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Impact of the COVID-19 pandemic on patients with peripheral arterial disease in China: a multicenter cross-sectional study

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This study aims to understand the repercussions of the COVID-19 pandemic on hospitalized patients with peripheral arterial disease (PAD) in China, who did not contract SARS-CoV-2. We conducted a multicenter cross-sectional analysis comparing the characteristics and outcomes of hospitalized PAD patients across two distinct periods: Pre-pandemic (P1, from January 2018 to December 2019) and during the pandemic (P2, from January 2020 to December 2021). During P1, 762 hospitalized patients were treated, with an average age of 72.3 years, while 478 patients were treated in P2, with an average age of 65.1 years. Notably, hospitalized patients admitted during the pandemic (P2) exhibited a significantly higher incidence of chronic limb-threatening ischemia (CLTI, 70% vs 54%), diabetic foot infection (47% vs 29%), and infra-popliteal lesions (28% vs 22%). Furthermore, these patients demonstrated a marked deterioration in their Rutherford category and an increased mean score in the Wound, Ischemia, and foot Infection classification system (WIfI). Treatment during the pandemic emerged as a predictor of reduced procedural success and increased major adverse limb events. Factors such as the presence of diabetic foot infection, renal impairment, and deteriorating WIfI scores were identified as independent risk indicators for major adverse limb events. Our results demonstrate that intensive care was provided to severe cases of PAD even during the challenging circumstances of the COVID-19 pandemic. Despite the unprecedented pressures on healthcare systems, patients with severe PAD, particularly those with CLTI, continued to receive necessary in-patient care. The findings underscore the importance of timely medical interventions and extended follow-up for patients exhibiting high-risk factors.

Keywords Peripheral arterial disease, Critical limb threatening ischemia, COVID-19, Diabetic foot infection, Amputation

Abbreviations

COVID 19 Coronavirus 2019 (SARS-CoV-2)
PAD Peripheral arterial disease
ALI Acute limb ischemia

WIfI Wound, ischemia and foot infection classification system

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CLTI Chronic limb threatening ischemia

DFI Diabetic foot infection AFS Amputation free survival

LS Limb salvages

MALE Major adverse limb events

F- MALE Freedom from major adverse limb events

MACE Major cardiovascular events
MAEs Major adverse events
ER Emergency room
LOS Length of hospital stay
DM Diabetes mellitus

The COVID-19 (SARS-CoV-2) pandemic has profoundly disrupted global healthcare service. Amidst a multitude of unfavorable consequences, the impact of COVID-19 on the cardiovascular system is prevalent, variable, and debilitating, thus warranting heightened attention^{1,2}. Peripheral arterial disease (PAD) patients, in particular, have manifested a range of symptoms from acute lower limb pain and gangrene to subtle chilblain-like signs during this period³. The systemic repercussions of the virus intensify the risk of severe complications in these patients[^3^], underscoring the need for prompt clinical intervention⁴. The pandemic's strain on healthcare resources in Western countries led to the postponement or cancellation of elective surgeries and revascularization procedures for PAD patients⁵⁻⁹. This shift in priorities, aimed at battling COVID-19, has unfortunately resulted in heightened complications for infected PAD patients, including critical limb ischemia and amputations¹⁰. However, the outcomes for PAD patients uninfected by SARS-CoV-2 during the pandemic remain ambiguous due to limited data on their prevalence and clinical presentation.

China, among nations with populations exceeding 100 million, boasts the lowest cumulative confirmed COVID-19 cases (503 K) and deaths (5.2 K) as of July 7, 2023¹¹. The nation's stringent Zero-COVID and lockdown strategies have been pivotal in curbing the virus's spread¹². Owing to these measures, COVID-19 cases in mainland China have been sporadic, with an exceedingly low transmission rate among hospitalized patients between 2020 and 2021. This unique scenario offers a distinctive perspective on the experiences and outcomes of PAD patients unaffected by SARS-CoV-2 during the pandemic. Our study endeavors to explore the impact and clinical characteristics of these hospitalized PAD patients.

Methods Study design

We conducted a cross-sectional study using data from four prominent tertiary medical centers in China that regularly admit Peripheral Arterial Disease (PAD) patients. Our aim was to discern the specific effects of the COVID-19 pandemic on PAD patient outcomes. We observed over 48 months, bifurcated into: Period 1 (prepandemic: January 2018-December 2019) and Period 2 (pandemic: January 2020-December 2021). Only PAD patients hospitalized during these times, with a negative test for SARS-CoV-2, were considered.

Ethics

The study protocol received approval from the Institutional Review Board of Beijing Friendship Hospital (No. 2020-P2-073) and was in line with the Declaration of Helsinki's guidelines.

Data collection and participants

Data was sourced from a shared database across the four medical centers. This database encompassed patient demographics, comorbidities, medications, presentation nature, symptom onset to presentation duration, presentation to intervention duration, intervention types, complications, and amputation types. The data reflects the characteristics and outcomes of PAD-related hospitalizations in Beijing, China, during our study's timeframe. Symptomatic PAD was categorized into intermittent claudication, acute limb ischemia (ALI), and chronic limb-threatening ischemia (CLTI) as following the guidelines^{13,14}.

Selection criteria and procedural data

CLTI patients, that is patients with symptoms like ischemic rest pain, gangrene, or ulcers lasting over two weeks, were included. Those with venous, traumatic, embolic, or non-atherosclerotic origins were excluded¹⁵. ALI of thrombotic origin was differentiated from embolic origin based on clinical presentation, imaging findings, and patient history, in accordance with established diagnostic criteria¹⁶. We gathered procedural and clinical data, including the Rutherford classification¹⁷ and the Wound, Ischemia, foot Infection (WIfI) Classification System by the Society for Vascular Surgery (SVS)^{18–20}. The WIfI mean score was computed as a clinical outcome predictor¹⁹. All participating patients provided informed consent for anonymous data collection and management.

Selection criteria and definitions

Patients with a Rutherford class of 3 or higher, including symptoms like intermittent claudication, rest pain, and rapidly deteriorating limb conditions, were considered. Procedural success for lower extremity interventions was marked by successful device or technique use to restore vessel patency with < 30% residual stenosis, without vessel rupture, distal embolization, thrombosis, access complications, and major adverse cardiovascular events (MACE)^{15,21}. Technical success for aortic and iliac artery revascularizations was noted by a lesion pressure

gradient reduction to < 10 mm Hg 8 . Both ischemic and neuropathic diabetic foot infections(DFI) were included in this studv 22 .

During lockdown, the Chinese government imposed stringent measures. Only essential outings were permitted, and COVID-19 patients had to be referred to specific facilities. Non-urgent surgeries were halted, but emergency treatments continued as usual. Based on evaluations, patients were medicated or underwent revascularization, which could be endovascular, surgical, or hybrid. An amputation was any procedure resulting in a lower extremity removal.

Outcomes

Primary outcome: the main focus was on the procedural volume throughout the study duration. We assessed procedural volumes for the entire cohort, further delineated by registry modality, and classified as elective or emergency procedures. We compared the relative volume every three months between Period 1 and Period 2, considering factors like anatomical location, urgency, and presenting symptoms.

Secondary outcomes: these encompassed the rates of procedural success and both major and minor amputations. We analyzed the differences in clinical outcomes between the two study periods for the entire cohort and further by presenting symptoms. Additionally, we conducted a multivariate logistic regression analysis to identify independent predictors for procedural success (successful revascularization) and Freedom from Major Adverse Limb Events (MALE, as defined by the Society for Vascular Surgery's reporting standards for endovascular treatment of chronic lower extremity PAD²¹). A major amputation was defined as any procedure resulting in amputation above the ankle¹⁸.

Statistical analysis

Continuous variables are displayed as means with SD and compared using t-tests, or as medians with IQR and compared with Mann–Whitney tests if non-normally distributed. Categorical variables are displayed as frequencies/percentages and compared using chi-squared or Fisher's exact test as appropriate. Mantel–Haenszel chi-square test was used for grading variables. Change of procedure volumes between P1 and P2 were computed and displayed graphically. Multivariate Cox regression analysis were used to determine potential independent factors which may predict primary patency and freedom from MALE. A two-tailed probability value less than 0.05 was considered statistically significant. Statistical analysis was performed using GraphPAD Prism* 9 (GraphPAD Software, San Diego, California, USA) and R (R Foundation for Statistical Computing, Vienna, Austria; http://www.r-project.org).

Results

Patient demographics and presentation

As shown in Table 1, the study was conducted over two distinct periods, encompassing 1240 patients who underwent medication, elective, or emergency interventions. Period 1 (P1) comprised 762 patients, while Period 2 (P2) included 478. For a more detailed breakdown of time periods, please refer to Fig. 1.. The average age differed significantly between the two periods: 72.3 ± 16.2 years in P1 compared to 65.1 ± 10.9 years in P2 (P < 0.001). Both cohorts had comparable rates of CAD, stroke, hypertension, and hypercholesterolemia. However, there were marked differences in gender distribution, smoking prevalence, DM, and instances of renal impairment. Specifically, P1 had a higher male-to-female ratio (543:219) than P2 (306:172) (P = 0.008). Smoking was more prevalent in P1 (82%) than in P2 (75%) (P = 0.003). DM was more common in P2 (64%) compared to P1 (58%) (P = 0.035), and renal impairment was also more frequent in P2 (17% vs. 9% in P1, P < 0.001).

In terms of clinical presentation, P2 patients were less likely to have claudication (8% vs. 31% in P1, P<0.001) but showed increased rates of acute limb ischemia (ALI) (18% vs. 12%, P=0.003), CLTI(70% vs. 54%, P<0.001), and diabetic foot infections or tissue loss (47% vs. 29%, P<0.001). Further analysis revealed that P2 patients with CLTI and ALI had more severe conditions, as evidenced by higher Rutherford grades (P<0.001) and WIf1 scores (P=0.009). Anatomically, while there were no significant differences in iliac, femoropopliteal, and multi-level lesions between the periods, P2 saw fewer iliac lesions (13% vs. 18% in P1, P<0.001) but more infra-popliteal lesions (28% vs. 22%, P=0.018).

Procedural characteristics

The procedural attributes of the study are detailed in Table 2, both for the entire cohort and when segmented by urgency and intervention type. Over the two periods, medication usage remained relatively consistent (23% in P1 vs. 19% in P2, P = 0.084). Elective procedures saw a significant drop in P2 (46% vs. 64% in P1, P < 0.001), while emergency interventions surged (35% vs. 13% in P1, P < 0.001). In P2, there was a noticeable rise in endovascular and amputation procedures, whereas surgical and hybrid procedures saw a decline. Limb preservation rates during the perioperative phase also decreased during P2 (92% in P1 vs. 79% in P2, P < 0.001). Figure 2 depicts the monthly procedural volume shifts and the emergency procedure proportions.

Of the 966 patients who underwent revascularization (526 in P1 and 440 in P2), 63 (12%) in P1 and 101 (23%) in P2 later had major or minor amputations. A significant drop in total procedures was evident at the start of the COVID-19 pandemic (Jan–Mar 2020) compared to the preceding months (Oct–Dec 2019). This decline was paired with a rise in emergency procedures (from 24 to 76%) and amputation rates (from 12 to 49%, Fig. 2). Although emergency procedures began reverting to pre-pandemic levels by mid-2020, they surged again towards the end of the year. This trend continued into 2021, though with a slight reduction in amputation and emergency procedures compared to 2020.

Endovascular interventions were predominant in both periods. While there was a slight increase in P2, it wasn't statistically significant (60% in P2 vs. 54% in P1, P = 0.051). On the other hand, surgical (10% in P2 vs. 18%

Variable	Period 1 (N=762)	Period 2 (N = 478)	P Value
Age (years)	72.3 ± 16.2	65.1 ± 10.9	< 0.001
Sex (M:F)	543:219	306:172	0.008
Smoker, n (%)	625 (82)	358 (75)	0.003
DM, n (%)	442 (58)	306 (64)	0.035
CAD, n (%)	236 (31)	163 (34)	0.251
Stroke, n (%)	84 (11)	39 (8)	0.101
Hypertension, n (%)	594 (78)	387 (81)	0.205
Hypercholesterolemia, n (%)	381 (50)	258 (54)	0.178
Renal impairment, n (%)	69 (9)	81 (17)	< 0.001
Clinical presentation, n (%)			
Claudication	236 (31)	38 (8)	< 0.001
ALI	91 (12)	86 (18)	0.003
CLTI	411 (54)	334 (70)	< 0.001
Others	24 (3)	20 (4)	1
DFI	220 (29)	224 (47)	< 0.001
Rutherford categories of CLTI, n (%)			
3-4	289 (38)	100 (21)	
5	381 (50)	272 (57)	
6	92 (12)	106 (22)	
Registration of critical lesion(s), n ([%)		
Iliac	137 (18)	63 (13)	0.471
Femoro-popliteal	274 (36)	191 (40)	0.156
Infra-popliteal	167 (22)	133 (28)	0.018
Multi-level	184 (24)	91 (19)	0.895
WIfI mean score, n (%)			
0-1	175 (23)	86 (18)	
2	458 (60)	254 (53)	
3	129 (17)	138 (29)	

Table 1. Patient demographics and presentation during Period 1 (prepandemic) and Period 2 (pandemic period). *DM* diabetes mellitus, *CAD* coronary artery disease, *Renal Impairment* indicated as eGFR < 60 ml/min, *ALI* acute limb ischemia, *CLTI* chronic limb-threatening ischemia, *WIfI* wound, ischemia and foot infection classification system, *DFI* diabetic foot infection.

in P1, P<0.001) and hybrid procedures (11% vs. 16%, P<0.018) saw a decline in P2. Notably, major amputation procedures rose significantly in P2 (13% vs. 5%, P<0.001), aligning with the increase in emergency interventions.

In-hospital outcomes

Table 3 provides a detailed breakdown of in-hospital outcomes, segmented by presenting symptoms. During the two periods, there were 23 deaths in P1 and 30 in P2. P2 witnessed a notable rise in both reintervention (9.6% vs. 5.0%, P = 0.002) and death rates (6.3% vs. 3.0%, P = 0.006) compared to P1. Concurrently, there was a significant drop in procedural success rates in P2 (83.1% vs. 88.1%, P = 0.013). The median total length of stay (LOS) was notably longer in P2, with 6 days (ranging from 1 to 10 days) compared to P1's 4 days (ranging from 0 to 6 days, P < 0.001).

The study participants were categorized into three subgroups based on their symptoms: claudication, CLTI, and ALI. For those with claudication and ALI, the procedural success and death rates remained consistent across both periods (P > 0.05, Table 3). Despite fewer hospitalizations for claudication in P2 (P < 0.001), reintervention rates surged (3.8% in P1 vs. 13.2% in P2, P = 0.015). On the other hand, hospitalizations for both CLTI (54% vs. 70%, P < 0.001) and ALI (12% vs. 18%, P = 0.003) saw a significant increase in P2. Specifically, the CLTI group experienced a higher death rate in P2 (2.7% vs. 5.7%, P = 0.038). Procedures in P2 were linked to decreased success rates but increased reintervention and death.

A logistic regression analysis was conducted to pinpoint predictors of procedural success and freedom from major adverse limb events (MALE, Fig. 3). Seven factors emerged from the univariate logistic regression analysis for both outcomes, DFI, amputation, renal impairment, presentation in P2, CLTI, ALI, and a WIfI mean score of 3 (Supplemental Table S2). In univariate analyses, renal impairment and treatment during P2 were significantly tied to procedural success. Yet, in the multivariate analysis, only presentation during P2 (OR 0.55, 95% CI [0.39-0.79], P = 0.001, Fig. 3A) stood out as a significant independent risk factor for diminished procedural success. In a further multivariate analysis, DFI (OR 0.50, 95% CI [0.29-0.856], p = 0.011), renal impairment (OR 0.37, 95% CI [0.21-0.62], P < 0.001), treatment during P2 (OR 0.52, 95% CI [0.36-0.74], P < 0.001), and a WIfI mean score of 3 (OR 0.18, 95% CI [0.12-0.28], P < 0.001) were identified as independent predictors of reduced

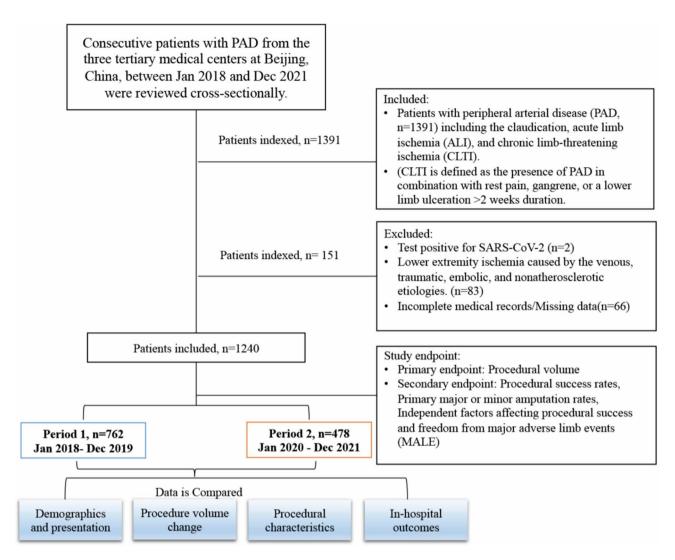


Fig. 1. Study flow diagram. *PAD* peripheral arterial disease, *ALI* acute limb ischemia, *CLTI* chronic limb threatening ischemia, *MALE* major adverse limb events.

Variable	Period 1 (N = 762)	Period 2 (N=478)	P Value
In-hospital management, n (%)			•
Medication	175 (23)	90 (19)	0.084
Elective intervention	488 (64)	220 (46)	< 0.001
Emergency intervention	99 (13)	168 (35)	< 0.001
Endovascular	37 (38)	84 (50)	
Surgical	20 (20)	18 (11)	1
Hybrid	26 (26)	15 (9)	1
Amputation	16 (16)	51 (30)	1
Revascularization, n (%)	N = 526	N=440	
Endovascular	284 (54)	265 (60)	0.051
Surgical	94 (18)	40 (10)	< 0.001
Hybrid	85 (16)	48 (11)	0.018
Major amputation	26 (5)	57 (12)	< 0.001
Minor amputation/debridement	37 (7)	44 (9)	0.098
Limb preservation, n (%)	699 (92)	377 (79)	< 0.001

Table 2. Procedural characteristics during Period 1 and Period 2. Major amputation defined as any above the ankle amputation.

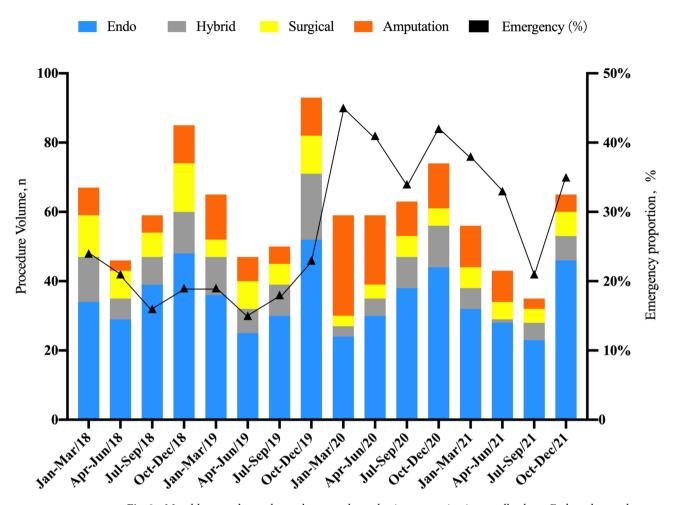


Fig. 2. Monthly procedure volume change and nonelective proportion in overall cohort. *Endo* endovascular procedure, *Hybrid* hybrid procedure, *Surgical* surgical repair, *Emergency*% proportion of emergency procedures in total volume. Black triangle accounted for emergency procedures of total procedures in each period.

Variable	Period 1 (N = 762)	Period 2 (N=478)	p value		
Overall					
Procedural success, n (%)	671 (88.1)	397 (83.1)	0.013		
Reintervention, n (%)	38 (5.0)	46 (9.6)	0.002		
Death, n (%)	23 (3.0)	30 (6.3)	0.006		
Total LOS, days, median (IQR)	4 (0, 6)	6 (1, 10)	< 0.001		
Claudication	236 (31.0)	38 (7.9)			
Procedural success, n (%)	222 (94.1)	34 (89.5)	0.289		
Reintervention, n (%)	9 (3.8)	5 (13.2)	0.015		
Death, n (%)	5 (2.1)	2 (5.3)	0.254		
CLTI	411 (53.9)	334 (69.9)			
Procedural success, n (%)	371 (90.3)	294 (88.0)	0.070		
Reintervention, n (%)	20 (4.9)	24 (7.2)	0.182		
Death, n (%)	11 (2.7)	19 (5.7)	0.038		
ALI	91 (12.0)	86 (18.0)			
Procedural success, n (%)	78 (85.7)	69 (80.2)	0.331		
Reintervention, n (%)	9 (9.9)	12 (14.0)	0.403		
Death, n (%)	7 (7.7)	9 (10.5)	0.520		

Table 3. In-hospital outcomes in overall population and by presenting symptom during Period 1 and Period 2. *CLTI* chronic limb-threatening ischemia, *ALI* acute limb ischemia, *IQR* interquartile range.

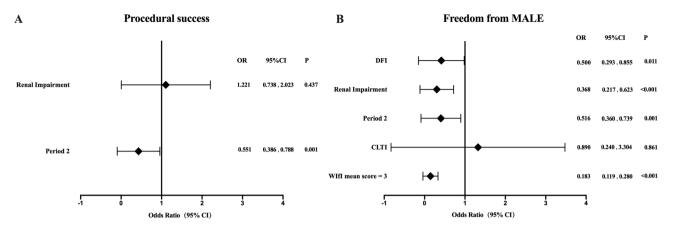


Fig. 3. Multivariate logistic regression analysis for the independent factors affecting procedural success and freedom from MALE. *MALE* major adverse limb events, *WIfI mean score* mean score of Wound, ischemia and foot infection classification system¹⁹.

freedom from MALE (Fig. 3B). Importantly, CLTI wasn't an independent risk factor for either procedural success or freedom from MALE.

Discussion

The COVID-19 pandemic has reshaped healthcare delivery globally, with a notable impact on PAD treatment^{8,9}. While there have been reports of reduced lower extremity revascularization in Europe and the USA^{9,10}, the effects on PAD and Diabetic Foot Infection (DFI) in Asia are less clear. Our study offers a detailed snapshot, revealing shifts in patient demographics, clinical features, and PAD procedural volumes during the pandemic. Key observations include a marked rise in patients (Table 1) with CLTI, ALI, and DFI during the pandemic (P2) compared to the pre-pandemic period (P1). These patients also showed a higher prevalence of DM and renal impairment upon admission during P2 (Table 1). Procedural volumes saw a significant dip in P2, with a corresponding rise in emergency procedures and major amputation rates.

In line with the Centers for Disease Control and Prevention guidelines, Beijing medical institutions suspended non-urgent elective cases from January 20, 2020. This led to a 25% drop in PAD cases in the initial three months, followed by a 10% rise in the next three months (Fig. 2). The suspension of elective cases resulted in a surge of emergency cases with complex arterial diseases and associated conditions like DM, DFI, and renal impairment during P2 (Table 1). To manage the pandemic's challenges, we adopted special triage systems and therapeutic modifications²³. Endovascular procedures for PAD were prioritized due to their reduced surgical trauma, quicker operation time, and shorter hospital stays. This strategy was vital in optimizing limited medical resources and minimizing COVID-19 transmission risks. Consequently, P2 saw a rise in endovascular procedures and a decline in open and hybrid surgeries.

However, global studies present varied findings regarding procedural volume changes during the pandemic. Many indicate that PAD patients experienced intervention delays, potentially heightening major limb amputation rates in P2^{8,9,24,25}. Contrarily, a study from Northern Italy showed stable urgent aortic cases but a drop in emergency room admissions for critical limb ischemia post-lockdown⁷. Our data indicates that P2 patients had a higher likelihood of presenting with ALI, CLTI, and DFI, leading to more emergency procedures. This shift might be attributed to pandemic-related restrictions and patients' fear of in-hospital infection^{6,7}. Other studies report²⁶ an increase in complex peripheral interventions for wound patients, yet high-volume centers with experienced operators performing endovascular treatments showed no rise in overall acute amputation rates. Our analysis revealed that P2 patients had worse Rutherford and WIf1 stages, which have been linked to prolonged wound healing and increased amputation rate^{10,18,25,27}. The rise in DFI and infra-popliteal lesions in P2 further exacerbated these stages. The pandemic's impact on PAD patients may be profound, with reduced physical activity leading to a heightened risk of thromboembolic diseases^{28,29}. This sedentary behavior, coupled with the therapeutic benefits of exercise on the vascular system³⁰, might explain the worsened Rutherford and WIfI stages in P2. Despite COVID-19 limitations, an efficient angioplasty service was sustained with reduced wait times. High mortality among hospitalized patients suggests the need for earlier, more aggressive referral and treatment of CLTI cases³¹.

DFI, a significant MALE risk factor, saw higher amputation rates in P2, possibly due to delayed admissions and elective procedure cancellations. These patients also faced reduced procedural success but increased reintervention and mortality rates. While some studies found no significant difference in limb salvage rates between the pre-pandemic and pandemic periods²⁷, others reported increased in-hospital amputation rates during the pandemic¹⁰. Our findings align with the latter, emphasizing the need for timely intervention, especially during pandemic outbreaks.

The COVID-19 pandemic has significantly altered healthcare-seeking behaviors and hospital admission practices, potentially influencing our study outcomes³². It is plausible that patients with milder symptoms of PAD, particularly those experiencing claudication, may have refrained from seeking hospital care during the P2. This behavioral shift could have resulted in an apparent increase in the proportion of severe PAD cases among

hospitalized patients. Furthermore, healthcare systems likely adapted their management strategies for mild PAD cases between the P1 and P2 periods. Patients who might have been hospitalized pre-pandemic may have been managed as outpatients or kept under observation during the pandemic, reflecting necessary adaptations in healthcare delivery³³. These changes in patient behavior and hospital practices could explain the observed differences in PAD severity between P1 and P2, rather than solely representing an actual increase in disease severity during the pandemic.

In conclusion, the COVID-19 pandemic has undeniably impacted PAD treatment, emphasizing the necessity for adaptive healthcare strategies to ensure optimal patient care during such global crises. While the acute phase of the COVID-19 pandemic has subsided, our findings have potential implications for future public health crises, highlighting the need for robust healthcare systems that can maintain essential services for patients with PAD even during emergencies.

Limitation

This study has several limitations that warrant consideration. Firstly, the findings are largely contingent on the severity of the COVID-19 wave in Beijing, China, potentially limiting their generalizability to other regions or countries. The impact of the pandemic varies geographically, influencing healthcare-seeking behaviors and disease presentations. Our study focused on hospitalized patients, which may not fully represent the entire spectrum of PAD cases during the pandemic³⁴. Patients with milder symptoms, especially those with claudication, might have avoided hospital visits due to fear of COVID-19 exposure, potentially leading to an overrepresentation of severe cases in our P2 cohort. Additionally, changes in hospital admission criteria and management strategies during the pandemic may have resulted in some mild PAD cases being treated as outpatients or kept under observation, rather than being admitted. These factors could have skewed our sample towards more severe cases in P2, potentially overstating the pandemic's impact on PAD severity. It is plausible that patients during the COVID-19 era may present with more severe clinical profiles due to delays in seeking medical care, resulting in advanced disease stages. This trend has been noted in various studies during the pandemic^{35,36}, underscoring its potential effect on disease severity and outcomes. Secondly, the cross-sectional design of the study precludes the establishment of causality or temporal relationships between variables. The lack of follow-up data during the pandemic restricts our understanding of long-term outcomes. Additionally, variations in patient management across different centers could introduce potential biases. While the zero-COVID policy was indeed unique and created limitations in our study, it also provided a rare and valuable opportunity to observe the treatment of PAD patients unaffected by COVID-19 during the pandemic, offering significant insights into the pandemic's impact on PAD management over a two-year period and highlighting areas for future research to broaden our understanding in this field.

Conclusion

During the COVID-19 pandemic, PAD patients' care was compromised, leading to fewer procedures but more emergencies and worsened health indicators. Treatment during this period predicted poorer outcomes, especially in those with DFI, renal issues, and declining WIfI scores, emphasizing the necessity for prompt interventions and prolonged follow-up in these patients.

Data availability

Data are however available from the authors upon reasonable request and with permission of the Bioethics Committee of Beijing Friendship Hospital, Capital Medical University. Data will be made available on reasonable request to Dr. Ming-Yuan Liu (Email: dr.mingyuanliu@pku.edu.cn).

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References

- Canale, M. P., Menghini, R., Martelli, E. & Federici, M. COVID-19-associated endothelial dysfunction and microvascular injury: From pathophysiology to clinical manifestations. *Card. Electrophysiol. Clin.* 14, 21–28. https://doi.org/10.1016/j.ccep.2021.10.003 (2022).
- Kwenandar, F. et al. Coronavirus disease 2019 and cardiovascular system: A narrative review. Int. J. Cardiol. Heart Vasc. 29, 100557. https://doi.org/10.1016/j.ijcha.2020.100557 (2020).
- 3. Fernandez-Nieto, D. et al. Characterization of acute acral skin lesions in nonhospitalized patients: A case series of 132 patients during the COVID-19 outbreak. J. Am. Acad. Dermatol. 83, e61–e63. https://doi.org/10.1016/j.jaad.2020.04.093 (2020).
- 4. Piazza, G. & Morrow, D. A. Diagnosis, management, and pathophysiology of arterial and venous thrombosis in COVID-19. *JAMA* 324, 2548–2549. https://doi.org/10.1001/jama.2020.23422 (2020).
- 5. Martelli, E. et al. How the first year of the COVID-19 pandemic impacted patients' hospital admission and care in the vascular surgery divisions of the southern regions of the Italian Peninsula. J. Pers. Med. 12. https://doi.org/10.3390/jpm12071170 (2022).
- de Athayde Soares, R., de Arruda Caceres, N., Barbosa, A. G., Matielo, M. F. & Sacilotto, R. The catastrophic impact of COVID-19 infection in patients with chronic limb-threatening ischemia. Surgery 171, 1422–1426. https://doi.org/10.1016/j.surg.2021.10.016 (2022)
- Piazza, M. et al. The challenge of maintaining necessary vascular and endovascular services at a referral center in Northern Italy during the COVID-19 outbreak. Vascular 29, 477–485. https://doi.org/10.1177/1708538120962964 (2021).
- 8. Miranda, J. A., Chung, J. & Mills, J. L. Influence of the COVID-19 pandemic on the management of chronic limb-threatening ischemia. Semin. Vasc. Surg. 34, 89–95. https://doi.org/10.1053/j.semvascsurg.2021.05.006 (2021).
- Lou, J. Y. et al. North American lower-extremity revascularization and amputation during COVID-19: Observations from the vascular quality initiative. Vasc. Med. 26, 613–623. https://doi.org/10.1177/1358863X211021918 (2021).
- Stabile, E. et al. A cross-sectional study evaluating hospitalization rates for chronic limb-threatening ischemia during the COVID-19 outbreak in Campania Italy. Vasc. Med. 26, 174–179. https://doi.org/10.1177/1358863X20977678 (2021).

- 11. Data, W. C. https://www.worldometers.info/coronavirus/country/china/. Worldometer manually analyzes, validates, and aggregates data from thousands of sources in real time and provides global COVID-19 live statistics for a wide audience of caring people around the world. (Accessed on July 7, 2023).
- 12. Jin, H., Lu, L., Liu, J. & Cui, M. COVID-19 emergencies around the globe: China's experience in controlling COVID-19 and lessons learned. *Int. J. Qual. Health Care* 33, 1. https://doi.org/10.1093/intqhc/mzaa143 (2021).
- 13. Rooke, T. W. et al. Management of patients with peripheral artery disease (compilation of 2005 and 2011 ACCF/AHA Guideline Recommendations): A report of the American College of Cardiology Foundation/American Heart Association Task Force on Practice Guidelines. J. Am. Coll. Cardiol. 61, 1555–1570. https://doi.org/10.1016/j.jacc.2013.01.004 (2013).
- 14. Norgren, L. et al. Inter-society consensus for the management of peripheral arterial disease (TASC II). J. Vasc. Surg. 45(Suppl S), S5-67. https://doi.org/10.1016/j.jvs.2006.12.037 (2007).
- Conte, M. S. et al. Global vascular guidelines on the management of chronic limb-threatening ischemia. Eur. J. Vasc. Endovasc. Surg. 58, S1-S109 e133. https://doi.org/10.1016/j.ejvs.2019.05.006 (2019).
- Obara, H., Matsubara, K. & Kitagawa, Y. Acute Limb Ischemia. Ann. Vasc. Dis. 11, 443–448. https://doi.org/10.3400/avd.ra.18-00074 (2018).
- Zeller, T. et al. Directional atherectomy followed by a paclitaxel-coated balloon to inhibit restenosis and maintain vessel patency: Twelve-month results of the DEFINITIVE AR study. Circ. Cardiovasc. Interv. 10, 1. https://doi.org/10.1161/CIRCINTERVENTIO NS.116.004848 (2017).
- 18. Zhan, L. X., Branco, B. C., Armstrong, D. G. & Mills, J. L. Sr. The Society for Vascular Surgery lower extremity threatened limb classification system based on Wound, Ischemia, and foot Infection (WIFI) correlates with risk of major amputation and time to wound healing. *J. Vasc. Surg.* 61, 939–944. https://doi.org/10.1016/j.jvs.2014.11.045 (2015).
- 19. Darling, J. D. *et al.* Predictive ability of the Society for Vascular Surgery Wound, Ischemia, and foot Infection (WIfI) classification system after first-time lower extremity revascularizations. *J. Vasc. Surg.* **65**, 695–704. https://doi.org/10.1016/j.jvs.2016.09.055 (2017).
- Mills, J. L. Sr. et al. The Society for Vascular Surgery Lower Extremity Threatened Limb Classification System: Risk stratification based on wound, ischemia, and foot infection (WIfI). J. Vasc. Surg. 59(220–234), e221-222. https://doi.org/10.1016/j.jvs.2013.08. 003 (2014).
- 21. Stoner, M. C. *et al.* Reporting standards of the Society for Vascular Surgery for endovascular treatment of chronic lower extremity peripheral artery disease. *J. Vasc. Surg.* **64**, e1–e21. https://doi.org/10.1016/j.jvs.2016.03.420 (2016).
- Sharma, S., Kerry, C., Atway, S., & Ramanujam, C. Diabetic Foot Infections. In StatPearls. Treasure Island (FL): StatPearls Publishing. Retrieved from https://www.ncbi.nlm.nih.gov/books/NBK441914/ (2023).
- 23. Li, W., Chen, X. & Feng, H. Strategies and recommendations for the safe implementation of vascular surgery during the pandemic period of novel coronavirus pneumonia. *J. Vasc. Surg.* 72, 377–378. https://doi.org/10.1016/j.jvs.2020.04.466 (2020).
- Sena, G. & Gallelli, G. An increased severity of peripheral arterial disease in the COVID-19 era. J. Vasc. Surg. 72, 758. https://doi. org/10.1016/j.jvs.2020.04.489 (2020).
- 25. Schuivens, P. M. E. et al. Impact of the COVID-19 lockdown strategy on vascular surgery practice: More major amputations than usual. Ann. Vasc. Surg. 69, 74–79. https://doi.org/10.1016/j.avsg.2020.07.025 (2020).
- 26. Noory, E. et al. Impact of COVID-19 pandemic on clinical care of peripheral arterial disease patients: A single-center experience. I. Clin. Med. 12, 1. https://doi.org/10.3390/jcm12030890 (2023).
- Zayed, H. et al. Impact of COVID-19 pandemic on the outcomes in patients with critical limb threatening ischaemia and diabetic foot infection. Ann. Surg. 275, 1037–1042. https://doi.org/10.1097/SLA.000000000004677 (2022).
- 28. Smolderen, K. G., Lee, M., Arora, T., Simonov, M. & Mena-Hurtado, C. Peripheral artery disease and COVID-19 outcomes: Insights from the Yale DOM-CovX registry. Curr. Probl. Cardiol. 47, 101007. https://doi.org/10.1016/j.cpcardiol.2021.101007 (2022).
- 29. Bilaloglu, S. et al. Thrombosis in Hospitalized Patients With COVID-19 in a New York City Health System. JAMA 324, 799–801. https://doi.org/10.1001/jama.2020.13372 (2020).
- 30. Batatinha, H. A. P., Kruger, K. & Rosa Neto, J. C. Thromboinflammation and COVID-19: The role of exercise in the prevention and treatment. Front. Cardiovasc. Med. 7, 582824. https://doi.org/10.3389/fcvm.2020.582824 (2020).
- 31. Rodway, A. D. *et al.* Understanding the impact of COVID-19 on angioplasty service and outcome of patients treated for chronic limb-threatening ischaemia: A single-centre retrospective cohort study. *Biomedicines* 11, 1. https://doi.org/10.3390/biomedicines11072034 (2023).
- 32. Ritti-Dias, R. M. et al. Impact of the COVID-19 pandemic on health lifestyle in patients with peripheral artery disease: A cross-sectional study. J. Vasc. Nurs. 40, 54–58. https://doi.org/10.1016/j.jvn.2022.01.001 (2022).
- 33. Sasko, B. et al. Impact of the COVID-19 pandemic on hospital admission rates for arterial hypertension and coronary heart disease: a German database study. Front. Cardiovasc. Med. 11, 1333749. https://doi.org/10.3389/fcvm.2024.1333749 (2024).
- 34. Bhatt, A. S. et al. Fewer hospitalizations for acute cardiovascular conditions during the COVID-19 pandemic. J. Am. Coll. Cardiol. 76, 280–288. https://doi.org/10.1016/j.jacc.2020.05.038 (2020).
- 35. Smith, A. C. et al. Telehealth for global emergencies: Implications for coronavirus disease 2019 (COVID-19). J. Telemed. Telecare 26, 309–313. https://doi.org/10.1177/1357633X20916567 (2020).
- 36. Katulanda, P. et al. Prevention and management of COVID-19 among patients with diabetes: An appraisal of the literature. Diabetologia 63, 1440–1452. https://doi.org/10.1007/s00125-020-05164-x (2020).

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Author contributions

MY Liu, X Chen and H Feng were contributed to the conception and study design/obtaining funding; MY Liu, B Liu, L Zhang, and WR Li writing the article; MY Liu, YX Zhang, L Zhang, and B Liu, critical revision of the article; X Guo, and W Yin, obtaining and processing the medical imaging data; MY Liu, Y Wang, J Zhang, WR Li, and X Guo, the data collection/analysis and interpretation.

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Competing interests

The authors declare no competing interests.

Ethics approval and consent for publication

The authors confirmed that all the experiment protocol for involving human data was in accordance to guidelines of national/international/institutional or Declaration of Helsinki in the manuscript. The study protocols were approved by the Bioethics Committee of Beijing Friendship Hospital, Capital Medical University and all the personal information was encrypted by the data system, making this study approved (No. 2020-P2-073) as an audit project. All the consents of the participants were obtained for the publication.

Additional information

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