Received: 17 October 2022 | Revised: 6 February 2023 | Accepted: 14 February 2023

DOI: 10.1002/dmrr.3626

WILEY

RESEARCH ARTICLE

Evidence of greater severity of diabetic foot ulcers during COVID-19 pandemic: A real-life single-centre cohort study

Stefano Radellini[1] | Enrica Vigneri[1] | Lucia Smeraldi[1] | Ettore Dinoto[2] | Giovanni Guercio[3] | Pierina Richiusa[1] | Piero Luigi Almasio[4] | Valentina Guarnotta[1] | Riccardo Salzillo[1] | Carla Giordano[1]

[1]Section of Endocrinology, Diabetology and Metabolism, Dipartimento di Promozione della Salute, Materno-Infantile, di Medicina Interna e Specialistica di Eccellenza "G. D'Alessandro" (PROMISE), Division of "Malattie Endocrine, del Ricambio e della Nutrizione", Università degli studi di Palermo, Palermo, Italy

[2]Department of Surgical, Oncological and Oral Sciences, Vascular Surgery Unit, AOUP Policlinico 'P. Giaccone', University of Palermo, Palermo, Italy

[3]Department of Surgical Oncological and Stomatological Disciplines, Division of Surgery, University of Palermo, Palermo, Italy

[4]Section of Gastroenterology and Hepatology, Dipartimento di Promozione della Salute, Materno-Infantile, Medicina Interna e Specialistica di Eccellenza "G. D'Alessandro", PROMISE, Università degli Studi di Palermo, Palermo, Italy

Correspondence

Valentina Guarnotta and Carla Giordano, Piazza delle Cliniche 2, Palermo 90127, Italy.
Email: carla.giordano@unipa.it and valentina.guarnotta@unipa.it

Funding information

Sicilian Health Department "PSN Piede Diabetico", Grant/Award Number: 37475

Abstract

Aims: In the Sars-Cov-2 pandemic era, patients with diabetes mellitus (DM) manifested more severe forms of Sars-Cov-2 with greater mortality than non-diabetic patients. Several studies documented more aggressive forms of diabetic foot ulcers (DFU) during the pandemic period even though the results were not unanimously confirmed. The aim of this study was to evaluate the clinical-demographic differences between a cohort of Sicilian diabetic patients hospitalised for DFU in the pre-pandemic 3 years and a cohort of patients hospitalised in the pandemic 2 years.

Materials and Methods: One hundred and eleven patients from the pre-pandemic period 2017–2019 (Group A) and 86 patients from the pandemic period 2020–2021 (Group B) with DFU, admitted to the division of Endocrinology and Metabolism of the University Hospital of Palermo, were retrospectively evaluated. The clinical assessment of the type, staging and grading of the lesion, and the infective complication from DFU was performed.

Results: No differences in HbA1c values were observed between the two groups. Group B showed a significantly higher prevalence of male subjects ($p = 0.010$), neuro-ischaemic ulcers ($p < 0.001$), deep ulcers with involvement of bones ($p < 0.001$), white blood count levels ($p < 0.001$), and reactive C protein ($p = 0.001$) compared to group A.

Conclusions: Our data show that in the COVID-19 pandemic, a greater severity of ulcers requiring a significantly greater number of revascularisations and more expensive therapy, but without an increase in the amputation rate, was observed. These data provide novel information on the impact of the pandemic on diabetic foot ulcer risk and progression.

KEYWORDS

diabetes mellitus, diabetic foot, pandemic, SARScov 2

1 | INTRODUCTION

Since the beginning of the Sars-Cov-2 pandemic era, it has been documented that patients with diabetes mellitus (DM) manifest more severe forms of SARS-COV2 infection with greater mortality than non-diabetic patients.[1–3] These data were confirmed by a recent meta-analysis that considered a total of 78,874 patients hospitalised for SARS COV2 infection from 83 observational studies, which documented a prevalence of pre-existing DM in 14.3% of patients and a significantly higher prevalence of the more severe forms of SARS COV2 pneumonia and a higher risk of hospital mortality in diabetic than non-diabetic patients.[4] The prevalence of DM in patients who died of COVID-19 was shown to be higher than in the general population.[1,5] These data have led clinicians to consider diabetic patients as having greater susceptibility to hospitalisation and mortality in case of SARS-COV2 infection, consequently leading to a more incisive vaccination campaign and more rigorous isolation rules.[6] In the diabetic area, distance medicine measures have been implemented in order to avoid the risk of contagion though with the risk of underestimating more severe conditions of DM and its complications, such as diabetic foot ulcers (DFU).[7–10] The aim of the study was to evaluate the clinical-demographic differences between a cohort of patients with DFU hospitalised in the pre-pandemic 3-year period and a cohort of patients hospitalised for DFU in the most recent 2-year pandemic period.

2 | MATERIALS AND METHODS

The clinical and demographic data of 111 patients from the pre-pandemic period 2017–2019 (Group A) and 86 patients from the pandemic period 2020–2021 (Group B) affected by DFU, admitted to the division of Endocrinology and Metabolism of the University Hospital of Palermo, were retrospectively evaluated. The clinical assessment of the type, staging and grading of the lesion, and the infective complications from DFU was performed according to the most recent recommendations of the International Working Group on the Diabetic Foot (IWGDF).[11,12] In both patient groups, we evaluated anthropometric and demographic data, such as age, sex, body mass index (BMI), type and duration of DM, clinical parameters such as type of ulcer (neuropathic, ischaemic, or neuro-ischaemic ulcer), grade and stage of the lesion according to the Texas wound classification system, the severity of infection according to Infectious Diseases Society of America (IDSA) classification, the presence of systemic inflammatory response syndrome (SIRS) in accordance with the recommendations of the main scientific societies in the sector, and the presence of osteomyelitis and its outcome in terms of major or minor amputation and revascularisation.[12–16] The Texas classification is a descriptive classification, rather than a scoring system, which classifies DFUs according to depth (grade from 0 to 3), presence of infection (stage B), ischaemia (stage C), or both (stage D).[13]

Ischaemic ulcer was defined by the clinical evaluation of absent pulses, ankle-brachial index (ABI) less than 0.9, and evidence of low arterial flow at triphasic pedal Doppler.[17] The decision to revascularise was based on clinical evaluation by a deputed vascular surgeon, low ABI (<0.5), low or absent arterial flow at triphasic pedal Doppler, and execution of computed tomography angiography only in cases of large ulcers that cannot consent to perform Doppler according to the guidelines on the diagnosis and treatment of peripheral arterial diseases.[17]

In addition, biochemical parameters, such as glycated haemoglobin (HbA1c), indices of inflammation such as ultrasensitive C-reactive protein (CRP), erythrocyte sedimentation rate (ESR), and number of white blood cells, were evaluated. The study was approved by the Local Ethical Committee, Policlinico Paolo Giaccone Hospital, and carried out in accordance with the Declaration of Helsinki for experiments involving humans. At the time of observation, all patients, regularly informed of the aim of the study, signed an informed consent for scientific use of their data.

2.1 | Statistical analysis

A statistical analysis was performed using the SPSS version 20. The normality test was assessed using the Kolmogorov–Smirnov test. Numerical data were presented as mean ± standard deviation (SD) or median and interquartile range. Analyses of variables were performed using the chi-square or Fisher's exact test for categorical variables and the independent *t*-test or Mann–Whitney test for continuous variables according to their distribution. A p value of <0.05 was considered statistically significant.

3 | RESULTS

The clinical, demographic, and biochemical data are shown in Table 1. As expected, longer foot ulcer duration was observed in group B compared to group A ($p < 0.001$). Patients hospitalised in the pandemic period had significantly higher indices of inflammation (WBC $p < 0.001$; ESR $p = 0.030$; CRP $p = 0.001$). In Group B, a significantly higher prevalence of male subjects ($p = 0.009$) was observed compared to group A. In Group B, a higher prevalence of ischaemic and neuro-ischaemic ulcers was observed compared to neuropathic ulcers (neuropathic ulcer in Group A 36.9% vs. Group B 10.5%; neuro-ischaemic ulcer Group A 53.2% vs. Group B 74.4% $p < 0.001$). In Group B, a significantly higher prevalence of deep ulcers with the involvement of the osteo-articular plane was observed compared to Group A (superficial ulcers in Group A 50.5% vs. Group B 18.6%; ulcer involving tendons/capsules Group A 36% vs. Group B 58.1%; ulcer with bone involvement Group A 12.6% vs. Group B 20.9%, $p < 0.001$) (Table 1). In Figure 1, grading of DFU shows the significant difference ($p < 0.001$) in the frequency of all lesions from pre-ulcerative ones to those involving superficial, tendon/capsule, and bone. Patients hospitalised during the pandemic period showed a higher prevalence of SIRS than the limit of statistical significance (SIRS Group A 12.6% vs. Group B 23.3% $p = 0.05$).

TABLE 1 Anthropometric, clinical, and biochemical characteristics of patients with diabetic foot ulcer hospitalised before (group A) and during (group B) COVID-19 pandemic.

	Group A ($N = 110$) Mean ± SD	Group B ($N = 84$) Mean ± SD	p
Age (years)	65.5 ± 12.4	65.8 ± 11.9	0.866
Duration of diabetes (years)	19.8 ± 12.7	19.6 ± 12.1	0.855
Foot ulcer duration (days)	22.2 ± 11.2	35.6 ± 20.7	<0.001
BMI (kg/m^2)	29.1 ± 4.1	28.7 ± 4.18	0.457
WBC	10.752 ± 3.714	16.227 ± 6.605	<0.001
Neutrophils (%)	67.9 ± 11.4	70.1 ± 13.5	0.235
ESR (mm)	52.8 ± 25.3	63.2 ± 42.9	0.030
CRP (mg/L)	62.8 ± 71.8	98.4 ± 79.9	0.001
HbA1c (%)	10.1 ± 2.14	10.1 ± 2.23	0.909
	Subjects (%)	**Subjects (%)**	
Gender			
Male	68 (61.9%)	66 (78.6%)	0.009
Female	42 (38.1%)	18 (21.4%)	
Diabetes mellitus			
Type 1	8 (7.2%)	5 (5.9%)	0.475
Type 2	102 (92.8%)	79 (94.1%)	
Cardiovascular disease			
Myocardial infarction	33 (30%)	27 (32.1%)	0.027
Stroke	9 (8.2%)	0	
Cardiac insufficiency	0	0	
Chronic kidney disease			
G1	50 (45.4%)	23 (27.4%)	0.151
G2	23 (20.9%)	26 (31%)	
G3a	13 (11.8%)	16 (19%)	
G3b	10 (9.1%)	9 (10.7%)	
G4	7 (6.4%)	4 (4.8%)	
G5	7 (6.4%)	6 (7.1%)	
Gangrene	29 (26.3%)	28 (33.3%)	0.289
Lesion area			
I toe	10 (9.2%)	16 (19%)	0.150
Distal extremities	11 (10.1%)	7 (8.3%)	
Lateral plantar	31 (28.4%)	19 (22.6%)	
Medial plantar	37 (33.9%)	30 (35.7%)	
Calcanear	10 (9.2%)	7 (8.3%)	
Dorsal	10 (9.2%)	5 (6%)	
IDSA			
Non-infected	0	0	<0.001
Mild	56 (50.5%)	0	
Moderate	40 (36.0%)	46 (54.7%)	
Severe	14 (12.6%)	38 (45.3%)	
Grading			
Shallow	56 (50.5%)	16 (18.6%)	<0.001
Tendon/capsule	40 (36.0%)	50 (58.1%)	
Bone	14 (12.6%)	18 (20.9%)	
Staging			
Negative	3 (3.6%)	1 (3.5%)	<0.001
Infected	64 (57.7%)	5 (5.8%)	
Ischaemic	0	10 (11.6%)	
Infected and ischaemic	43 (38.7%)	68 (79.1%)	
Osteomyelitis	12 (10.8%)	16 (18.6%)	0.105
Diagnosis of SIRS	14 (12.6%)	20 (23.3%)	0.051

Abbreviations: BMI, body mass index; ESR, Eritrosedimentation rate; IDSA, Infectious disease society of America; PCR, ultrasensitive C reactive Protein; SIRS, Systemic Inflammatory related Syndrome; WBC, White Blood Cells.

Revascularisation and minor or major amputation outcome data are shown in Table 2. Patients hospitalised in the pandemic period showed a significantly higher prevalence of revascularisations with equal outcomes in minor or major amputations compared to patients hospitalised in the pre-pandemic period (revascularisations in Group A 19.8% vs. Group B 40.7%, $p = 0.001$; minor amputations: Group A 5.4% vs. Group B 2.3%; major amputations: Group A 21.6% vs. Group B 24.4% $p = 0.5$). Figure 2 shows the trend of use or otherwise of revascularisation or revascularisation procedures in the two periods examined, confirming the higher necessity than in the previous non-COVID period. This result is confirmed by the evidence in Figure 3 of the greater number of minor amputations in the period 2019–2021, which in any case did not involve a greater number of major amputations, whose trend continued to decline from 2017 and decline even in the COVID period, revealing that the increase in revascularisation procedures had a limiting effect on the extent of amputation.

4 | DISCUSSION

Numerous studies have documented that patients with DM have a higher risk of developing more severe forms with greater mortality in case of SARS-COV2 infection than non-diabetic subjects.[1–3] However, few studies have investigated the impact of the pandemic on the management of DM and its complications. Subjects presenting with DFU are to be seen as subjects with a greater burden of morbidity and a greater risk of mortality.[18–21] The objective of our

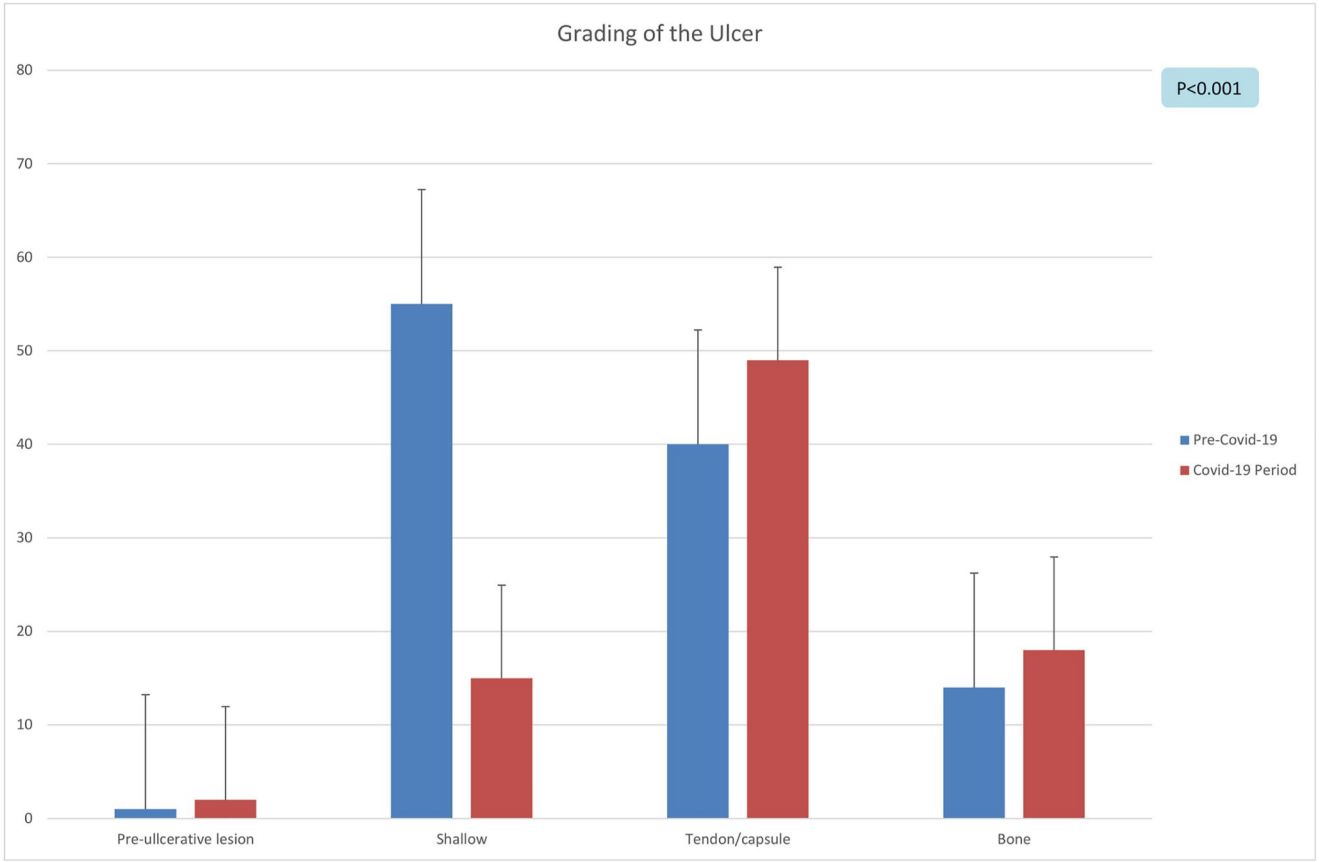

FIGURE 1 Comparison of diabetic foot ulcers during and before the pandemic period.

TABLE 2 Outcome of patients with diabetic foot ulcer hospitalised before (group A) and during (group B) COVID-19 pandemic.

	Group A (No = 110) Subjects (%)	Group B (No = 84) Subjects (%)	*p*
Surgery			
None	80 (72.7%)	61 (72.6%)	0.5
Major amputation	24 (21.8%)	21 (25%)	
Minor amputation	6 (5.4%)	2 (2.3%)	
Re-vascularisation	22 (20%)	35 (41.6%)	0.001

study was to investigate the clinical and demographic characteristics of patients hospitalised for DFU in the pandemic period by comparing them with patients hospitalised for the same disease in the immediately preceding 3 years, using the standards already established by the multidisciplinary team for diagnosis and treatment of DFU in hospitalised patients in accordance with the most recent international guidelines.[12] In our study, a higher prevalence of more severe forms of ulcers was documented in patients hospitalised in the two pandemic years compared to patients hospitalised in the three pre-pandemic years. This finding is documented by a significantly higher prevalence of ulcers with deep tissue involvement and by greater systemic inflammatory compromise in patients admitted for DFUs in the two pandemic years. In our study, the severity of clinical presentation of the DFU picture in patients hospitalised in the pandemic period also involved a greater severity in terms of ischaemia, which resulted in a greater number of revascularisations but not in a higher rate of amputations compared to patients hospitalised in the three pre-COVID years. These findings are difficult to interpret, but in the context of the greater severity in general of DFU cases in Group B, they could be explained by the delay in referral of these subjects to our observation and consequently the greater severity of the clinical picture, as demonstrated by the longer duration of foot ulcers. In our hospital, clinical activity was only maintained during the lockdown for patients with urgent medical conditions, but some patients were afraid of contracting COVID, causing a further delay. The latter clinical observation made revascularisation necessary for limb salvage. The need for re-vascularisation was directly related to the stage of the wound. In addition, during the COVID pandemic period, patients had more accessibility to the OR\angio-room because outpatients were not admitted.

Our data are in agreement with numerous other studies that have documented the greater severity of the presenting picture of DFU in the pandemic period, sometimes with an increase in the rate of amputations.[10,19] A recent study by Schuivens et al. documented a

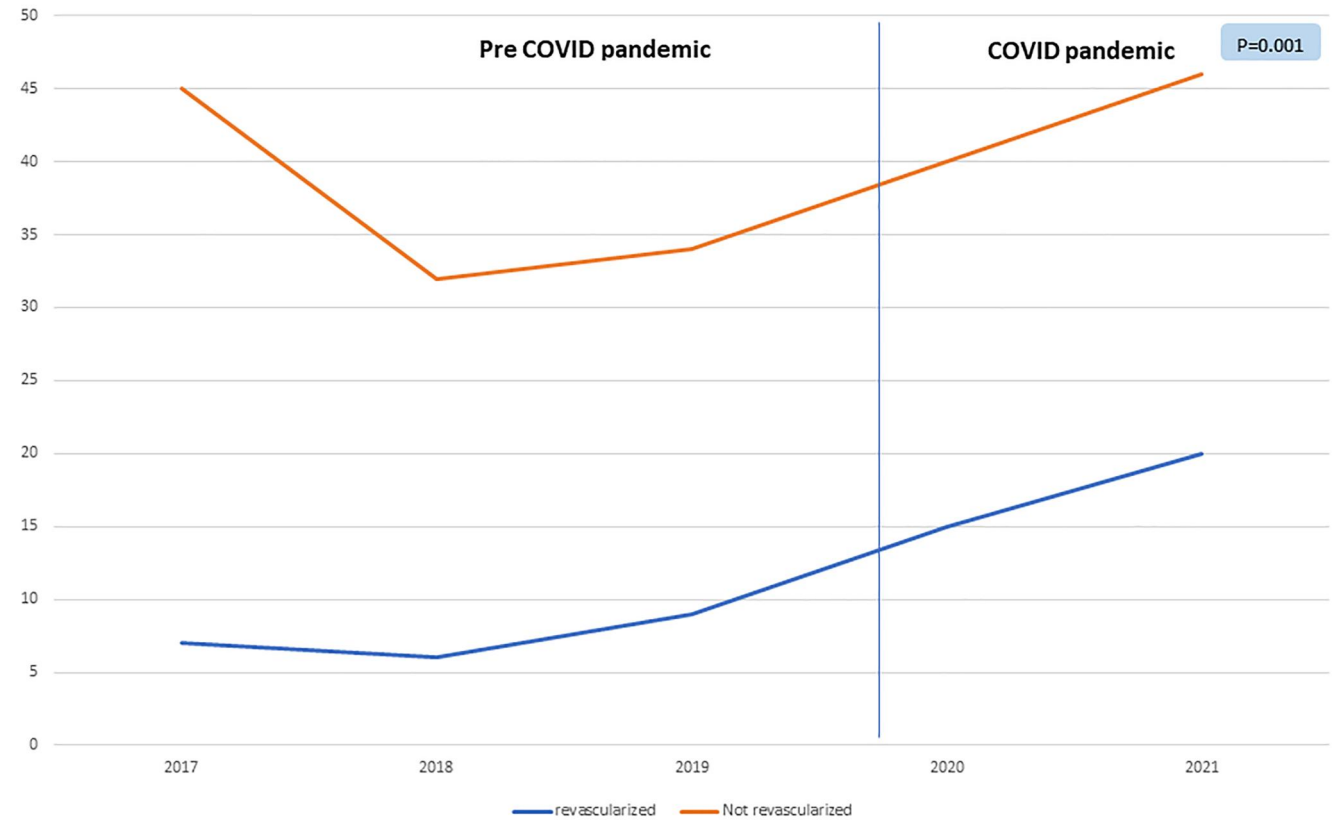

FIGURE 2 Distribution of revascularisation and non-revascularisation in diabetic patients hospitalised at the Division of Endocrinology and Diabetology, AOUP Paolo Giaccone, University of Palermo, Italy, in the pre-pandemic period and during the COVID pandemic.

higher incidence of major amputations in the pandemic period attributed to the greater extent of ischaemic tissue.[22] However, a cohort study conducted in Canada, which examined a large population of patients with DM evaluating the minor and major amputation rates in the pre-pandemic versus the pandemic period, showed no significant differences.[23] In this cohort study on the diabetic population residing in Ontario (where there is a public health system), 8 parameters relating to indicators of diabetes care and outcomes were studied: diabetic examination including clinical examination of the foot, evaluation of HbA1c, access to the emergency area or hospitalisation for ulcer, osteomyelitis or gangrene, minor amputation (toes or partial foot), major amputation (above the ankle), and endovascular or surgical revascularisation. This study compared two 10-week periods relating to the pandemic period (year 2020–2021) and the pre-pandemic control period (2019–2020). Ontario ordered a state of emergency with the suspension of scheduled activities from March until May 2020 and in the first 2 months of 2021. Access to the emergency area and hospitalisation for ulcer, osteomyelitis or gangrene, minor amputations, and endovascular and open revascularisations decreased in the first weeks after the onset of the pandemic to subsequently increase in the levels of the period 2019–2020. In conclusion, in this large study, limited access to treatment due to COVID-19 did not lead to an increase in major amputations, and this appears to be confirmed by our data indicating the greater severity of the presentation of DFU in terms of ischaemia and infection but without this, resulting in a larger number of major amputations. However, in our cohort of patients, the amputation rate was slightly higher than that reported in the literature. The reasons can be assigned to the high rate of bedridden patients with rapid worsening of their clinical conditions, which would not allow rescue of the patient limbs and involved contraindications for revascularisation in patients with severe renal insufficiency (eGFR less than 30 mL/min).

The Canadian study conducted by De Mestral and collaborators clearly appears to be in contrast to what is described in other countries, including Italy.[24–27] In the Neapolitan situation, Caruso and collaborators described a clear increase in the risk of amputation and urgent presentation during the lockdown.[24] So how are we to interpret the results of the Canadian study with respect to what was found in our small cohort of patients? The authors of the Canadian study report that restrictions on non-COVID activity of relatively short duration (10 weeks) only occurred during the first wave and that they did not limit surgical activity on the foot or revascularisations. The Canadian study, although with the significant contribution made by an observation from the population register, has the limit of examining a vast series of diabetics with probable non-homogeneity of the sample in terms of the presence of comorbidities and people coming from different care settings. Another recent study evaluated the effects of COVID pandemic on the outcomes and mortality of patients with DFU without finding any significant differences in

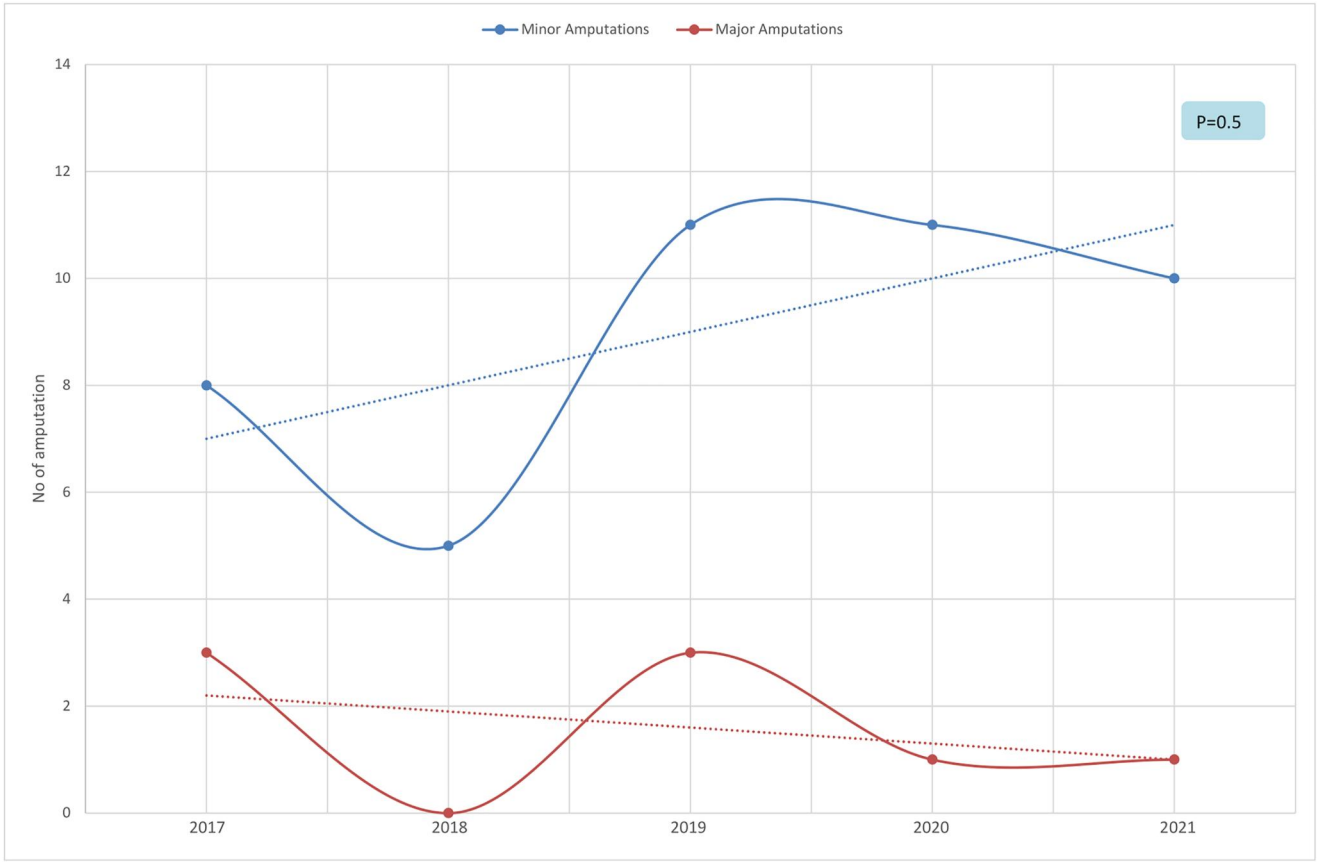

FIGURE 3 Distribution of amputation in diabetic patients admitted to the Division of Endocrinology and Diabetology, AOUP Paolo Giaccone, University of Palermo, Italy, during the COVID-19 pandemic in 2019–2020 and in the previous 3 years.

amputation rates and mortality in patients with DFU before and during the pandemic.[28] To avoid late referral and the risk of major amputation, the scientific community developed a tool to be adopted during the pandemic period and beyond in the case of similar condition, the COVID-19 fast-track pathway.[29] This tool is useful for clinicians to distinguish non-limb from limb-threatening conditions.

4.1 | Limitations and strength of the study

The strength of our study is to be considered the observation of a series of monocentric patients, all hospitalised for acute DFU conditions and compared taking into consideration the 2-year pandemic and an immediately preceding 3-year period to avoid the bias linked to a different territorial microbiological spectrum, different antibiotic resistances, and different procedural methods. The limits include the small number of the sample and the retrospective observation.

4.2 | Conclusions

Our study documented a greater severity of ulcers in terms of deep tissue involvement, systemic inflammatory involvement, and severity of ischaemia, requiring a significantly higher number of revascularisations and more expensive therapy but without increasing the amputation rate observed in the pandemic period. The main message of our study is that the collaboration of several professional figures is confirmed as fundamental as is the timeliness of diagnosis and intervention in the diagnostic and therapeutic pathway of DFU, which were probably deficient due to the pandemic emergency.

AUTHOR CONTRIBUTIONS

Stefano Radellini, Enrica Vigneri, Pierina Richiusa, Riccardo Salzillo, Lucia Smeraldi, Ettore Dinoto, Giovanni Guercio, Piero Luigi Almasio, and Carla Giordano were involved in the conception, design, and conduct of the study, and the analysis and interpretation of the results. Carla Giordano wrote the first draft of the manuscript, and all authors edited, reviewed, and approved the final version of the manuscript. Carla Giordano is the guarantor of this work, and as such, had full access to all the data in the study, and takes responsibility for the integrity of the data and the accuracy of the data analysis. The datasets generated during and/or analysed in the current study are available from the corresponding author upon reasonable request.

ACKNOWLEDGEMENTS

This research received specific funds from the Sicilian Health Department "PSN Piede Diabetico" that contributed to create the

Diabetic Foot Centre in 2013; these funds were provided in the form of a grant (No. 37475) awarded to CG.

Open Access Funding provided by Universita degli Studi di Palermo within the CRUI-CARE Agreement.

CONFLICT OF INTEREST STATEMENT

The authors declare no conflict of interest.

DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available on request from the corresponding author. The data are not publicly available due to privacy or ethical restrictions.

ETHICS STATEMENT

The study was approved by the Local Ethical Committee, Policlinico Paolo Giaccone Hospital, and carried out in accordance with the Declaration of Helsinki for experiments involving humans. At the time of observation, all patients, regularly informed of the aim of the study, signed an in-formed consent for scientific use of their data.

ORCID

Carla Giordano https://orcid.org/0000-0003-1731-9395

PEER REVIEW

The peer review history for this article is available at https://www.webofscience.com/api/gateway/wos/peer-review/10.1002/dmrr.3626.

REFERENCES

1. Silverii GA, Monami M, Cernigliaro A, et al. Are diabetes and its medications risk factors for the development of COVID-19? Data from a population-based study in Sicily. *Nutr Metab Cardiovasc Dis*. 2021;31(2):396-398. https://doi.org/10.1016/j.numecd.2020.09.028
2. Zhou Y, Chi J, Lv W, Wang Y. Obesity and diabetes as high-risk factors for severe coronavirus disease 2019 (Covid-19). *Diabetes Metab Res Rev*. 2021;37(2):e3377. https://doi.org/10.1002/dmrr.3377
3. Hussain A, Bhowmik B, do Vale Moreira NC. COVID-19 and diabetes: knowledge in progress. *Diabetes Res Clin Pract*. 2020;162:108142. https://doi.org/10.1016/j.diabres.2020.108142
4. Mantovani A, Byrne CD, Zheng M, Targher G. Diabetes as a risk factor for greater COVID-19 severity and in-hospital death: a metaanalysis of observational studies. *Nutr Metabol Cardiovasc Dis*. 2020;30(8):1236e48. https://doi.org/10.1016/j.numecd.2020.05.014
5. Fadini GP, Morieri ML, Longato E, Avogaro A. Prevalence and impact of diabetes among people infected with SARS-CoV-2. *J Endocrinol Invest*. 2020;43(6):867e9. https://doi.org/10.1007/s40618-020-01236-2
6. Palmieri L, Vanacore N, Donfrancesco C, et al; Italian National Institute of Health COVID-19 Mortality Group. Clinical characteristics of hospitalized individuals dying with COVID-19 by age group in Italy. *J Gerontol A Biol Sci Med Sci*. 2020;75(9):1796-1800. https://doi.org/10.1093/gerona/glaa146
7. Sayed S. COVID-19 and diabetes; Possible role of polymorphism and rise of telemedicine. *Prim Care Diabetes*. 2021;15(1):4-9. https://doi.org/10.1016/j.pcd.2020.08.018
8. Danne T, Limbert C, Puig Domingo M, et al. Telemonitoring, telemedicine and time in range during the pandemic: paradigm change for diabetes risk management in the post-COVID future. *Diabetes Ther*. 2021;12(9):2289-2310. https://doi.org/10.1007/s13300-021-01114-x
9. de Kreutzenberg SV. Telemedicine for the clinical management of diabetes; implications and considerations after COVID-19 experience. *High Blood Press Cardiovasc Prev*. 2022;17:1-8.
10. Carro GV, Carlucci EM, Torterola I, Breppe P, Ticona Ortiz MÁ, Palomino Pallarez JE. Diabetic foot and COVID-19. Medical consultation and severity of lesions compared to 2019. *Medicina*. 2020;80:30-34.
11. Bakker K, Apelqvist J, Lipsky BA, Van Netten JJ; International Working Group on the Diabetic Foot. The 2015 IWGDF guidance documents on prevention and management of foot problems in diabetes: development of an evidence-based global consensus. *Diabetes Metab Res Rev*. 2016;32:2-6. https://doi.org/10.1002/dmrr.2694
12. Monteiro-Soares M, Russell D, Boyko EJ, et al; International Working Group on the Diabetic Foot (IWGDF). Guidelines on the classification of diabetic foot ulcers (IWGDF 2019). *Diabetes Metab Res Rev*. 2020;36:e3273.
13. Armstrong DG, Lavery LA, Harkless LB. Validation of a diabetic wound classification system. The contribution of depth, infection, and ischemia to risk of amputation. *Diabetes Care*. 1998;21(5):855-859. https://doi.org/10.2337/diacare.21.5.855
14. Lipsky BA, Berendt AR, Cornia PB, et al; Infectious Diseases Society of America. 2012 Infectious Diseases Society of America clinical practice guideline for the diagnosis and treatment of diabetic foot infections. *Clin Infect Dis*. 2012;54(12):e132-e173. https://doi.org/10.1093/cid/cis346
15. Singer M, Deutschman CS, Seymour CW, et al. The third international consensus definitions for sepsis and septic shock (Sepsis-3). *JAMA*. 2016;315(8):801-810. https://doi.org/10.1001/jama.2016.0287
16. Sun Y, Ma L, Ji M, Wang Z. Evidence map of recommendations on diabetic foot ulcer care: a systematic review of 22 guidelines. *J Tissue Viability*. 2022;31(2):294-301. https://doi.org/10.1016/j.jtv.2022.03.001
17. Hinchliffe RJ, Forsythe RO, Apelqvist J, et al; International Working Group on the Diabetic Foot (IWGDF). Guidelines on diagnosis, prognosis, and management of peripheral artery disease in patients with foot ulcers and diabetes (IWGDF 2019 update). *Diabetes Metab Res Rev*. 2020;36(Suppl 1):e3276. https://doi.org/10.1002/dmrr.3276
18. Guarnotta V, Radellini S, Vigneri E, et al. Diabetic foot ulcers: retrospective comparative analysis from Sicily between two eras. *PLoS One*. 2021;16(12):e0259405. https://doi.org/10.1371/journal.pone.0259405
19. Dietrich I, Braga GA, de Melo FG, da Costa Silva Silva ACC. The diabetic foot as a proxy for cardiovascular events and mortality review. *Curr Atheroscler Rep*. 2017;19(11):44. https://doi.org/10.1007/s11883-017-0680-z
20. Jeyaraman K, Berhane T, Hamilton M, Chandra AP, Falhammar H. Mortality in patients with diabetic foot ulcer: a retrospective study of 513 cases from a single centre in the Northern Territory of Australia. *BMC Endocr Disord*. 2019;19:1. https://doi.org/10.1186/s12902-018-0327-2
21. Liu C, You J, Zhu W, et al. The COVID-19 outbreak negatively affects the delivery of care for patients with diabetic foot ulcers. *Diabetes Care*. 2020;43(10):e125-e126. https://doi.org/10.2337/dc20-1581
22. Schuivens PME, Buijs M, Boonman-de Winter L, et al. Impact of the COVID-19 lockdown strategy on vascular surgery practice: more major amputations than usual. *Ann Vasc Surg*. 2020;69:74-79. https://doi.org/10.1016/j.avsg.2020.07.025
23. de Mestral C, Gomez D, Wilton AS, et al. A population-based analysis of diabetes-related care measures, foot complications, and amputation during the COVID-19 pandemic in Ontario, Canada. *JAMA Netw Open*. 2022;5(1):e2142354. https://doi.org/10.1001/jamanetworkopen.2021.42354

24. Caruso P, Longo M, Signoriello S, et al. Diabetic foot problems during the COVID-19 pandemic in a tertiary care center: the emergency among the emergencies. *Diabetes Care*. 2020;43(10):e123-e124. https://doi.org/10.2337/dc20-1347
25. Du C, Li Y, Xie P, et al. The amputation and mortality of inpatients with diabetic foot ulceration in the COVID-19 pandemic and post-pandemic era: a machine learning study. *Int Wound J*. 2022;19(6):1289-1297. https://doi.org/10.1111/iwj.13723
26. Mariet AS, Benzenine E, Bouillet B, Vergès B, Quantin C, Petit JM. Impact of the COVID-19 epidemic on hospitalization for diabetic foot ulcers during lockdown: a French nationwide population-based study. *Diabet Med*. 2021;38(7):e14577. https://doi.org/10.1111/dme.14577
27. Yunir E, Tarigan TJE, Iswati E, et al. Characteristics of diabetic foot ulcer patients pre- and during COVID-19 pandemic: lessons learnt from a National Referral Hospital in Indonesia. *J Prim Care Community Health*. 2022;13:21501319221089767. https://doi.org/10.1177/21501319221089767
28. Rubin G, Feldman G, Dimri I, Shapiro A, Rozen N. Effects of the COVID-19 pandemic on the outcome and mortality of patients with diabetic foot ulcer. *Int Wound J*. 2022:1-6.
29. Meloni M, Bouillet B, Ahluwalia R, et al. Fast-track pathway for diabetic foot ulceration during COVID-19 crisis: a document from International Diabetic Foot Care Group and D-Foot International. *Diabetes Metab Res Rev*. 2021;37(3):e3396. https://doi.org/10.1002/dmrr.3396

How to cite this article: Radellini S, Vigneri E, Smeraldi L, et al. Evidence of greater severity of diabetic foot ulcers during COVID-19 pandemic: a real life single-centre cohort study. *Diabetes Metab Res Rev*. 2023;e3626. https://doi.org/10.1002/dmrr.3626