

## COVID 19

# SARS-COV-2 Pandemic for Patients with Chronic Obstructive Peripheral Arterial Disease: Impact of Interruption to Access According to Gender in a Single Center Experience

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**Background:** This retrospective study aims to evaluate the impact of interrupted services for peripheral arterial disease (PAD) patients and especially women in a single north-eastern Italian center over a period of 3 months prior to the pandemic, during the first (2020) and the second (2021) wave of contagion in northern Italy.

**Methods:** Patients with PAD at Rutherford stages 3 to 6 that required revascularization between March 2019 and March 2021 were classified into 3 groups, according to the period of treatment: the pre-pandemic period, the pandemic-20 period, and the pandemic-21 period.

**Results:** Twenty-eight patients were treated in the pre-pandemic period, 21 in the pandemic-20 period, and 39 in the pandemic-21 period. It was observed that in the both pandemic periods patients presented with more severe stages of limb ischemia, Rutherford 5 and 6 stages. During pandemic-20, patients underwent mostly open surgery, followed by hybrid procedures. No differences were observed between the 3 groups in major amputations, length of hospital stay, type of discharge, limb salvage and mortality. During long-term follow-up, limb salvage appeared to be significantly better in the pandemic-21 group. The gender analysis revealed a significantly reduced female proportion of overall treated patients in 2020 and 2021 compared to the pre-pandemic period. In the pandemic-20 this difference appears even more evident since treatments on females represented 19% of the total while in the same period of the previous year the male/female percentage was comparable (54% vs. 46%). The women admitted presented higher stages of disease and tended to have a longer hospital stay than men. At 12-month follow-up, limb salvage was similar between the 2 genders but was slightly worse in women.

**Conclusions:** An efficient reorganization of the vascular surgery services during the pandemic period guaranteed the quality and standard of treatment offered in the preceding periods. Among patients suffering from PAD the impact of the pandemic was greater for the female gender. It is therefore important that in addition to a reorganization of hospital services to provide adequate care for patients with ACOP in the pandemic period, greater information and awareness of women.

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Ann Vasc Surg 2023; 89: 129–134

<https://doi.org/10.1016/j.avsg.2022.09.046>

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Manuscript received: August 18, 2022; manuscript accepted: September 19, 2022; published online: 29 October 2022

## INTRODUCTION

The SARS-CoV-2 pandemic changed worldwide health service management organization, causing interruptions to diagnosis and treatment for all patients, including cancellation and delay of chronic illness surveillance.<sup>1</sup> As authors report, following the first wave of contagion (2020), patients with chronic peripheral arterial disease (PAD) presented with more severe stages of disease due to a delayed or absent health access.<sup>2</sup> Moreover as health services decline a significant rise also in lower limb amputations was observed<sup>3-4</sup>. Data regarding the effects of interrupted services during the initial and second waves of the pandemic are continuously emerging however little is known about gender differences in PAD patients during pandemic. Generally, gender-specific data on PAD are lacking and for women the disease is still under-recognized.<sup>5</sup>

This retrospective study aims to assess the impact of interrupted services for chronic PAD patients and especially in women, according to access type (elective versus urgent) and outcome (limb salvage versus amputation) in a single north-eastern Italian center over a period of 3 months prior to the pandemic, during the first (2020) and during the second (2021) wave of contagion in northern Italy.

## MATERIALS AND METHODS

This single-center retrospective observational study was conducted at Unit of Vascular and Endovascular Surgery at the University Hospital of Ferrara. The observational study was approved by the local Ethics Committee (Approval number 277/19) and patients provided informed consent to data collection. Patients were included in the analysis if they presented PAD at Rutherford stages 3 to 6 that required revascularization between March 2019 and March 2021. Patients diagnosed with acute ischemia of the lower limbs from distal embolization of cardiac origin were excluded. Then patients were classified into 3 groups, according to the period of treatment:

- Prepandemic period from March 2019 to May 2019.
- Pandemic-20 period from March 2020 to May 2020.
- Pandemic-21 period from March 2021 to May 2021.

The demographics characteristics, risk factors, comorbidities, previous revascularizations and all the factors related to the PAD revascularization, including type of intervention, major and minor amputation and length of hospital stay, were collected. In addition, for each patient, a follow-up period of 12 months was scheduled, when reinterventions, mortality, and other issues were monitored. For the stratification of the state of PAD the Rutherford classification was utilized.<sup>6</sup>

## Interventions

The strategy of revascularization was based on symptoms, disease extension, anatomic complexity, and patients' comorbidities and included endovascular procedures (PTA, stenting) and/or open surgery (endarterectomy, bypass surgery, minor or major amputation). The type of amputation was defined as the highest level of amputation performed for each patient. Minor amputation was defined as an amputation at the level of ankle joint and below. Amputations above this level were defined as major amputations.

The endpoints of the study included: successful revascularization defined as arterial or graft patency verified by ultrasound evaluation before discharge and at 30 days, reintervention at 30 days, major amputation at 30 days and 12 months, and limb salvage and mortality at 30 days and 12 months.

## The Pandemic Period and the Surgical Reorganization

Nationally, all elective surgical activities were suspended at the beginning of the SARS-COV-2 pandemic, with interventions reserved for urgent cases only.<sup>7</sup> Outpatient clinics were also suspended and follow-up controls interrupted. For patients with acute and critical limb requiring treatment, hospital admission and rapid revascularization were undertaken (depending upon hospital bed, disease severity, and operating theater availability).

At our center, a single weekly operating session and outpatient clinics were reintroduced in May 2020, with 3 operating sessions and 100% ward capacity reestablished by September 2020. As per hospital protocol, COVID patients requiring urgent vascular interventions were hospitalized in dedicated COVID wards and surgery was performed in dedicated COVID operating theaters. From September 2020, chronic PAD patients' clinical pathway included follow-up controls at the

**Table I.** Patients risk factors and comorbidities

Parameters	Pre-pandemic	Pandemic 20	Pandemic 21	P Value
Patients	28	21	39	
Age - y	77 ± 10	76 ± 8	73 ± 10	0.14
Female sex	13 (46)	4 (19)	10 (25)	0.047
Comorbidities				
Hypertension	23 (82)	20 (95)	34 (87)	0.39
Ischemic heart disease	15 (54)	12 (57)	21 (54)	0.96
Diabetes	11 (39)	11 (52)	21 (54)	0.47
CKD	6 (21)	7 (33)	8 (21)	0.50
COPD	2 (7)	0 (0)	10 (27) <sup>a</sup>	0.011
Obesity	0 (0)	2 (11)	8 (21) <sup>c</sup>	0.035
COVID-19 <sup>d</sup>	N/A	0 (0)	1 (3)	0.87
ASA class				
3	23 (82)	13 (62)	25 (64)	0.44
4	5 (17)	8 (38)	14 (36)	
Peripheral artery disease severity				
Rutherford stage 3/4	16 (57)	7 (33) <sup>b</sup>	14 (36) <sup>c</sup>	<0.001
Female patients	7 (54)	1 (25)	2 (20)	
Rutherford stage 5/6	12 (43)	14 (67) <sup>b</sup>	25 (74) <sup>c</sup>	
Female patients	6 (46)	3 (75)	8 (80)	
Previous vascular surgery				
Lower limb <sup>e</sup>	12 (86)	11 (84)	11 (100)	0.41
Aorta	0 (0)	1 (8)	0 (0)	
Carotid	2 (14)	0 (0)	0 (0)	
Other	0 (0)	1 (8)	0 (0)	

CKD, chronic kidney disease; COPD, chronic obstructive pulmonary disease.

<sup>a</sup> $P < 0.05$  respect to Pre-pandemic and Pandemic 20.

<sup>b</sup> $P < 0.05$  respect to Pre-pandemic.

<sup>c</sup> $P < 0.05$  respect to Pre-pandemic.

<sup>d</sup>Data available from 2020 season.

<sup>e</sup>Including both lower limbs.

outpatient clinics with imaging investigations (DUS, CTA, and peripheral angiography).

### Statistical Analysis

Data are presented as mean ± standard deviations or median (interquartile range) or number (percentage) according to data nature and distribution. Data distribution was verified with the Shapiro–Wilk test. The between-period comparison was carried out by means of chi-squared tests for categorical variables and by one-way analysis of variance or Kruskal–Wallis test for continuous variables. A  $P$ -value  $< 0.05$  was considered as statistically significant. Statistical analysis has been performed with MedCalc® Statistical Software version 20.014 (MedCalc Software Ltd., Ostend, Belgium).

### RESULTS

The analyses included 28 patients in the prepandemic period, 21 in pandemic-20, and 39 in

pandemic-21. During the first period, as expected, a reduced number of patients with chronic PAD was admitted, compared to prepandemic activity. However, it was observed that in the both pandemic periods patients presented with more severe stages of limb ischemia, Rutherford 5 and 6 stages (Table I). The mean age of patients was similar in the 3 periods but gender analysis revealed a significantly reduced female proportion of overall treated patients in 2020 and 2021 compared to the prepandemic period ( $P = 0.047$ ; Table I).

Differences were also found between the 3 periods in terms of hospital access. In pandemic-20, the majority of patients presented to emergency department as scheduled admissions were canceled (Table II).

As reported in table (2) in the prepandemic period and in the pandemic-21 period endovascular treatment was more frequently performed followed by open surgery and hybrid treatment. Interestingly during pandemic-20, patients underwent mostly open surgery, followed by hybrid procedures. No

**Table II.** Hospitalization characteristics

Parameters	Pre-pandemic	Pandemic 2020	Pandemic 2021	P Value
	28	21	39	
Hospital access type				
Emergent/Urgent	12 (43)	15 (71) <sup>b</sup>	16 (41) <sup>a</sup>	0.049
In Females (N°in tot)	6/13	3/4	4/10	
Elective	16 (57)	6 (29) <sup>b</sup>	23 (59) <sup>a</sup>	
Type of intervention				
Open surgery	8 (29)	11 (50)	10 (25)	0.76
In Females	3 (25)	3 (75)	3 (38)	
Major amputation	1 (f)	1 (m)	3 (1 f 2 m)	
Endovascular	15 (53)	4 (18)	21 (52)	
Hybrid	5 (18)	6 (27)	9 (23)	
Revascularization + minor amputation	2 (7)	4 (20)	5 (14)	
Length of hospital stay – d	13 ± 15	15 ± 12	11 ± 10	0.41
In females	14.1 ± 14.39	11 ± 5.23	12.20 ± 8.12	
Type of discharge				
Ordinary	23 (82)	18 (86)	35 (88)	0.51
Support structure	2 (7)	2 (10)	0 (0)	
In-hospital mortality	3 (11)	1 (5)	4 (10)	
Outcomes				
30 Days follow up				
Successful revascularization	25 (93)	16 (80)	30 (83)	0.31
Reintervention	3 (11)	4 (15)	6 (17)	
Revascularization	1 (3)	1 (5)	6 (17)	0.031
In females	0	0	4/10	
Minor amputation	0 (0)	1 (5)	0 (0)	
Major amputation	2 (7)	2 (10)	0 (0) <sup>a,c</sup>	
Limb salvage	26 (93)	18 (90)	36 (100)	0.11
In females	12 (92)	4 (100)	9 (90)	
12 months follow up				
Major amputation	1 (f)	2 (1f)	0	0.56
Limb salvage	25 (89)	16 (80)	36 (100)	0.07
In females	11 (85)	3 (75)	9 (90)	
Time to first reintervention, months (range)	6 ± 5	3 ± 1	4 ± 2	0.47
Follow-up, months	10 ± 5	10 ± 5	10 ± 4	0.99

<sup>a</sup>P < 0.05 respect to Pandemic 2020.

<sup>b</sup>P < 0.05 respect to Pre-pandemic and Pandemic 2021.

<sup>c</sup>P < 0.05 respect to Pre-Pandemic and to Pandemic 2020.

differences were observed between the 3 groups regarding major amputations. Nevertheless the rate of patients who underwent revascularization together with a minor amputation was higher in the pandemic-20 period. Length of hospital stay, type of discharge, and inhospital mortality were similar in all groups. Early outcomes were also comparable including successful revascularization although it was higher in the prepandemic group. No differences were observed in mortality, as described in Table II. In the pandemic-21 group it was observed a higher rate of reinterventions within 30 days but it did not include any minor or major amputation. In addition, the rate of limb salvage was higher in the latter group although not statistically significant. During long-term follow-up, rates

of limb salvage was observed to be significantly higher in the pandemic-21 group. Data regarding the female sex are reported in Tables II and III. Besides the low rates of hospital admissions in both pandemic periods, women were admitted in a higher stage of disease. No statistical differences were observed in length of hospital stay although appeared slightly greater in women. At 12-month follow-up, limb salvage was similar between the 2 genders but slightly worse in women.

## DISCUSSION

The SARS-CoV-2 pandemic has led to a singular modification and reorganization of all hospital

**Table III.** Data regarding early and late mortality in males and females in the 3 periods

	Prepandemic	Pandemic 20	Pandemic 21	P Value
Patients	28	21	39	
Mortality				
30 days	2 (7)	1 (5)	3 (8)	0.32
In Females (N°in tot)	0	1/4	2/10	
12 months	8 (29)	4 (20)	7 (18)	0.32
In Females (N°in tot)	6/13	1/4	0/10	

services worldwide. Being in 1 of the regions most affected by the pandemic in Italy, also in our hospital it was necessary to limit the flow of patients (e.g., the reduction of surgical activities and the suspension of outpatient activities) and enhance the assistance to patients with SARS-CoV-2.<sup>8</sup> Therefore, the bed capacity of intensive care unit was firstly increased, consequently reducing the number of ordinary hospital beds for all other pathologies and all outpatient checks were suspended. This reorganization made the care pathways insufficient both in terms of diagnosis, follow-up, and treatment for all clinical conditions other than SARS-CoV-2 infection.

In the field of vascular surgery, vascular surgical societies published guidelines regarding the management of patients with vascular disease during the pandemic, indicating as a priority the aortic aneurysmal pathology in the rupture phase or symptomatic carotid stenosis.<sup>9,10</sup> As reported in literature also in our study we observed a reversal of hospitalizations in the COVID period with a decrease in those in election and an increase in urgent ones.<sup>11,12</sup> This inversion was linked to the suspension of the scheduled operating sessions in the first pandemic period, which in turn prolonged the waiting list for treatment, even if not in a statistically significant manner.

Lancaster et al.<sup>2</sup> report that in the pandemic period, patients with PAD came to medical attention in more serious conditions than in the pre-COVID period, with the need to choose treatments already aimed at controlling complications and perioperative mortality. In our experience, a significant increase in the most advanced stages, 4 and 6, has been highlighted in the whole pandemic period, with a reduction of cases to stage 3. This reduction is probably also linked to the known fear of patients with controllable symptoms of going to hospital due to the risk of contagion and also due to the absence of outpatient activities that would have allowed them to be taken in charge for any treatment.

In the COVER study, a COVID-19 vascular service study,<sup>13</sup> it is described how in the pandemic period it was necessary to change the therapeutic

indications for patients with PAD with greater indication for amputation or palliative treatments compared to revascularization procedures for those with severe chronic ischemia and greater use of endovascular procedures such as first therapeutic option in cases of critical ischemia. In our experience, no significant changes in the indications for treatment have been observed thanks to an optimal organization of the surgical and anesthesia department which has allowed us to offer the best treatment for each case. However, endovascular treatments were less frequently performed due to the more severe stages of disease presentation but also due to the lack of personnel occupied for the pandemic emergencies. The lower rates of successful revascularization in both pandemic-20 and 21 groups together with the need of reintervention were predictable due to the more severe stage of disease at presentation. As reported in literature also in our study was found a higher rate of minor and major amputations during the pandemic.<sup>14</sup> Such finding was due to the higher number of patients with more severe disease in this period rather to more stringent surgical indications. During pandemic-21 after a better organization of all vascular surgery services, although patients presented still with advanced disease, management turned to be minimally influenced by the pandemic with an increase in elective treatments and a higher rate of limb salvage in the 12-month follow up.

An unexpected finding from this study is the significant reduction in female patients throughout the pandemic period (pandemic-20 and pandemic-21 groups) compared to the previous year when there were no differences between the 2 sexes. In pandemic-20, this difference appears even more evident since treatments on females represented 19% of the total while in the same period of the previous year the male/female percentage was comparable (54% vs. 46%). The reason for this difference could be attributed to several sociocultural factors. Galasso et al.,<sup>15</sup> argue that women have shown a greater perception of the severity of the pandemic

and greater compliance with the restrictive measures. Furthermore the arrival of the pandemic has resulted in an increase in family and domestic organization activities for the female population, giving priority to these activities and with a greater tendency to neglect their health.<sup>16</sup> Additionally, although the prevalence of PAD does not vary by gender,<sup>17</sup> women present a higher prevalence of asymptomatic and atypical PAD.<sup>18</sup> As a result of that, PAD, like cardiovascular diseases, remains underdiagnosed and undertreated. Taking into account the restricted population of this study, women were characterized by more severe stages of disease, required a longer hospital stay, and had lower rates of limb salvage.

The main limitations of this study are inherent in its single center, retrospective design. However, this small study highlights the increased incidence of more severe comorbidities and disease, which have important implications for the allocation of vascular resources for chronic PAD patients. Greater efforts in atherosclerotic disease and the risk of limb loss information and awareness, especially for women, are necessary.

## CONCLUSIONS

In conclusion, despite the restrictions imposed by the pandemic, the good reorganization of the local vascular surgery service ensured as much as possible the quality and standard of treatment offered in the preceding periods. Our experience, albeit limited, has also shown that among patients suffering from PAD the impact of the pandemic was greater for the female gender. It is therefore important that in addition to a reorganization of hospital services to provide adequate care for patients with PAD in the pandemic period, greater information and awareness of women about atherosclerotic disease and the risk of limb loss.

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