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Sudden Rupture of Abdominal Aortic Aneurysm in COVID19 Patients

Antonio Bozzani, MD[1], Vittorio Arici, MD[1], Giulia Ticozzelli, MD[2], Mila Maria Franciscone, MD[1], Antonio V. Sterpetti, MD, FACS[3], and Franco Ragni, MD[1]

Abstract

Purpose: The purpose of the paper is to report the clinical outcomes of 4 patients with ruptured abdominal aortic aneurysm (AAA) during (3 patients) or immediately after (1 patient) moderate-severe SARS-CoV-2 infection. We discuss COVID-19-related mechanisms which could impact AAA rupture.

Patients and Methods: During the period of the pandemic (March 2020—May 2021), we performed surgery in 18 patients with ruptured AAA. Four patients were affected by moderate or severe SARS-CoV-2 infection (in 3 patients the rupture occurred during the infection and in 1 patient 3. months after discharge from the hospital). Two patients underwent open repair and 2 endovascular surgery.

Results: No postoperative mortality and no major complication occurred. Rapid growth of the AAA in comparison with a previous Duplex scan was evident in all 4 patients.

Conclusions: Family doctors and vascular surgeons should be aware about the possibility of AAA degeneration in patients with moderate-severe COVID19 infection. The risk is increased by steroid therapy which is essential in more advanced stages of the infection. In this clinical setting, endovascular repair is a valid choice.

Keywords

abdominal aortic aneurysm, endovascular aneurysm repair, COVID19, inflammation, mortality

Introduction

The recent COVID-19 pandemic has deeply changed medical practice. COVID-19 pandemic has brought to reduced visits and surgical procedures for patients with cardiovascular disease.[1,2] The general attitude of surgeons, not rarely forced by the patient desire to avoid operations in this period, was to modify therapeutic approaches.[3,4] Screening for abdominal aortic aneurysms (AAA) and follow-up of patients with AAA have been postponed. During the first lockdown, the U.K. National Joint Vascular Implementation Board suggested that in individuals with AAA measuring 5.5 to 6.0 cm elective surgery could be delayed for up to 12 months, and up to 6 months for those with AAA measuring 6.0 to 7.0 cm. The capacity to offer elective AAA repair has been severely reduced and the number of elective AAA repairs during the lockdown period fell dramatically.[5] Steroid therapy has been a cornerstone in the treatment of patients with moderate-severe COVID19 infection; steroid therapy may lead to deregulation of the immune system and of collagen metabolism which are well known risk factors for AAA degeneration.[6] COVID19 infection may influence AAA degeneration. The cytokine storm which accompanies viral and bacterial infections activates several metallic proteinases involved in elastin and collagen digestion with consequent weakening of the aneurismal wall. The cytokine storm is more evident in advanced COVID19 infection[7].

During the overwhelming pandemic period, epidemiological studies were inevitably inaccurate. It was not possible to determine the real prevalence of AAA rupture, directly or indirectly related with COVID19 infection.

We report the clinical outcomes of 4 patients with ruptured AAA which occurred during or soon after moderate-severe COVID19 infection, speculating about the possible

[1]Vascular and Endovascular Surgery Unit, Fondazione IRCCS Policlinico San Matteo, Pavia, Italy
[2]Anesthesiology and Intensive Care Unit, Fondazione IRCCS Policlinico San Matteo, Pavia, Italy
[3]The Sapienza University of Rome, Rome, Italy

Corresponding Author:
Antonio V. Sterpetti, Visiting Professor, The Sapienza University of Rome, Viale Del Policlinico 00167, 00185 Rome, Italy.
Email: antonio.sterpetti@uniroma1.it

Table 1. Clinical Characteristics of Patients With Abdominal Aortic Aneurysm Rupture During COVID-19 Pandemia.

	COVID-19 free (14 patients)	COVID-19 (4 patients)	
Age (range)	74.1 (54-87)	76.7 (67-81)	
Sex (M/F)	12/2	3/1	
Arterial hypertension	13/14 (92.8%)	4/4 (100%)	
CAD	4/14 (28.5%)	2/4 (50%)	
Diabetes	3/14 (21.4%)	1/4 (25%)	
COPD	6/14 (42.8%)	2/4 (50%)	
Renal failure	1/14 (7.1%)	1/4 (25%)	
Pulmonary embolism	1/14 (7.1%)		
Previous EVAR	0	2/4 (50%	
Type of surgery			
OPEN	9/14 (64.3%)	2/4 (50%)	
EVAR	5/14 (35.7%)	2/4 (50%)	
Mean serum CRP values at rupture (mg/dl)	2.1 (0.04-7.81)	5.7 (0.55-14.32)	$P<0.001$

Abbreviations: COPD, chronic obstructive pulmonary disease; CAD, coronary artery disease; CRP, C Reactive Protein; EVAR, endovascular aortic repair.

correlations between AAA degeneration and SARS-CoV-2 infection.

Patients and Methods

This study was approved by our Institutional Review Board and informed consent was obtained from the patients or from their families. We analyzed the prospective data of patients treated for ruptured AAA from March 2020 to May 2021 at our Tertiary Care Hospital. Patients were divided into 2 groups: COVID-19-free group (14 patients) and COVID-19 group (4 patients). Analyzed data included age, sex, COVID-19 disease, other underlying chronic diseases like arterial hypertension (HTN), diabetes mellitus (DM), chronic renal disease (CRD), history of symptomatic coronary artery disease (CAD), chronic obstructive pulmonary disease (COPD), pulmonary embolism (PE), and previous vascular surgery. Serum C-reactive protein (CRP) values at the time of aneurysm rupture were recorded. We describe separately the 4 patients with AAA rupture potentially correlated with COVID19 infection.

Statistical Analysis

To prepare the database and perform descriptive analysis, the Statistical Package for Social Sciences software (SPSS Inc., Chicago, IL, USA) version 14.0 for Windows was used. The results are presented in tables. Categorical variables are expressed as frequencies and percentages. Continuous variables with normal distribution were expressed as mean and standard deviation. Student's *t* test and Chi square were used when appropriate.

Results

We observed 18 patients with ruptured AAA during the pandemic period March 2020 to May 2021. Four patients (Table 1) suffered from moderate-severe COVID-19 infection with fever and dyspnea. In all 4 COVID19 patients, the aneurysm showed a sudden increase in diameter (Table 2). In 3 of these 4 patients the maximum transverse diameter was less than 55 mm 6 months before rupture: Two patients had postponed duplex scan control due to organizational directives imposed during the pandemic. The remaining 2 patients were scheduled for endovascular treatment of an endo-leak, and they decided to postpone surgery during the pandemic, fearing the risk for contamination.

At the diagnosis of AAA rupture, these 4 patients had a statistically significant higher mean value of C Reactive Protein ($p<0.001$) in comparison with COVID-19 free patients (Table 1). Patients with COVID19 infection had more co-morbidities, even if these differences were not statically significant ($p>0.9$).

There was no mortality or major postoperative morbidity in the 4 COVID19 patients (2 open and 2 endovascular surgeries).

Four out of the 14 COVID19 free patients died in the postoperative period (1 out of 5 Endovascular Aneurysm Repair-[EVAR], 3 out of 9 open surgeries). The overall mean postoperative intensive care unit (ICU) hospital stay was 6.3 days (range: 0-38 days). We describe separately the 2 patients with primary rupture of the AAA (Patient 1,2) from the 2 patients who have had a previous endovascular repair (Patient 3,4).

Table 2. Characteristics of Four COVID19-Positive Patients With Sudden Increase in Diameter and Rupture of Abdominal Aortic Aneurysm.

	Age/sex	Characteristics AAA	Postponed US or surgery	Previous AAA maximum diameter (date)	Maximum diameter at rupture (date)	Growth rate (mm) and time	Type of surgery	Follow up
1	67/M	Fusiform, infrarenal (contained rupture)	Postponed US	47 mm (December 2019)	58 mm (November 2020)	11 mm/11 months	EVAR	Alive and well at 9 months
2	77/F	Fusiform, iuxtarenal (contrast extravasion at CT scan)	Postponed US	42 mm (November 2019 and October 2020)	53 mm (May 2021)	11 mm/17 months	OPEN	Alive and well at 4 months
3	82/M	Previous EVAR (rupture)	Waiting list/ patient postponed	68 mm (November 2020)	85 mm (December 2020)	17 mm/1 month	OPEN	Alive and well at 8 months
4	81/M	Previous EVAR (rupture pararenal AAA above EVAR)	Postponed US and severe COVID19	57 mm (October 2019)	80 mm (April 2020)	26 mm/7 months	EVAR	Alive and well at 12 months

Abbreviations: AAA, abdominal aortic aneurysm; EVAR, endovascular aortic repair; F, female; M, male; US, ultrasonography.

Case 1

A 67-year-old man was admitted with moderate COVID19 infection (confirmed by RT-PCR assay on rhino-pharyngeal swab-RPS) with fever, cough, and dyspnea in November 2020. His medical history was consistent with HTN, moderate CRD, CAD and infrarenal AAA with a 47-mm diameter at the last ultrasound (US) (December 2019). Due to respiratory distress, corticosteroid therapy (dexamethasone 4 mg/ 2 times per day) and oxygen (Venti mask, FiO2 = 30%) were administered. Five days after admission the patient complained abdominal pain. The patient was hemodynamically unstable with hypotension and tachycardia. Computed tomography (CT) angiography showed rupture of the AAA, contained in the retroperitoneum, with a maximum diameter of 58 mm. The patient underwent EVAR under local anesthesia. The postoperative course was uneventful, with normalization of clinical and serum inflammatory parameters within 7 days from surgery.

Case 2

A 77-year-old female was admitted for abdominal and back pain and hypotension in May 2021. Her medical history was consistent with HTN, CAD, and COPD. The patient was previously hospitalized in October 2020 for moderate COVID19 infection; treatment consisted in corticosteroid therapy (dexamethasone 4 mg/ 2 times per day) and oxygen (c-PAP). During this admission, the diameter of the aneurysm was unchanged in comparison with a Duplex scan performed 10 months before (4.2 cm). She was discharged in January 2021 in good general conditions. At the last admission in May 2021, a CT scan was immediately performed showing a 5.2 cm maximum transverse diameter of the AAA with extra-luminal contrast. The AAA showed a short, hostile neck and open surgery under general anesthesia was preferred. The postoperative course was uneventful (ICU stay 3 days).

Case 3

An 82-year-old man was admitted for moderate COVID19 infection (confirmed by RT-PCR assay on rhino-pharyngeal swab [RPS]) with fever and bilateral interstitial pneumonia in December 2020. His medical history was consistent with HTN and DM. Three years before the patient had EVAR for aorto-iliac aneurysm and he was followed up for type 2 endo-leak from the right hypogastric artery (sac diameter 68 mm in November 2020). The previous endovascular repair extended to the external iliac artery in both sides. He was scheduled for endo-leak embolization, but the procedure was postponed during the pandemic. Corticosteroid therapy (dexamethasone 4 mg/ 2 times per day) and oxygen (c-PAP) were administered. Ten days after admission the patient suddenly complained of abdominal pain. He was hemodynamically unstable with hypotension and tachycardia. Angio CT showed retroperitoneal contained rupture of the right common and internal iliac aneurysm with a maximum diameter of 85 mm. The AAA had a short neck. The patient underwent immediately open surgery under general anesthesia. Surgery consisted of removal of the endoprosthesis and aortic reconstruction with a bifurcated Dacron graft. The postoperative course was uneventful with a 3-days ICU stay. CT scan performed 4 months after surgery showed no complications of the aortic reconstruction.

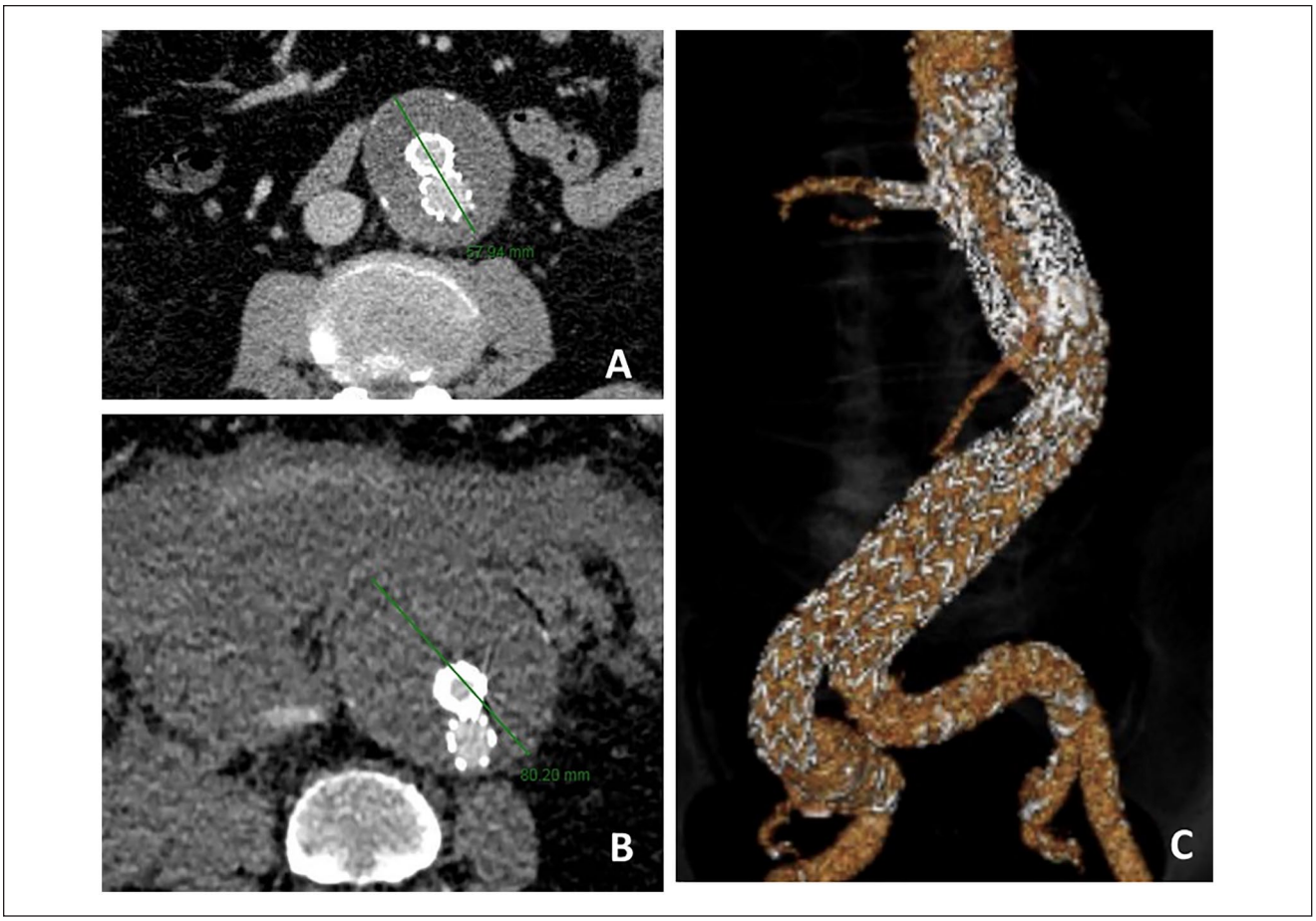

Figure 1. Patients N 4: CT scan shows abdominal aortic aneurysm sac with a diameter of 57 mm in October 2019 (A) and sudden increase of diameter (80 mm) in April 2020, (B) during admission for severe COVID-19 infection. The patient underwent immediate endovascular proximal aortic cuff placement with a double chimney (right renal and superior mesenteric arteries; the left renal artery was chronically occluded), (C): control CT scan control 12 months from surgery. CT, computerized tomography.

Case 4

An 81-year-old man underwent EVAR in 2018 for an AAA and he was followed up for type 2 endo-leak from lumbar arteries with serial U.S. scans (sac diameter 54 mm in October 2019). The patient was scheduled for endovascular treatment of the endo-leak, but he preferred to avoid admission during the pandemic. In April 2020, the patient was admitted for severe COVID-19 infection (confirmed by RT-PCR assay on rhino-pharyngeal swab [RPS]) with dyspnea and bilateral interstitial pneumonia. During hospitalization, the patient complained of sudden onset of abdominal and back pain; CT scan showed rupture of the AAA in the pararenal segment. The maximum transverse diameter of the aneurysm was 80 mm. The patient underwent endovascular proximal aortic cuff placement with a double chimney (right renal and superior mesenteric arteries; the left renal artery was chronically occluded). The postoperative course was uneventful with a 11-days ICU stay. No endo-leak and/or gutter were found at the 12-month CT scan follow-up (Figure 1).

Discussion

COVID-19 infection may increase directly or indirectly the risk for AAA rupture. “Indirect” potential influence of COVID19 infection on increased AAA rupture rate is related with the situation determined by the overwhelming severity of the pandemic. The pandemic has brought to several, unexpected consequences, including shortage of medical personnel and reluctance from patients to ask for medical help unless symptoms are severe. Admissions to hospitals have been reduced, avoiding visits for not-urgent conditions and deferrable elective surgeries. 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. During the COVID19 pandemic, it was not possible to perform an

accurate and timely follow-up of patients with AAA and vascular procedures were reserved only for emergency conditions.[1–3]

To these "indirect" risk factors for AAA rupture we should add the conceptual possibility of direct effects of COVID19 infection on AAA degeneration.

The inflammatory storm associated with SARS-CoV-2 infection and the deregulation of the immune system secondary to steroid therapy have the potentials to trigger different mechanisms, traditionally considered risk factors for altered collagen metabolism and consequent aneurysm degeneration. Although intracranial and coronary arterial aneurysms have been described with a higher prevalence than usual in adults and children with COVID-19 infection,[7] the relationship between COVID19 infection and AAA degeneration has been rarely described.[8–13] Several COVID19-related mechanisms may impact AAA degeneration, including augmented angiotensin converting enzyme (ACE)-II-AT1 receptor activity, increased elastin and collagen digestion by enzymes triggered by viral spike proteins in ACE2-negative myeloid cells, hypoxemia related with thrombosis of micro vessels of the aneurismal wall[13–16] In general, viral and bacterial systemic infections are associated with high levels of inflammatory cytokines. High systemic levels of inflammatory cytokines are characteristic of the so-called cytokine storm, a condition in which inflammation, a physiological defense response to infection, become overwhelming, representing a damaging factor for the host. It has been shown that the so-called "cytokine storm" may be severe in advanced COVID19 infection. Systemic high levels of inflammatory cytokines in COVID19 severe infection have been found in many studies. High levels of interleukin-1β, interleukin-6, IP-10, tumor necrosis factor, interferon-γ, macrophage inflammatory protein 1α and 1β have been documented in patients with COVID19 infection and correlated with the severity and clinical outcome of the disease[13]. These cytokines may activate enzymes (metallic proteinases) able to digest collagen and elastin favoring degeneration of the aneurismal wall. Inflammasome NLRP3 levels are correlated with aneurysm degeneration and are correlated also with disease severity in COVID19 infection.[13–18]

Another important "indirect" risk factor is represented by steroids therapy, which represents a cornerstone in hospitalized COVID19 patients. Inhibition of excessive inflammation through timely administration of steroids in the early stage of the inflammatory cytokine storm effectively prevents the occurrence of ARDS and protects the functions of the organs. For patients with progressive deterioration of oxygenation indicators, rapid imaging progression, and excessive inflammatory response, steroids improve clinical outcome.[13,17,18] Corticosteroid therapy have a potential double, contrasting effect: steroids may attenuate the inflammatory reaction reducing the activation of metallic proteinases and AAA degeneration; at the same time, steroids may determine reduced host immunological response and may lead to altered collagen metabolism, which could facilitate AAA rupture.

In all 4 patients, preoperative CT scan showed a significant peri-aneurismal inflammatory reaction. The inflammatory reaction may be just a consequence of the sudden increase in diameter of the aneurysm with compression of the peri-aneurismal lymphatic and venous system and/or a reaction of blood in the retroperitoneal space.

Finally, we should underline the importance of endovascular surgery in this clinical setting. Endovascular surgery can be performed often under loco-regional anesthesia, avoiding tracheal intubation, with reduced postoperative pain and intensive care unit permanence. The possibility of pulmonary complications, which may predispose and aggravate COVID-19 contamination and clinical course, is therefore potentially reduced. Hospital stay is shorter. Endovascular procedures which have the same results of standard surgery, or even a marginal less effective result, represent a valid option. During the acute phase of the pandemic outbreaks, we have preferred to perform endovascular procedures whenever possible.

Conclusion

AAA rupture is one of the possible collateral problems resulting from patient reluctance to seek timely medical attention and from the difficulties to perform an adequate screening and follow-up in patients with AAA in the acute phases of the pandemic.[5,19,20] Furthermore, patients with AAA suffering or recovered from COVID19 infection should be monitored more carefully because the inflammatory storm secondary to SARS-CoV-2 infection may favor AAA rupture.[21,22]

Declaration of Conflicting Interests

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ORCID iDs

Antonio Bozzani https://orcid.org/0000-0003-3274-6248
Antonio V. Sterpetti https://orcid.org/0000-0003-2125-1151

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