



# Diabetic Foot Problems During the COVID-19 Pandemic in a Tertiary Care Center: The Emergency Among the Emergencies

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As a consequence of the coronavirus disease 2019 (COVID-19) pandemic, profound changes in daily lives have occurred. In Italy, the exponential spread of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection required extraordinary measures to limit viral transmission, leading to an almost complete lockdown of the country (1).

The mandatory lockdown significantly affected patients with chronic diseases, including people with diabetes and diabetic foot ulceration (DFU), which represents a heavy burden for health care systems in terms of mortality and reduced quality of life (1,2). The interruption of preventive education, early treatment, and diagnosis may have led to increased hospitalization of patients with severe DFU at high amputation risk (3). The aim of this study was to evaluate clinical features and amputation risk of individuals with diabetes and DFU admitted to a tertiary care center during the COVID-19 lockdown compared with a population admitted in the first 5 months of 2019.

Patients with diabetes and DFU admitted to the Division of Endocrinology and Metabolic Diseases at the Teaching

Hospital of University of Campania “Luigi Vanvitelli” (Naples, Italy) from 9 March 2020 to 18 May 2020 were included in this study. This cohort was compared with a population of patients admitted for DFU from January to May 2019. Demographics, clinical and biochemical parameters, and DFU treatments were collected from the hospital medical records and entered in an internal electronic database. We also recorded whether patients came from outpatient clinics and were admitted as an emergency.

Continuous variables were compared with *t* test or Mann-Whitney *U* test according to their distribution, whereas Fisher exact test was used for categorical variables. Relative risk and 95% CI was calculated from a log-binomial regression model. Data were analyzed using Stata version 16.1.

The study population included 63 patients, of whom 25 patients were admitted in 2020 (2020 group) and 38 patients in 2019 (2019 group). The main findings are reported in Table 1. There were no significant differences between groups in age, diabetes duration, and HbA<sub>1c</sub> levels. A greater number of males was found in

both groups, with a higher male-to-female ratio in the 2020 group ( $P = 0.055$ ). Moreover, in the 2020 group, the proportion of patients coming from the outpatient clinic was significantly lower (16% vs. 45%,  $P = 0.028$ ), whereas the proportion of patients admitted for emergency was significantly higher (76% vs. 26%,  $P < 0.001$ ). There were no significant differences in clinical and biochemical parameters, except for urinary albumin-to-creatinine ratio, which was significantly higher in the 2020 group (median 58 mg/g [interquartile range 23, 319] vs. 36 [9, 76],  $P = 0.050$ ). No differences were found in ulcer duration, prevalence rate of peripheral artery disease, neuropathy, and osteomyelitis, or in the percentage of patients reporting previous history of DFU. A significantly higher prevalence was found in the 2020 group as compared with the 2019 group for gangrene (64% vs. 29%,  $P = 0.009$ ) and for the proportion of patients requiring amputation (60% vs. 18%,  $P = 0.001$ ). No differences were found in the number of revascularization and other surgeries. The relative risk for amputation of the 2020 group versus the 2019 group was 3.26 (95% CI 1.55–6.84), and it was 2.50 (95% CI 1.18–5.29) after adjustment for sex.

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**Table 1—Demographics, clinical characteristics, and interventions among participants in the study**

Parameter	2020 group (n = 25)	2019 group (n = 38)	P
Age, years	62.6 ± 11.1	65.4 ± 16.8	0.47
Male/female, n	21/4	23/15	0.055
Outpatient patients, n (%)	4 (16)	17 (45)	<b>0.028</b>
Patients admitted for emergency, n (%)	19 (76)	10 (26)	<b>&lt;0.001</b>
Diabetes duration, years	15 (10, 24)	20 (10, 28)	0.91
HbA <sub>1c</sub> , %	8.1 ± 1.8	8.3 ± 1.8	0.60
HbA <sub>1c</sub> , mmol/mol	65 ± 20	67 ± 20	0.60
GFR, mL/min/1.73 m <sup>2</sup>	67 ± 28	78 ± 31	0.18
UACR, mg/g Cr	58 (23, 319)	36 (9, 76)	<b>0.050</b>
CRP, mg/dL	2.35 (1.01, 7.86)	1.45 (0.45, 3.98)	0.31
PAD, n (%)	23 (92)	31 (82)	0.30
Neuropathy, n (%)	22 (98)	30 (79)	0.50
Previous ulcers, n (%)	16 (64)	23 (61)	0.99
Ulcer duration, months	5 (2, 7)	4 (2, 12)	0.95
Osteomyelitis, n (%)	20 (80)	23 (61)	0.17
Gangrene, n (%)	16 (64)	11 (29)	<b>0.009</b>
Intervention, n (%)			
Revascularization	8 (32)	6 (16)	0.21
Amputation*	15 (60)	7 (18)	<b>0.001</b>
Other surgeries†	9 (36)	8 (21)	0.31

Data are reported as mean ± SD or median (interquartile range) unless otherwise specified. Boldface type indicates statistically significant difference between groups. Cr, creatinine; CRP, C-reactive protein; GFR, glomerular filtration rate; PAD, peripheral artery disease; UACR, urinary albumin-to-creatinine ratio. \*Amputation refers to the transverse removal of part of the lower limb below the ankle joint (minor amputation). Major amputation was not required for any patient. †Other surgeries include surgical debridement, abscess drainage, and reconstructive/regenerative surgeries. The latter were not performed during COVID-19 lockdown, as they were considered elective procedures.

Our data show for the first time that, during COVID-19 lockdown, patients with diabetes admitted to a tertiary care center for DFU had more than threefold risk of amputation compared with those in 2019. DFU represents the most common cause of nontraumatic lower limb amputation worldwide and is responsible for prolonged hospitalization and massive health care costs due to related infection, critical limb ischemia, and gangrene (2,4). DFU care and prevention remain highly recommended to avoid dramatic outcomes (5).

Interestingly, patients of the 2020 group had higher albuminuria and were diagnosed more frequently with gangrene, which are both well-known risk factors for amputation

(2,4). The COVID-19 lockdown may have had a detrimental impact on amputation risk because of the sudden interruption of DFU care and lower limb preservation pathways, resulting in delayed diagnosis and treatment (3). DFU is often characterized by progressive clinical course, which can rapidly lead patients to critical worsening of their ulcers. Of note, we found a higher proportion of patients admitted for emergency and a lower number of patients coming from regular outpatient access among the individuals admitted during the lockdown than those of the 2019 cohort.

In conclusion, the higher risk of amputation observed during COVID-19 lockdown confirms the need for proper

and timely management of DFU patients to prevent dramatic outcomes responsible for a reduction of quality of life and increased morbidity and mortality.

**Duality of Interest.** M.I.M. received honoraria for speaking at meetings from AstraZeneca, Novo Nordisk, Bruno, Mundipharma, and Merck. G.B. received honoraria for speaking at meetings from Roche and Novo Nordisk. D.G. has been an advisory board member for and/or has received speaker's fees from Eli Lilly, Boehringer Ingelheim, Novo Nordisk, Novartis, Mundipharma, and Sanofi. K.E. received honoraria for speaking at meetings from Novartis, Sanofi, Lilly, AstraZeneca, Boehringer Ingelheim, Novo Nordisk, and Mundipharma. No other potential conflicts of interest relevant to this article were reported.

**Author Contributions.** P.Ca. and M.L. conceived the study and wrote the manuscript. S.S. did the statistical analyses and contributed to the data analysis. M.G. collected data and contributed to writing the manuscript. M.I.M. contributed to data analysis and to writing the manuscript. G.B. contributed to the data analysis and reviewed the manuscript for intellectual content. P.Ch. did the statistical analyses and contributed to the data analysis. D.G. and K.E. conceived the study, contributed to the data analysis, and reviewed and edited the manuscript. All authors approved the final version of the manuscript. K.E. 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.

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