	52	M	None	Severe chest + abdominal pain; Low grade fever 37.6 C; No cough or dyspnea	Type A Aortic dissection	Ascending + hemiarch aortic repair	EXITUS 11th postop progressive respiratory failure + acute renal failure-> multi-organ failure	Tested and positive on sixth day p.o, but not tested on admission
Giacomelli [28]	67	M	Chronic hypertension 2014: aorto-bi-iliac Dacron open repair for 60 mm abdominal aortic aneurysm patent on follow up (2019)	Eighth day hospitalization for COVID-19 ARDS: pallor + bilateral lower limb hypothermia mottled skin from umbilical line absence of femoral and peripheral pulses	Abdominal aortic graft complete thrombosis	Exitus before surgery	EXITUS cardiac arrest before surgery planning	Tested positive on admission
He [32]	51	M	Hypertension	Fever 37.6°C; RX pulmonary inflammatory changes; No respiratory symptoms; Low lymphocyte count	Type A Aortic dissection	Surgical aortic substitution	ALIVE Successful surgery no post operative follow up	Clinically suspected on admission
	51	M	Hypertension	Fever 37.6°C; RX pulmonary inflammatory changes; No respiratory symptoms; Low lymphocyte count	Type A Aortic dissection	Surgical aortic substitution	ALIVE Successful surgery no post operative follow up	Clinically suspected on admission
	62	M	None	RX pulmonary inflammatory changes; No respiratory symptoms; Low lymphocyte count	Type A Aortic dissection	Surgical aortic substitution	ALIVE Successful surgery no post operative follow up	Clinically suspected on admission
	59	F	Hypertension	Fever 38.5°C RX pulmonary inflammatory changes No respiratory symptoms low lymphocyte count	Type A Aortic dissection	Surgical aortic substitution	ALIVE Successful surgery no post operative follow up	Clinically suspected on admission

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**Table 1** (continued)

Author	Age	Sex	Comorbidities	Clinical presentation	Aortic involvement	Surgical management	Outcome	COVID +
Martens [33]	64	M		Acute onset chest pain + Right leg ischemia	Type A Aortic dissection	Surgical aortic substitution	ALIVE But on 6th day post-op low-grade fever, dyspnea+ dry cough desaturation+ bilateral pleural fluid + ground glass opacification lesions + alveolar infiltration + Hemophilus influenzae -> medical treatment. Discharged 14 day p.o.	Tested as protocol on 1 st postop
Resch [34]	65	M	Hypertension; Myocardial infraction + stenting Stroke without residual deficit Renal a. stenting (nephrogenic hypertension); Stable Crohn's disease; Hypothyroidism; gout; Chronic lower back and hip pain at 500 mt; palpable pulses, ankle brachial index 0.86	Programmed 2 stage aortic repair for abdominal aortic aneurysm	Type III Crawford thoracic-abdominal aortic aneurysm (6.3 × 7.3 cm)	Stage 1 percutaneous thoracic endovascular repair (TEVAR) -thoracic stent-graft left subclavian a. -> 4 cm proximal to celiac origin. Waiting for planned 2nd stage exclusion of the aneurysm with a fenestrated stent-graft	ALIVE 2nd day after discharge claudicatio + legs asthenia 25meters. Foot pulses and ABI's were unchanged; no signs of lower limb weakness or sensory loss. No fever on admission-> 38 AT DAY 2. Diarrhea. Negative for spinal cord or thrombus embolism . well-positioned TEVAR graft, patent visceral and iliac arteries. On day 2 fever 38,1°C. COVID positive needing oxygen supplementation and respiratory therapy. Discharged to home after 9 days in good clinical condition.	Tested on day 2 of second hospitalization (7 days after symptoms, 10 days after first discharge)

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**Table 1** (continued)

Author	Age	Sex	Comorbidities	Clinical presentation	Aortic involvement	Surgical management	Outcome	COVID +
Rinaldi [35]	80	M	EVAR abdominal aortic aneurysm (2013); Rectal cancer-Hartman + colostomy; Chronic kidney failure+ left kidney shrinkage	Free rupture of the para-renal abdominal aorta above previous endo-graft (renal a. level); Massive intraperitoneal hematoma	Ruptured pararenal abdominal aorta above previous endograft	Monolateral renal a. stenting + aortic cuff below origin of superior mesenteric a. Postoperative day 2, type IA endoleak - caudal aortic cuff migration ->new endograft aortic cuff below coeliac trunk	ALIVE constant recovery during the post-operative course of COVID pneumonia	Positive on admission
Shihi [36]	54	M	Hypertension; Coronary a. disease; Coronary stenting; Wolff-Parkinson-White syndrome; left nephrectomy	Abdominal pain for 1 day + Fever, cough, dyspnea 5 days	Ruptured Abdominal aortic aneurysm 5.8 cm	Bifurcated EVAR	ALIVE at 2 weeks follow up stable endograft sac size (5.8 cm) + small type II endoleak. Patent limbs with no mural thrombus. Resolving retroperitoneal hematoma and ground glass opacities in the lungs.	Tested negative on admission, but positive during hospitalization (3 days)
Akgul [25]	68	F	Diabetes Hypertension	Pulseless right femoral a. Pulmonary hypertension. Lung bilateral ground-glass opacities	Type A aortic dissection	Aortic transection above commissures and distally before the innominate a. +28mm Dacron graft + distal anastomosis sutured with pledgets in order to affix dissection flap to aortic wall	ALIVE discharged on 14th postoperative day with antiaggregant	On admission (test not specified)

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**Table 1** (continued)

Author	Age	Sex	Comorbidities	Clinical presentation	Aortic involvement	Surgical management	Outcome	COVID +
Azouz [37]	56	F	Not reported	Acute ischemic stroke (right middle cerebral a. occlusion); On 2nd day abdominal pain + vomiting	free-floating aortic arch thrombus + superior mesenteric a. occlusion	Endovascular thrombectomy + open resection small bowel	NOT SPECIFIED	Positive on admission
Mori [14]	54	M	Family history for aortic aneurysm and dissection	Sudden onset chest pain, no respiratory symptoms	52 mm dilated Aortic root and arch intramural hematoma + ground-glass opacities in the lung	Valve-sparing root+ hemiarch replacement (dacron) + coronary bypass	ALIVE discharged on 6 po day	Positive on admission (PCR)
	82	F	Atrial fibrillation, sick sinus syndrome, diastolic heart failure, pacemaker, COPD	sudden onset chest pain and facial weakness, anuria and acute kidney injury, no COVID symptoms on admission	Type A aortic dissection	Ascending aorta and hemiarch replacement + coronary sinus reconstruction	ALIVE (renal failure requiring dialysis, + COVID-19 pos 66 p.o.day)	Positive 66 days p.o (respiratory symptoms)
Mamishi [18]	14	M	Williams Syndrome supraaortic stenosis, coronary involvement	Fever, shortness of breath and cough	Type A aortic dissection	Exitus before surgery	EXITUS (acute dissection after 3 weeks steroid therapy for COVID treatment)	Positive on admission
Tabaghi [16]	47	F	None	Fever, dry cough and bloody diarrhea	Type A aortic dissection	Exitus before surgery	EXITUS cardiac arrest before surgery	Positive on admission
Shergill [19]	71	M	None	Fever, dry cough, diarrhea 2 weeks. Acute Chest pain (left side)	Circumferential aortitis	Prednisolone 40mg	ALIVE (discharged after 2 weeks)	Positive on admission

Details on author, age and sex of patients, comorbidities, aortic pathology, surgical management, outcome and timing of positive test in relation to hospitalization have been reported in column.

to aortic dissection; new pathology on previous aortic graft in 2 cases (specifically 1 bilateral branch thrombosis; 1 embolizing aortic thrombosis; 1 recurrent aneurysm rupture on the proximal end point of an infrarenal abdominal aortic graft); 1 ruptured abdominal aortic aneurysm; 1 thoracoabdominal aortic aneurysm. Rupture, as reported above, occurred in 2 cases, the abdominal aortic aneurysm and the recurrent aneurysm on previous abdominal aortic graft.

As for treatment, exitus before surgery has been reported in 3 cases, 17.6% (in 1 case because of acute thrombosis on previously implanted endovascular aortic bifurcated graft; in 1 because of acute type A dissection on enlarged ascending aorta; the third because of acute type A aortic dissection on aortitis after prolonged COVID steroidal treatment in a patient with William syndrome). Open surgery was the most frequently reported surgical option (10 cases, 58.8%) consisting in 9 open

surgical procedures for type A aortic dissection and 1 embolectomy of a free floating aortic arch thrombus, associated with bowel resection for mesenteric ischemia. Endovascular treatment was carried out in 3 cases (17.6%), including 1 EVAR procedure planned in 2 steps for an unbroken thoraco-abdominal aortic aneurysm, 1 EVAR for ruptured abdominal aortic aneurysm and 1 endovascular embolectomy for aortic acute embolic thrombosis.

Exitus was reported in 4 cases, with a total mortality of 23.5%. Specifically, death was due to multiorgan a failure occurred on the 11th day post-aortic arch repair for type A dissection; to cardiac arrest while waiting for surgery, in a patient diagnosed with previous abdominal aortic endograft thrombosis; to acute aortic type A dissection in 2 patients hospitalized for COVID, during treatment for the infectious disease condition. Results have been summarized in [Table 2](#).

## DISCUSSION

Many matters of concern have been raised when analyzing the occurrence and managing of acute aortic syndromes during COVID-19 pandemic, from organizational level of vascular emergencies, challenged by lockdown provisions, to the hypothesis of a likely direct link of the infectious agent as a cause of major acute aortic events.

### Challenges in Aortic Patients Access to Emergency Assessment and Diagnostic Issue

COVID-19 pandemic has initially forced health care systems to delay elective operations, including abdominal aortic aneurysm (AAA) repair, because of shortage of resources and high patients' comorbidities related to acute vascular disease in this specific infectious setting.

A report by El-Hamamsy on the experience on acute aortic dissections occurring since the pandemic outbreak in New York has observed a 76.5% drop in the monthly surgical case volume of acute type A aortic dissection and an 8- to 10-fold increase of at-home deaths compared to the same time period in 2019, causing delayed or missed diagnoses.<sup>12</sup> Similar findings of a dramatic drop in the number of cardiovascular admissions after the establishment of containment have been reported from a French group.<sup>1</sup>

Observations from the Cleveland Clinic comparing baseline to pandemic data on cardiovascular daily transfers for aortic emergencies

presented a relative reduction of 21%, even though not statistically significant.<sup>13</sup>

However, new data have forced to reconsider delay in cardiovascular disease management during pandemics at a level of benefit-risk assessment of procrastinating treatment.

Mori et al., who reported 2 cases of surgical thoracic aortic emergencies, 1 undergoing an operation with known COVID-19 positive status and another who contracted COVID-19 in the postoperative period, suggested the possibility of favorable recovery from the combination of the highly morbid vascular pathology undergoing high-risk operations in the setting of highly virulent respiratory illness.<sup>14</sup>

Recent probabilistic sensitivity analyses suggest that the decision to delay operative repair of AAA should consider both patient age and local COVID-19 prevalence in addition to aneurysm size. Patients with large aneurysms (>7 cm) faced a 5.4% to 7.7% absolute increase in the probability of mortality with a delay of repair of 3 months, but demonstrated a higher probability of survival when treated with immediate endovascular repair or open surgery. Immediate endovascular repair had a higher probability of survival for smaller aneurysms (5.5–6.9 cm) except in settings with a high probability of COVID-19 infection (10–30%) and advanced age (70–85 years).<sup>15</sup>

### Patients' Clinical Presentation: Special Considerations

Analyzing the reported clinical/microbiological positivity for SARS-CoV-2 infection in relation to timing of hospitalization for aortic event, we can observe that the majority of patients were either positive or highly clinically suspected on admission in 52.5% of the cases. Along with symptoms due to the aortic condition, clinical features that may be referred to the associated COVID-19 infection were also present on presentation, including fever, respiratory symptoms, low white cell blood count, in some cases associated to positivity for radiological pulmonary imaging confirming the co-occurrence of vascular aortic involvement and SARS-CoV-2 infection ([Table 1](#)).

Because vascular acute complications have occurred in known COVID-19 patient during hospitalization due to the infectious condition, there is a need to assess any concomitant clinical condition (including vascular acute syndromes) that may occur in COVID-19 patients and not merely viewing them as purely infectious patients.<sup>16</sup>



**Table 2.** Summary of data from case reports

	<i>n</i> ( <i>N</i> tot = 17)	%
<i>Anagraphic data</i>		
Age	58.6 ± 15.2	
M/F	12/5	70.5%/29.5%
Days of COVID symptoms/diagnosis prior to vascular event	6.1 ± 15.4	
Diagnosed through clinical presentation	4	23.5%
COVID+ on admission/first day	9	52.5%
COVID+ during hospitalization	4	23.5%
<i>Comorbidities</i>		
	<i>N</i> tot available	
	16	
Comorbidities present	11	64.7%
None	5	29.4%
Hypertension	8	47.0%
Renal pathology	3	17.6%
Previous coronary artery disease	3	17.6%
Previous aortic surgery	2	11.7%
Arrhythmia	2	11.7%
Previous cerebrovascular disease	1	5.8%
Diabetes	1	5.8%
Autoimmune disease (Crohn disease)	1	5.8%
Previous neoplastic condition	1	5.8%
BPCO	1	5.8%
Heart failure	1	5.8%
<i>Clinical presentation</i>		
Fever	8	47.0%
Thoracic pain	8	47.0%
Respiratory symptoms	6	35.2%
Low lymphocyte count	3	17.6%
Ruptured aneurysm	2	11.7%
Ischemic stroke	2	11.7%
Abdominal pain	2	11.7%
Acute renal insufficiency	1	5.8%
<i>Aortic pathology</i>		
Type A aortic dissection	11	64.7%
New pathology of previous aortic graft (1 bilateral branch thrombosis; 1 aneurysm rupture proximal end point)	2	11.7%
Aortitis (associated to dissection in 1 case)	2	11.7%
thoracoabdominal aortic aneurysm	1	5.8%
Abdominal aortic aneurysm with rupture	1	5.8%
Embolizing aortic thrombosis	1	5.8%
<i>Management</i>		
Open surgery	10	58.8%
Endovascular	3	17.6%
Exitus before treatment	3	17.6%
Conservative	1	5.8%
<i>Outcome</i>		
Total mortality	4	23.5%
• multi-organ failure 11th day postaoortic arch repair for type A dissection	1	5.8%
• waiting for surgery previous endo-graft thrombosis	1	5.8%
• aortitis and acute aortic dissection after steroidal therapy for COVID	1	5.8%
• Acute aortic dissection on aortic root enlargement after 1 week hospitalization for COVID symptoms	1	5.8%

Anagraphic data, details on comorbidities, aortic pathology clinical presentation, management and outcome have been analyzed.

At this purpose, vasculitic sequelae of SARS-CoV-2 have been well documented in the pediatric population,<sup>17</sup> and have involved also the aorta, as in the 14 years old patient with William syndrome who presented acute type A aortic dissection complicating a prolonged steroidal therapy for COVID-19 infection,<sup>18</sup> which was included in our review. Adult aortitis has also been described.<sup>19</sup> Features that include both acute vascular syndromes due to wall damage, such as aneurysm or dissections, or major vessels thrombosis, which may present in variable clinical scenarios, such as acute abdomen, intestinal or peripheral ischemia should raise a clinical suspect of COVID-19 infection also in patients otherwise free of classical presenting symptoms, given the specific anatomopathological features attributed to virion damage which specifically targets the arterial wall. These features have been analyzed in detail in a recent paper by Manenti et.al, findings that we summarize in a dedicated section of this paper.<sup>20</sup>

If it's true that vascular conditions need to be considered as a complicating feature in COVID-19 patients, we should also keep in mind that vascular pathology may mimic in some cases COVID-19 symptoms in COVID-19 negative patients, thus challenging differential diagnosis. Differential diagnosis of acute aortic conditions in pregnancy, for example, is usually challenging due to confounding overlapping features of labor and vascular conditions,<sup>21</sup> but has been reported to be additionally challenged by similarity of COVID-19 infection features and acute aortic symptoms, in a patient actually negative to the disease, finally diagnosed with pregnancy related aortic dissection.<sup>22</sup>

### **Physiopathology Hypothesis and Observations: Direct Arterial Damage and Thromboembolic Conditions**

Because of its supposed direct viral effect on endothelium (inducing endothelial dysfunction) and because of the effect of viral induced late inflammatory burden, COVID-19 has been suggested to be involved in both venous and arterial thromboembolic diseases, as occurred in the thoracic aortic thromboembolic conditions described in the case reported by Azouz et al. and included in our review,<sup>23</sup> or in native arterial wall damage, as in the case of otherwise rare lesions such as coronary artery dissections.<sup>24</sup> Two cases of coronary dissection have been reported in literature, 1 in a 39 years old male patient without cardiovascular risk factors, which was additionally complicated by a coronary/ pulmonary fistula,

successfully treated conservatively<sup>24</sup> and the other in a 48 years old female patient with dyslipidemia, also conservatively treated because of absence of suitable coronary outflow.<sup>25</sup>

Even though coronary complications are not the direct object of this paper, we think it is important to consider these lesions while speculating on the likeliness of a link between aortic pathology and COVID-19. Given that the association between otherwise rare coronary artery dissection events and COVID-19 induced inflammatory endothelial damage seem to be straightforward, we could speculate a possible link between COVID-19 and other vessel wall pathology, including aortic dissection.

Thickening of the wall (as seen in inflammatory aortopathies) has been observed during surgical treatment of aortic type A dissection in a COVID-19 positive patient reported by Akgul et al., which appeared to be "pronounced" when compared to the authors monocentric experience of previous aortic dissections. In the same report, the possibility of "similarity" of virulence and therapy between HIV and SARS CoV- 2 and their infections has been interestingly suggested by the authors.<sup>26</sup>

This hypothesis becomes more interesting as the authors add considerations on the complications occurring at distal anastomotic site of the aortic repair performed through aortic synthetic graft implant in their patient: as occurs in aortic conditions related to other infectious or autoimmune disease,<sup>9,27</sup> the authors have observed the occurrence of bleeding in the suture line (usually due to aortic wall loss of elastic structure and strength). These complications may be frequent in inflammatory aortopathy in its acute phase, which may later evolve, in a chronic phase, to formation of aneurysms. It has been suggested that SARS-CoV-2 viremia may have had a role in the observed aortic wall inflammation and in the surgical complications induced by it, as preoperative measurement of C-reactive protein and erythrocyte sedimentation rate were high, requiring immunosuppressive therapy after surgery.<sup>25</sup>

Interesting consideration on physiopathology mechanisms underlining aortitis in COVID-19 patients has been summarized by Manenti et. Al, that have described 2 main processes leading to arterial damage. The first is an acute endothelitis, due to endothelial infiltration by virions and, by neutrophils and mononuclear elements involved in an inflammatory/prothrombotic response. Acute endothelitis may be followed by peri/panarteritis and leukocytoclastic vasculitis with deposition of polyclonal antigen-antibody immune complexes

(IgG, IgA IgM, C3 complement fraction proteins), featuring a type III hypersensitive acute vasculitis, which predisposes to thrombosis. According to this model, aortic endothelium, provided of angiotensin-converting enzyme-2 receptors, is directly attacked by virions, leading to an endotheliitis that could later be complicated by a hypersensitive vasculitis. This process can be favored by a pre-existing pathology, like atherosclerotic plaques or by facilitating hemodynamic conditions, such as a turbulent flow and a reduced parietal elasticity, common in elderly patients or after endovascular procedures.<sup>20</sup>

### Challenges for Patients With Previous Vascular Graft Implant

Not only the native arteries seem to be at risk. Specifically referring to patients with positive history for previous vascular surgery, it has been suggested that thrombotic risk related to Sars-CoV-2 infection might be much higher in a patient with a vascular prosthesis. As observed in the report by Giacomelli et al., while aortic graft thrombosis is an uncommon event (occurring in less than 1% of all aortic reconstructions) this complication may occur in COVID -19 patients also in the absence of structural abnormalities involving the graft or its inflow or outflow, or of proximal and distal anastomosis stenosis or severe occlusive disease of distal vessels, thus suggesting to consider these patients as candidates to an aggressive treatment with heparin at therapeutic dosage, given the high mortality linked to acute aortic thrombosis.<sup>28</sup>

Additionally, free rupture of the para-renal abdominal aorta, above a previous abdominal aortic endo-graft implanted for aneurysm in an 80 years old patient, was reported by Rinaldi et. Even though the timing of proximal aortic aneurysm formation can't be determined, recurrent complicated aortic pathology has previously been described in patients with inflammatory conditions, such as autoimmune disease, due to histological changes leading to weakening of aortic wall.<sup>27</sup>

### Considerations on Treatment

When it comes to treatment option, it has been underlined that the postoperatory of aortic surgery may be challenged by severe pulmonary associated conditions even in healthy nonsmoker patients after uneventful surgery.<sup>29</sup>

Furthermore, the shortage of available places in intensive care unit during pandemic may influence patient's management decisions, such as the preference of open or endovascular option for treatment, wherever they are both potentially

feasible. Patients with ruptured abdominal aortic aneurysms are among those who may need the intensive care unit postoperatively. Open repair treatment increases both the intraoperative complexity of treatment and the need for postoperative intensive care. On the other hand, endovascular aneurysm repair (EVAR) can be performed under local anesthesia and a successful outcome is usually accompanied by short recovery and quick turnover.<sup>30</sup>

Thus, endovascular repair has been proposed as a preferable option, if anatomically suitable, as the pulmonary burden from cardiopulmonary bypass usage and associated induced inflammatory cascade can be avoided.<sup>29,31</sup>

### Prevention Issues

Last but not least, the literature has invited to consider the consequences of the fall in aneurysm surveillance and lower screening attendance (from 90% to 59% in United Kingdom) which has been denounced recently, because it could lead to an increase in incidence of aneurysm-related deaths and presentation of ruptured aortic aneurysms.<sup>31</sup>

### CONCLUSIONS

Acute aortic events have occurred during the actual pandemic in patients with clinically suspected/microbiologically confirmed COVID-19 infection.

Clinical features at presentation, anamnestic details (as previous vascular graft implant), the observed surgical and postoperative challenges in these patients may suggest the need for further studies, analyzing the link between acute aortic events and the emerging infectious disease, in order to better define eventual physiopathology links between aortic diseases and SARS-CoV-2 infection and involvement of major vessel in the form of acute aortic events or vascular involvement sequelae.

### AUTHOR'S CONTRIBUTIONS

The authors have contributed equally to the review process, the writing of the manuscript and the approval of the definitive version for submission.

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