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# The Limitations of Social Behaviour Imposed by CoVid-19 Impacted the Perception and the Evolution of Peripheral Arterial Disease Negatively

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**Background:** The novel acute respiratory syndrome coronavirus 2 (SARS-CoV-2) pandemic imposed a national lockdown at the beginning of 2020. People faced social distancing, being forced to stay at home. Peripheral arterial disease (PAD) typically influences life habits and psycho-social relationship. It is now questionable how PAD can be affected by changes in lifestyle imposed by the Sars-CoV-19 Pandemic. This study's main objective is to evaluate how the limitations of social behavior set by Sars-CoV-19 Pandemic impact the perception and evolution of the disease in a group of patients with a diagnosed PAD.

**Methods:** The changes in the in the perception and the evolution of the PAD were evaluated by comparing results of a modified VascuQoI-6 quality of life (QoL) survey referring to the time frame defined "No-Sars-CoV-2 period" (from July to December 2019) with results referring to the time frame defined "Sars-CoV-2 period" (from January to June 2020). An overall score (range 4-60) was calculated, and a comparison between the two period studies was reported. Receiver Operating Characteristics (ROC) Curves evaluated a delta value for each patient with revascularization of lower limb peripheral arteries. Optimal cut-offs were chosen based on their specificity, sensitivity.

**Results:** One-hundred-two PAD patients gave their informed consent to take part in the study. A significant general worsening of patients PAD perception in the Sars-CoV-2 period was recorded for the following items: lower limbs health status perception; overall activity limitation; walking ability limitation; overall daily walking distance; lower limbs fatigue perception; concerns about PAD worsening; pain discomfort (P < 0.05). The pain intensity changed from  $4.7 \pm 2.9$  in the No-Sars-CoV-2 period to  $6.3 \pm 2.9$  in the Sars-CoV-2 period significantly (P < 0.001), even though analgesic drug intake did not increase considerably in Sars-CoV-2 period (P = 0.15). The overall score was 20.3  $\pm$  7.4 for the No-Sars-CoV-2 period and 27.4  $\pm$  7.6 in the Sars-CoV-2 period (P = 0.0001). The ROC curve built to analyze the relation between Delta-score and the need for revascularization identifies a cut-off > 8.5 (Area Under the Curve 0.5436; CI 95% 0.4252 to 0.6620) with a sensitivity and specificity respectively of 52.6% (CI 95% 37.26–67.52%) and 65.6% (CI 95% 53.40–76.08%).

**Conclusions:** Patients with PAD were significantly hit by all the restrictions and the social limitations imposed to reduce the Sars-CoV-19 virus diffusion. Our study confirms that the perception and the evolution of PAD were significantly affected during the "Sars-CoV-2 period".

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Abbreviations: PAD, Peripheral Artery Disease; QoL, Quality of Life; AF, Atrial Fibrillation; VAS, Visual Analogue Scale; ROC, Receiver Operating Characteristics.

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#### **INTRODUCTION**

The novel acute respiratory syndrome coronavirus 2 (SARS-CoV-2) pandemic hit Italy as one of the first Nations in Europe. The Italian Government imposed a national lockdown on the 11th of March, with an extreme restriction on people's movement. The whole healthcare system underwent great modifications in the following months, allocating appropriate resources to treat COVID-19 patients, increasing dedicated Intensive Care Unit beds, and identifying hub hospital and COVID-19-free hospital. With the decreasing number of COVID-19 affected and the reduction of hospitalization, from the 11th of June the national Government authorized the recovery of most activities, reducing the previous months' limitations.

These circumstances led to changes in social behavior.<sup>1</sup> People faced social distancing, being forced to stay at home. Therefore, stress levels raised and mental health support was provided though not equally distributed.<sup>2</sup> Patients' management also transformed. Several solutions to prevent inhospital and out-patients clinics infection were activated. However, due to the fear of getting affected, some patients did not come to clinicians' attention. The outbreak of COVID-19 caused overcrowding of Intensive Care Units - since the need for continuous vital function monitoring - and a more significant commitment of health care professionals. As a result, elective surgical procedures were delayed.<sup>3</sup>

The above situation hit different medical areas, including managing patients affected by the peripheral arterial disease (PAD). It is known that PAD influences life habits and psycho-social relationship. It is now questionable how PAD can be affected by changes in lifestyle imposed by the Sars-CoV-19 Pandemic.

This study's main objective is to evaluate how the limitations of social behavior imposed by the Sars-CoV-19 Pandemic impacted the disease's perception and evolution in a group of patients with a diagnosed PAD.

#### **MATERIALS AND METHODS**

# **Patient Population**

The inclusion criterion was a known condition of PAD before July 2019. PAD was defined as a chronic disease affecting the lower limbs characterized by a reduction of the vessel lumen from stenosis to occlusion and a brachial/ankle index <0.9.

The main exclusion criterion was the contemporary or previous affection of COVID-

**Table I.** Population baseline characteristics

Variables	N (Total population = 102)
Male (N, %)	60 (58.8%)
Age (years $\pm$ SD)	$75.1 \pm 11.3$
Diabetes (N, %)	42 (41.2%)
Dyslipidemia (N, %)	46 (45.1%)
Hypertension (N, %)	60 (58.8%)
Chronic kidney disease (N, %)	28 (27.5%)
Overweight (N, %)	24 (23.5%)
COPD ( <i>N</i> , %)	19 (18.6%)
Smoke ( <i>N</i> , %)	23 (22.5%)
Previous peripheral intervention	70 (68.6%)
(N, %)	
Leriche-Fontaine grading of PAD	
(N, %)	6 (5.9%)
Ι	16 (15.7%)
IIa	16 (15.7%)
IIb	2 (1.9%)
III	62 (60.8%)
IV	

\*COPD: Chronic Obstructive Pulmonary Disease.

19 to avoid any influence on the outcomes. The investigation does not aim to demonstrate a correlation between PAD and COVID-19 infection. Still, it only seeks to evaluate how the limitations of social behavior imposed by Sars-CoV-19 Pandemic impacted the perception and the evolution of the PAD. Patients were also excluded if they had a revascularization procedure in 2019.

#### Design

The study was realized through a prospective submission of a questionnaire to assess Quality of Life (QoL) in PAD people presenting at our out-patient vascular lab from July to September 2020. Patients were asked to participate voluntarily. Any participant gave informed consent for data processing for scientific research purposes.

We investigated changes in the perception and the evolution of the PAD by comparing results of the QoL survey referring to the time frame defined "No-Sars-CoV-2 period" (from July to December 2019) with those referring to the time frame defined "Sars-CoV-2 period" (from January to June 2020).

#### Survey

The questionnaire submitted to patients was based on VascuQol-6.<sup>4</sup> Some parts of the survey had been modified to better identify changes in the perception and the evolution of the PAD in the "Sars-CoV-2 period" compared to the "No-Sars-CoV-2 period".

The survey included demographic data, and ten items investigated: anamnestic connection,

motor ability limitation, disease burden, pain perception, and fulfillment of lower limb controls. Coronary artery disease, hypertension, diabetes mellitus, chronic obstructive pulmonary disease, renal disease (chronic renal insufficiency defined by serum creatinine >1.2 mg/dl), smoking history (any current or past regular use of tobacco), congestive heart failure, overweight (defined as Body Mass Index  $\geq$  25), history of cerebrovascular events (stroke and/or transient ischemic attacks), dyslipidemia and atrial fibrillation (AF) were taken in account as comorbidities.

It was also collected if the patient had any intervention for PAD during the two study periods.

The total questionnaire scores for each period ranged from 8 to 40. The first seven items had four options, which were scored from 1 to 4. Question #8 (pain Intensity) was scored from 0 to 10 based on VAS scale; question #9 (analgesic drugs intake) was scored from 0 (no drug) to and 1; question #10 regarding the execution of planned vascular follow-up examinations was scored to 0 (the patient fulfilled the protocol follow-up) to 1 point (miss vascular evaluation for any reason).

The Institutional Review Board approved the study protocol and informed consent, and all subjects gave informed consent. The ethical committee of the hospital was informed of the no-experimental design of the retrospective investigation and endorsed the study.

# **Statistical Analysis**

Continuous data were shown as mean values  $\pm$  standard deviation. Categorical variables were expressed as fractions. Student test was used for independent tests to match groups on continuous variables after demonstrating a normal distribution of the data.

Results of items 1-7 were graphically highlighted using a Radar graph reporting the percentage of patients' answers. The total score of each patient regarding the Sars-CoV-2 Period and No-Sars-CoV-2 period were also compared, and the resulting difference – defined Delta-Score - was calculated. The Delta-Score was studied by Receiver Operating Characteristics (ROC) Curves with revascularization of lower limbs peripheral arteries. Optimal cut-offs were chosen based on their specificity, sensitivity. All statistical analyses were performed using GraphPad Prism 9 (GraphPad Software Inc. San Diego, Calif).

# RESULTS

One-hundred-two PAD patients gave their informed consent to take part in the study. Sixty were males

(59%) and 42 females (41%) with an overall mean age of 75.1  $\pm$  11.3 years. Table I shows baseline patients' characteristics.

The most common comorbidities were diabetes (41%), dyslipidemia (45%), and hypertension (59%). Most of the patients were graded in stage II (n = 32, 31.4%) and IV (n = 62, 60.8%) of Leriche-Fontaine classification.

Table II reports results for the ten items under investigation and compares results for the two study periods. A significant general worsening of patients' PAD perception in Sars-CoV-2 period was recorded. The answers #1-7 regarding lower limbs health status perception, overall activity limitation, walking ability limitation, overall daily walking distance, lower limbs fatigue perception, concerns about PAD worsening, pain discomfort showed a significant worsening (P < 0.05). Fig. 1 gives an overview of changes in the scores by items.

The pain intensity changed from  $4.7 \pm 2.9$  in the No-Sars-CoV-2 period to  $6.3 \pm 2.9$  in the Sars-CoV-2 period significantly (P < 0.0001), even though analgesic drug intake did not increase considerably in COVID-19 period (P = 0.15).

Moreover, in the Sars-CoV-2 period, 22 patients (21.6%) did not fulfil the scheduled vascular examinations (P < 0.001).

The overall score was  $20.3 \pm 7.4$  for the No-COVID-19 period and  $27.4 \pm 7.6$  in the COVID-19 period (*P*=0.0001) (Fig. 2).

Thirty-eight patients underwent а revascularization procedure (29 endovascular vs. 9 surgical interventions) during the Sars-CoV-2 period. The score difference between the Sars-CoV-2 and the No-Sars-CoV-2 periods, defined as Delta-Score, was calculated for each patient and analyzed as a link to the need for revascularization. The ROC curve built to analyze the relation between Delta-score and the need for revascularization is shown in Figure 3. The ROC curve identifies a cut-off > 8.5 of the Delta-score (Area Under the Curve 0.5436; CI 95% 0.4252 to 0.6620) with a sensitivity and specificity respectively of 52.6% (CI 95% 37.26-67.52%) and 65.6% (CI 95% 53.40-76.08%). However, the curve was not informative enough, as it intercepted more than once the reference line, and no further analysis was made.

# DISCUSSION

Patients' perception of disease and QoL is often underestimated in clinical practice. However, it does have a significant impact on physical illness. According to the World Health Organization, "Health is a state of complete physical, mental and



**Fig. 1.** N° 1-8 survey's items results. Comparison between answers of "No-Sars-CoV-2 period" and "Sars-CoV-2 period" are shown in each graph.

N°	Item	Options	Answers No-Sars-CoV period	Answers Sars-CoV period	<i>P</i> value (<0.05)
1	Lower limbs	1-Very Good	22 (21.6%)	6 (5.9%)	P < 0.0001
	health status	2-Good	30 (29.4%)	10 (9.8%)	
		3-Poor	44 (43.1%)	56 (54.9%)	
		4-Very Poor	6 (5.9%)	30 (29.4%)	
2	Overall activity	1-Not limited at all	26 (25.5%)	8 (7.8%)	P < 0.0001
	-	2-Mild limitation	38 (37.2%)	14 (13.7%)	
		3-Moderate limitation	26 (25.5%)	38 (37.2%)	
		4-Severe limitation	12 (11.8%)	42 (41.2%)	
3	Walking ability	1-Not limited at all	28 (27.5%)	10 (9.8%)	P < 0.0001
		2-Mild limitation	46 (45.1%)	16 (15.7%)	
		3-Moderate limitation	24 (23.5%)	50 (49%)	
		4-Severe limitation	4 (3.9%)	26 (25.5%)	
4	Overall daily	1-At least 3 km	46 (45.1%)	16 (15.7%)	P< 0.0001
	walking	2-At least 2 km	16 (15.7%)	16 (15.7%)	
	U	3-At least 1 km	28 (27.5%)	26 (25.5%)	
		4- Zero km	12 (11.8%)	44 (43.1%)	
5	Lower limbs	1-Never	24 (23.5%)	14 (13.7%)	P = 0.0017
	weakness or	2-Few times	40 (39.2%)	28 (27.4%)	
	fatigue	3-Most of the times	30 (29.4%)	42 (41.2%)	
	0	4-Always	8 (7.8%)	18 (17.6%)	
6	Concern about	l-Never	24 (23.5%)	8 (7.8%)	P< 0.0001
	disease	2-Few times	58 (56.9%)	42 (41.2%)	
	worsening	3-Most of the times	16 (15.7%)	42 (41.2%)	
	0	4-Always	4 (3.9%)	10 (9.8%)	
7	Pain discomfort	1- None	28 (27.5%)	12 (11.8%)	P< 0.0001
		2-A little	32 (31.4%)	12 (11.8%)	
		3-Moderate	32 (31.4%)	30 (29.4%)	
		4-Very Much	10 (9.8%)	48 (47.1%)	
8	Pain intensity	1 to 10	$4.7 \pm 2.9$	$6.3 \pm 2.9$	P< 0.0001
9	Analgesic drugs	0-No	62 (60.8%)	48 (47.1)	P = 0.15
	use	1-Yes	40 (39.2%)	54 (52.9%)	
10	Lower limbs	0-Yes	98 (98%)	80 (78.4%)	P < 0.0001
	Examination fulfilment	1-No	4 (2%)	22 (21.6%)	

Table II. Questionnaire Items and results for No-COVID-19 period and COVID-19 period





Fig. 2. "No-Sars-CoV-2" and "Sars-CoV-2 periods' scores (mean  $\pm$  standard deviation)

social well-being and not merely the absence of disease or infirmity". In this line, the traditional clinical parameters only describe the physical state, while overall patients' wellness may be much more

**Fig. 3.** Receiver Operators Characteristics (ROC) curve of Delta-Score for reintervention.

complex to depict. As an example, it is known that from 30% to 60% of patients with PAD

have symptoms of depression, which are often unrecognized by their primary physician.<sup>5</sup>

The worldwide spread of the SARS-CoV-2 infection led National Government to apply unprecedented containment measures leading to the ban to get outside the home, except for essential activities. Quarantine was imposed, determining a substantial change in daily life, forcing the population to social distancing and self-isolation.

This social distancing and limitation may worsen the mental and emotional aspect of the disease and generated further psycho-physical stress<sup>6</sup> with a negative impact on the disease's perception and evolution, especially of those with documented benefits from regular physical activities.<sup>7</sup>

At the same time, COVID-19 pandemic conduced to the most important and radical reorganization of national healthcare systems. In Italy, highspecialized regional healthcare centers became a hub hospital for COVID patients while other centers remained exclusively COVID-free. The COVID-19 effect interested all areas of health care systems regarding not only the patients but also all the healthcare workers, from doctors, residents<sup>8</sup> and nurses. Access to hospitals was limited. Wearing masks became mandatory; no visitors were allowed to visit patients.

Most elective surgical and interventional procedures had been delayed. Also, vascular services reduced both surgical practice and clinic activity as abdominal aortic aneurysm screening.<sup>9</sup> Some out-patients clinics were closed temporarily, carrying the risk of diagnostic delay and eventual worsening of patients' clinical conditions. During COVID-19 pandemic, a significant reduction of hospital admissions for emergency events of acute myocardial infarction and stroke have been reported,<sup>10–11</sup> demanding attention by the scientific and healthcare communities and public regulatory agencies.

Also, medical therapy and rehabilitation programs got interrupted. Personal well-being for rare disease patients,<sup>12</sup> and oncological diagnosis got also impacted negatively.<sup>13</sup>

Vascular medicine and vascular surgery activities were adversely impacted: a reduction of revascularization rate for PAD associated with worse outcomes has been reported.<sup>14</sup> Li et al. confirmed that less patients underwent surgical procedures during the pandemic and the disease stage was more severe than expected.<sup>15</sup>

However, PAD is a chronic disease strongly related to general health status, mental health status, and physical activity needing a scheduled follow-up and precise medical management.<sup>16</sup> A

6-Minute Walking Time distance independently<sup>17</sup> predicted better physical and social aspects of QoL in people with intermittent claudication. It supports how physical activity and QoL, which experienced a revolution by the COVID-19 restrictions, are strictly intertwined in PAD patients.

Our study aimed to describe the patient's perception and evolution of PAD during the COVID-19 pandemic, as never reported by focusing on patients' QoL.

During the Sars-CoV-2 period the overall lower limb health status worsened, as demonstrated by the significant increase of our pre-defined score (from 20.3  $\pm$  7.4 to 27.4  $\pm$  7, P = 0.0001). It was due to substantial limitations towards carrying out the overall activity. Also, walking ability resulted in more limitations because of the impossibility of walking outside due to restrictions disposals. The fear of contagion also contributed to forcing people to stay at home. These elements led to a progressive reduction of the patients' physical activity with a significant worsening of the perception of their condition. The overall daily walk was strictly linked to the limitations of social behavior imposed by the pandemic; in No-Sars-CoV-2 period 45% of patients were able to walk at least 3 km a day, while in Sars-CoV-2 period they decrease to 16%, and 43% walk less than 1 km a day or do not walk anymore. The reduced mobility and the reduction of overall activity also led to weakness or fatigue in the lower limbs (Figure 1).

Notably, the "concerns about disease worsening" (item 6) was significantly changed as well (*P* <0.0001).

Pain is an aspect to be considered, as it is a substantial part of PAD spectrum of symptoms. Improvement or worsening of the pain can also affect patients' autonomy, activity, and emotional discomfort. PAD patients' mobility is already reduced due to age and comorbidities, so pain is an essential factor in standard immobilization. Our survey revealed a significant increase in pain intensity during Sars-CoV-2 period (VAS from 4.7  $\pm$  2.9 to 6.3  $\pm$  2.9, P < 0.0001), without an equivalent growth of analgesic drug intake (P=0.15). At first impression, this could be a misleading circumstance. We hypothesized that the general restrictions and the fear of being infected could have forced patients not to go to their general practitioners and pharmacies to have prescriptions and buy analgesics.

Another critical point from our investigation was the rate of non-accomplishment of scheduled vascular follow-up examinations: 21% of patients did not undergo their regular exams due to fear of in-hospital infection. Of note, there was only a small reduction in, and not a cessation of, out-patient services in our hospital, and vascular emergency surgery was always guaranteed.

Our survey also tried to remark as an initial fall in PAD evolution may influence PAD prognosis and outcome severely. The ROC curve built to analyze the relationship between the Delta-score and the need for revascularization failed to identify a cut-off value with significant sensitivity and specificity. However, the information contained in the curve (Area Under the Curve for value > 8.5 was 0.5436; CI 95% 0.4252 to 0.6620) reveals a trend of correlation between worsening of QoL scores and the need for revascularization, which may be further analyzed in a larger cohort of patients.

Finally, our investigation's main deduction is that PAD patients were affected negatively by the limitations of social behavior. Considering that the epidemic condition is still ongoing worldwide, and there is no reason to think about a natural decrease in vascular disease incidence, the prompt diagnosis, and treatment of the latest should not be disregarded. It is unfair that the management of a potentially treatable condition is euthanized at the price of another. We want to recommend that: in-patient vascular surgery facilities should not be reduced or stopped in any hospital; care systems should be prone to offer high-quality care for the symptomatic vascular disease at all time but in particular at times of crisis; general practitioners and the public should be aware that vascular team is fully operative all time.

Everybody involved in the health care system should be aware that the task of a correct diagnosis and prompt treatment of PAD and all vascular emergencies should continue irrespectively from the terrible COVID-19 pandemic situation we all are experiencing.

## CONCLUSION

PAD patients were significantly hit by all the restrictions and the social limitations imposed to reduce the Sars-CoV-19 virus diffusion. Even when moderate, physical activity has a significant positive impact on the disease and the perception of PAD patients' illness and should always be evaluated by QoL surveys. Our study confirms that the perception and the evolution of PAD were significantly affected during the "COVID-period".

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