## Supplementary Materials for

Ulcer-risk classification and plantar pressure distribution in patients with diabetic polyneuropathy: exploring the factors that can lead to foot ulceration

Claudia Giacomozzi, Cristina D. Sartor, Rafael Telles, Luigi Uccioli and Isabel C.N. Sacco

## Corresponding author:

Claudia Giacomozzi, Dipartimento Malattie Cardiovascolari, Dismetaboliche e dell'Invecchiamento, Istituto Superiore di Sanità, Viale Regina Elena 299, 00161 Rome, Italy. E-mail: claudia.giacomozzi@iss.it.

Published on

Ann Ist Super Sanità 2018 Vol. 54, No. 4: 284-293

DOI: 10.4415/ANN\_18\_04\_04

This PDF file includes:

Analysis of patients with the additional BMI-based classification: Tables S1-S5 and Figure 1.

## ANALYSIS OF PATIENTS WITH THE ADDITIONAL BMI-BASED CLASSIFICATION

Several patients in the studies were obese (in the Italian study the percentage of obese patients was > 50%). As excessive loads on one's foot structure can modify one's gait pattern and foot-loading distribution, patients within each group of both studies were further divided into below (B) and above (A) an obesity threshold of 31.3kg/m<sup>2</sup>; the threshold was increased slightly to account for the additional weight of equipment and clothing. Group C in the Italian study (healthy controls) was not divided as all volunteers in the group were below the BMI threshold. ANOVAs (p < 0.05) with multiple comparisons based on post-hoc Holm-Bonferroni correction (critical p values adjusted accordingly) were repeated for each dataset (Italian and Brazilian) after each group was divided. Table S1 shows main clinical and anthropometric data within each sub-group: Tables 2S and 3S show the results from the statistical analysis on the Italian study and the Brazilian study respectively.

In both databases, no statistically significant differences were found either among (R1-R3)<sub>B</sub> or among (R1-R3)<sub>A</sub>. However, intra-group variability decreased, and some heel and forefoot trends were observed in the below-threshold groups. This suggests that R1<sub>B</sub> slightly differed from the more compromised groups, while (R1-R3)<sub>A</sub> were very similar to one another, regarding almost all parameters and foot regions. Interestingly, differences were found between B-groups and A-groups in each dataset, and when compared to either C in the Italian study or to non-neuropathic patients in the Brazilian study (R0). More specifically:

- a) in the Italian study, the following parameters were significantly altered:
  - PP: R1<sub>B</sub> lower than C (total foot and heel) and R3<sub>A</sub> higher than C (midfoot);
  - 2. CA: (R1-R3)<sub>B</sub> smaller than C (all areas) and (R2-R3)<sub>A</sub> wider than C (forefoot and toes);
  - MF: all groups, but R1<sub>A</sub> lower than C (forefoot; (R2-R3)<sub>A</sub> also lower at heel and R1<sub>A</sub> also lower at toes);

- 4. PTI: all A-groups higher than C (midfoot and fore-foot):
- 5.v) CT: with respect to C, longer absolute, overall stance in R1<sub>A</sub>, and longer relative stance in all groups (heel and forefoot; R1<sub>B</sub> at forefoot only).
- b) In the Brazilian study, the majority of patients in R0, R1 and R2 belonged to the below-threshold group, with as low as three patients only in R2<sub>A</sub>. Anyway, some differences were observed in the following parameters:
  - 6. PP: both R3A and R3B had higher PP than R0B at forefoot, also higher than the corresponding values in all other groups. The total foot PP was also higher for R3, but differences were only highlighted between R0B and R3B;
  - 7. CA: high variability was found in all groups; differences (without statistical significance) were observed for R2B (total foot smaller than R0A, heel smaller than R2A, midfoot smaller than R1A), and for R3B heel (smaller than R2A);
  - 8. MF: no linear trend was found among the groups; R1A only was lower than R0<sub>B</sub>.

Besides data in the *Tables*, and since statistical significance might have been limited by high variability and relatively small samples, some interesting trends, and even lack of trends, are shown in *Figure S1* for CT, PP, and PTI at heel and forefoot.

## COMPARISON BETWEEN THE TWO STUDIES

The three neuropathic groups – i.e. all patients in each group, without further BMI-based split – from the Italian study were also compared with corresponding Brazilian groups using 30 two-way ANOVAs (p < 0.05). Factor A was the study (Italian or Brazilian) and Factor B was the neuropathic risk group (R1, R2, or R3). Results from the statistical analysis are reported in *Table S4*.

Corresponding statistical analysis on neuropathic subgroups classified as below- and above- BMI threshold delivered the results summarized in the following *Table S5*. Basically, the analysis seems to highlight greater similarities between corresponding groups of the two studies when BMI is taken into account. However, due to the reduced sample size, this results should be only considered as a suggestion for further investigations.

Table S1
Groups, clinical variables and anthropometric features for patients within the Italian and the Brazilian study, without and with BMI-based classification (mean and SD, % mean)

	c	R0	RO <sub>A</sub>	RO <sub>B</sub>	R1	R1 <sub>A</sub>	R1 <sub>B</sub>	R2	R2 <sub>A</sub>	R2 <sub>B</sub>	R3	R3 <sub>A</sub>	R3 <sub>B</sub>
Italian study													
n	20				18	10	8	37	20	17	28	13	15
Sex (M/F)	5/15				8/10	7/3	1/7	17/20	7/13	10/7	17/11	8/5	9/6
Age (years)	67.1 (9.8)				65.5 (13.8)	63.5 (12.8)	68.6 (15.2)	70.0 (11.1)	68.7 (10.8)	71.9 (11.5)	69.3 (13.9)	68.6 (15.5)	69.7 (13.5)
BMI (kg/m²)	27.4 (6.9)				32.8 (19.8) c	37.2 (13.2) C,R1 <sub>B</sub> ,R2 <sub>B</sub> ,R3 <sub>B</sub>	27.2 (10.3) R1 <sub>A</sub> ,R2 <sub>A</sub> ,R3 <sub>A</sub>	32.6 (22.0) c	37.5 (15.5) C,R1 <sub>B</sub> ,R2 <sub>B</sub> ,R3 <sub>B</sub>	26.9 (12.4) R1 <sub>A</sub> ,R2 <sub>A</sub> ,R3 <sub>A</sub>	32.1 (20.3) ⊂	37.2 (14.6) C,R1 <sub>B</sub> ,R2 <sub>B</sub> ,R3 <sub>B</sub>	27.7 (11.9) R1 <sub>A</sub> ,R2 <sub>A</sub> ,R3 <sub>A</sub>
Stance (ms)	822.5 (7.1)				957.0 (21.7)	934.3 (12.4) c	985.4 (29.7)	940.8 (36.7)	936.0 (46.5)	946.5 (21.9)	894.0 (18.2)	834.7 (14.0)	945.4 (19.3)
Type of diabetes (1/2)					1/17	1/9	0/8	1/36	1/19	0/17	7/21	0/13	7/8
DNI					4.3 (19.8) R2,R3	4.1 (18.0) R2 <sub>A</sub> ,R2 <sub>B</sub> ,R3 <sub>A</sub> ,R3 <sub>B</sub>	4.6 (21.3) R2 <sub>A</sub>	5.6 (13.2) R1	5.6 (12.4) R1 <sub>A</sub> ,R1 <sub>B</sub>	5.5 (14.6) R1 <sub>A</sub>	5.7 (15.0) R1	5.6 (18.9) R1 <sub>A</sub>	5.7 (12.6) R1 <sub>A</sub>
VPT					35 (21)	38 (17)	32 (26)	34 (21)	34 (20)	34 (22)	37 (22)	35 (31)	38 (15)
ABI					1.1 (16.4)	1.1 (17.5)	1.0 (11.7)	1.1 (17.7)	1.1 (19.4)	1.1 (16.1)	1.1 (21.1)	1.0 (23.1)	1.2 (18.9)
YOD					18.8 (62.2)	18.1 (69.8)	19.8 (54.8)	19.1 (63.5)	20.7 (64.2)	17.0 (61.7)	25.6 (61.2)	23 (66.0)	27.5 (59.7)
Brazilian study													
n		58	15	43	29	8	21	30	3	27	17	8	9
Sex (M/F)		28/30	7/8	21/22	16/13	4/4	12/9	11/19 R3	0/3	11/16	14/3 RO,R2	5/3	9/0
Age (years)		57.2 (11.4)	57.2 (15.0)	57.3 (9.9)	56.9 (8.1)	55.4 (9.6)	57.5 (7.3)	58.6 (9.9)	54.7 (9.1)	59.0 (10.0)	58.1 (9.1)	58.1 (10.7)	58.0 (8.1)
BMI (kg/m²)		28.8 (16.3)	34.5 (9.3)	26.8 (11.9)	29.3 (14.7)	34.8 (11.5)	27.4 (7.7)	27.6 (13.0)	34.6 (9.0)	26.8 (10.1)	30.4 (17.4)	34.9 (10.9)	26.5 (8.7)
Stance (ms)		696.4 (46.8)	659.4 (12.5)	709.3 (52.9)	663.0 (8.3)	669.4 (7.2)	661.3 (9.0)	660.4 (7.5)	697.3 (7.3)	655.8 (7.5)	670.2 (8.2)	676.4 (6.1)	670.3 (10.3)
Type of diabetes (1/2)		0/58	0/15	0/43	0/29	0/8	0/21	0/30	0/3	0 / 27	0/17	0/8	0/9
NSS		3.7 (102.7)	4.6 (84.8)	3.3 (112.1)	7.6 (34.2) RO	5.4 (61.1)	8.5 (20.0)	7.3 (34.2) RO	9.3 (6.5)	7.0 (37.1)	7.7 (27.3) RO	8.1 (19.8)	7.3 (34.2)
HbA1c (%)		7.8 (17.9)	8.0 (10.0)	7.6 (23.7)	8.8 (13.6)	9.4 (8.5)	8.1 (14.8)	8.5 (30.6)	10.9 (43.1)	8.1 (25.9)	8.3 (34.9)	6.2	10.3
YOD		8.8 (87.5)	8.6 (101.2)	8.9 (83.1)	11.0 (69.1)	8.5 (90.6)	12.0 (65.8)	15.7 (66.9) ro	14.3 (58.7)	15.9 (67.9)	13.4 (50.0)	14.0 (55)	12.9 (46.5)

n: number of patients. Groups: C = healthy volunteers (all below BMI threshold);  $RO_A =$  non-neuropathic patients above BMI threshold;  $RO_A =$  non-neuropathic patients without deformities and above BMI threshold;  $RO_A =$  neuropathic patients without deformities and below BMI threshold;  $RO_A =$  neuropathic patients with deformities and above BMI threshold;  $RO_A =$  neuropathic patients with previous ulceration and above BMI threshold;  $RO_A =$  neuropathic patients with previous ulceration and above BMI threshold;  $RO_A =$  neuropathic patients with previous ulceration and below BMI threshold;  $RO_A =$  neuropathic patients with previous ulceration and below BMI threshold (IWGDF international consensus, Bus et~al, 2016). BMI threshold: 31.3kg/m²). PO(A = al) Parameters: PO = peak pressure; PO(A = al) Parameters: PO = peak pressure; PO(A = al) Parameters: PO = peak pressure; PO(A = al) Parameters: PO(A = al)

Table S2
Italian study. PPD main parameters. Mean values, SD (% of mean) and results of ANOVA on clinical subgroups below (B) and above (A) BMI threshold

old								
Variable	Foot area	Control	R1 <sub>A</sub>	R1 <sub>B</sub>	R2 <sub>A</sub>	R2 <sub>B</sub>	R3 <sub>A</sub>	R3 <sub>B</sub>
PP (kPa)	Total (F=1.774;	254.2	279.7	212.9	279.9	257.6	280.4	257.1
	p=0.113)	(9.1) R1 <sub>B</sub>	(21.4)	(15.5) c	(22.3)	(30.1)	(21.7)	(23.7)
	Heel (F=1.517;	215.1	209.4	179.8	205.2	181.3	203.3	211.1
	p=0.181)	(8.5) R1 <sub>B</sub>	(24.0)	(16.2) c	(20.2)	(25.9)	(31.4)	(19.4)
	Midfoot (F=2.753;	92.0	103.1	84.5	105.1	90.7	114.4	89.0
	p=0.016)	(9.1) <sub>R3<sub>A</sub></sub>	(9.9)	(18.3) r3 <sub>a</sub>	(29.9)	(33.8)	(14.6) c,r1 <sub>B</sub>	(32.0)
	Forefoot (F=1.818;	246.6	270.0	196.7	250.9	224.4	258.4	216.8
	p=0.104)	(15.4)	(23.6)	(18.1)	(31.4)	(33.3)	(25.1)	(29.3)
	Toes (F=0.428;	144.4	126.4	130.4	144.3	147.5	154.6	122.4
	p=0.859)	(19.8)	(47.4)	(26.6)	(45.6)	(61.6)	(54.0)	(63.0
CA	Total (F=9.304;	74.9	71.6	67.9	73.0	63.1	70.7	64.6
(%insole)	p<0.001)	(5.3) R1 <sub>B</sub> ,R2 <sub>B</sub> ,R3 <sub>B</sub>	(6.1) R2 <sub>B</sub>	(8.1) c	(8.5) R2 <sub>B</sub> ,R3 <sub>B</sub>	(7.5) c,r1 <sub>A</sub> ,r2 <sub>A</sub>	(11.6)	(11.6) c,r2 <sub>A</sub>
	Heel (F=4.358;	25.7	24.6	24.2	24.8	23.5	24.9	22.8
	p<0.001)	(4.7) <sub>R2<sub>B</sub>,R3<sub>B</sub></sub>	(11.4)	(9.3)	(7.9) <sub>R3<sub>B</sub></sub>	(7.5) c	(9.3)	(6.7) c,R2 <sub>A</sub>
	Midfoot (F=6.464;	18.8	18.5	15.9	19.0	14.4	19.2	15.3
	p<0.001)	(6.2) R1 <sub>B</sub> ,R2 <sub>B</sub> ,R3 <sub>B</sub>	(18.6)	(21.1) c	(20.7) R2 <sub>B</sub>	(21.9) c,r2 <sub>A</sub> ,r3 <sub>A</sub>	(17.5) R2 <sub>B</sub>	(21.5) c
	Forefoot (F=7.608;	31.3	29.0	27.9	28.7	26.2	26.2	26.2
	p<0.001)	(5.0) R1 <sub>B</sub> ,R2 <sub>A</sub> ,R2 <sub>B</sub> ,R3 <sub>A</sub> ,R3 <sub>B</sub>	(9.3)	(9.2) ⊂	(10.0) ∈	(11.5) c	(10.5) c	(16.1) ⊂
	Toes (F=3.911;	10.8	8.9	9.7	8.5	8.1	8.0	7.4
	p=0.002)	(18.1) R2 <sub>A</sub> ,R2 <sub>B</sub> ,R3 <sub>A</sub> ,R3 <sub>B</sub>	(17.1)	(13.0)	(26.5) c	(30.9) ⊂	(32.7) ⊂	(45.6) c
MF (%N)	Total (F=2.180;	104.2	97.9	96.5	96.4	96.6	97.7	98.5
	p=0.051)	(10.0)	(6.9)	(9.5)	(7.3)	(8.8)	(4.6)	(7.7)
	Heel (F=3.779;	65.5	56.3	58.4	53.8	59.3	54.2	58.7
	p=0.002)	(13.5) R2 <sub>A</sub> ,R3 <sub>AR</sub>	(17.5)	(18.4)	(15.3) c	(15.0)	(15.8) c	(11.8)
	Midfoot (F=2.339;	21.7	21.3	18.5	21.0	18.0	24.5	18.2
	p=0.038)	(14.5)	(23.5)	(36.6)	(36.9)	(34.8)	(22.4)	(28.9)
	Forefoot (F=5.880;	82.9	70.5	63.9	62.3	65.6	61.1	58.1
	p<0.001)	(16.7) R1 <sub>B</sub> ,R2 <sub>A</sub> ,R2 <sub>B</sub> ,R3 <sub>A</sub> ,R3 <sub>B</sub>	(14.7)	(12.8) ∈	(24.9) ⊂	(22.2) c	(23.6) ∈	(30.7) ⊂
	Toes (F=1.677;	15.5	9.5	15.1	11.8	14.0	11.8	11.3
	p=0.135)	(25.7) R1 <sub>A</sub>	(40.5) c	(28.2)	(57.0)	(62.6)	(50.9)	(64.1)
PTI (kPa*s)	Total (F=1.031;	139.2	164.4	139.2	160.2	145.7	149.4	159.9
	p=0.410)	(10)	(22.4)	(29.6)	(38.9)	(22.6)	(20.5)	(17.6)
	Heel (F=1.164;	82.8	93.2	84.6	95.3	81.6	83.2	104.7
	p=0.332)	(17.9)	(33.9)	(38.4)	(53.7)	(24.2)	(22.0)	(31.0)
	Midfoot (F=1.284;	45.6	58.5	46.4	62.6	48.0	57.6	46.3
	p=0.272)	(15.1) R1 <sub>A</sub>	(18.0) c	(41.3)	(78.8)	(37.0)	(24.5)	(30.5)
	Forefoot (F=1.640;	86.6	121.4	94.9	114.9	102.0	108.9	104.2
	p=0.144)	(10.5) R1 <sub>A</sub> ,R3 <sub>A</sub>	(20.4) ∈	(32.4)	(52.1)	(30.8)	(24.6) ⊂	(32.1)
	Toes (F=0.710;	35.6	34.8	47.1	44.4	40.8	45.8	40.1
	p=0.642)	(17.0)	(39.1)	(40.8)	(53.0)	(54.3)	(64.2)	(56.1)
FTI (%N*s)	Total (F=0.553;	67.5	69.1	68.5	65.1	67.7	60.9	68.3
	p=0.766)	(15.0)	(12.4)	(25.6)	(35.2)	(16.2)	(12.4)	(14.6)
	Heel (F=1.355;	24.7	23.4	26.6	23.4	26.3	21.4	28.7
	p=0.241)	(24.4)	(24.7)	(34.7)	(44.9)	(30.1)	(15.8)	(31.0)
	Midfoot (F=0.978;	8.7	10.7	8.8	10.7	8.7	11.0	8.4
	p=0.444)	(21.3)	(32.8)	(48.5)	(71.0)	(48.3)	(28.7)	(36.6)
	Forefoot (F=1.292;	30.6	32.4	28.9	27.7	29.0	25.2	27.8
	p=0.268)	(16.3)	(11.5) <sub>R3<sub>A</sub></sub>	(24.7)	(35.0)	(21.7)	(20.1) R1 <sub>A</sub>	(34.8)
	Toes (F=0.753;	3.6	2.5	4.3	3.3	3.8	3.3	3.4
	p=0.609)	(27.0)	(27.0)	(46.8)	(32.8)	(64.6)	(63.5)	(66.1)
CT (ms)	Stance (ms)	822.5	934.3	985.4	936.0	946.5	834.7	945.4
	(F=0.933; p=0.475)	(7.1) R1 <sub>A</sub>	(12.4) c	(29.7)	(46.5)	(21.9)	(14.0)	(19.3)
CT	Heel (F=5.111;	72.7	83.2	77.7	82.7	82.6	82.9	83.8
(%stance)	p<0.001)	(8.6) R1 <sub>A</sub> ,R2 <sub>A</sub> ,R2 <sub>B</sub> ,R3 <sub>A</sub> ,R3 <sub>B</sub>	(11.4) ∈	(11.9)	(10.6) c	(7.4) ⊂	(6.5) c	(9.1) c
,	F	(-10) A A. I. ZBII DAI DB	( ) C	( )	(10.0)	(, , , , , ,	(0.0)	(>/ C

(Continues)

**Table S2** (Continued)

Variable	Foot area	Control	R1 <sub>A</sub>	R1 <sub>B</sub>	R2 <sub>A</sub>	R2 <sub>B</sub>	R3 <sub>A</sub>	R3 <sub>B</sub>
	Midfoot (F=2.689;	83.2	85.2	79.1	83.1	79.2	84.6	77.9
	p=0.019)	(5.2)	(4.1)	(9.8)	(7.5)	(10.3)	(4.9)	(11.5)
	Forefoot (F=14.261; p<0.001)	91.8 (2.7) R1 <sub>A</sub> ,R1 <sub>B</sub> ,R2 <sub>A</sub> ,R2 <sub>B</sub> ,R3 <sub>A</sub> ,R3 <sub>B</sub>	97.4 (1.5) c	95.3 (2.3) c	96.7 (2.5) c	96.2 (2.2) c	97.1 (2.4) c	97.6 (2.3) c
	Toes (F=0.508;	67.0	64.2	72.3	69.7	61.9	66.4	66.1
	p=0.801)	(16.1)	(20.6)	(17.1)	(26.6)	(30.1)	(36.9)	(25.1)

n: number of patients. Groups: C = healthy volunteers (all below BMI threshold);  $R1_A = neuropathic$  patients without deformities and above BMI threshold;  $R2_b = neuropathic$  patients with deformities and above BMI threshold;  $R2_b = neuropathic$  patients with deformities and below BMI threshold;  $R3_b = neuropathic$  patients with previous ulceration and above BMI threshold;  $R3_b = neuropathic$  patients with previous ulceration and below BMI threshold;  $R3_b = neuropathic$  patients with previous ulceration and below BMI threshold (IWGDF international consensus, Bus etal, 2016). BMI threshold:  $31.3 kg/m^3$ ). etal  $R3_b = neuropathic$  patients with previous ulceration and below BMI threshold;  $R3_b = neuropathic$  patients with previous ulceration and below BMI threshold;  $R3_b = neuropathic$  patients with previous ulceration and below BMI threshold;  $R3_b = neuropathic$  patients with previous ulceration and below BMI threshold;  $R3_b = neuropathic$  patients with previous ulceration and below BMI threshold;  $R3_b = neuropathic$  patients with previous ulceration and below BMI threshold;  $R3_b = neuropathic$  patients with previous ulceration and below BMI threshold;  $R3_b = neuropathic$  patients with previous ulceration and below BMI threshold;  $R3_b = neuropathic$  patients with previous ulceration and below BMI threshold;  $R3_b = neuropathic$  patients with previous ulceration and below BMI threshold;  $R3_b = neuropathic$  patients with previous ulceration and below BMI threshold;  $R3_b = neuropathic$  patients with previous ulceration and below BMI threshold;  $R3_b = neuropathic$  patients with previous ulceration and below BMI threshold;  $R3_b = neuropathic$  patients with previous ulceration and below BMI threshold;  $R3_b = neuropathic$  patients with previous ulceration and below BMI threshold;  $R3_b = neuropathic$  patients with previous ulceration and below BMI threshold;  $R3_b = neuropathic$  patients with previous ulceration and below BMI threshold;  $R3_b = neuropathic$  patients with previous ulcerat

Table S3
Brazilian study. PPD main parameters. Mean values, SD (% of mean) and results of ANOVA on clinical subgroups below (B) and above (A) BMI threshold

Variable	Foot area	RO <sub>A</sub>	RO <sub>B</sub>	R1 <sub>A</sub>	R1 <sub>B</sub>	R2 <sub>A</sub>	R2 <sub>B</sub>	R3 <sub>A</sub>	R3 <sub>B</sub>	
PP (kPa)	Total	360.1 (27.8)	327.3 (14.7) <sup>a</sup>	397.5 (22.3)	366.8 (16.8)	315.9 (8.5)	344.9 (20.7)	399.1 (21.7)	406.1 (16.5) <sup>a</sup>	F = 2.985; P = 0.0062 $RO_B < R3_B$
	Heel	298.4 (31.5)	278.8 (17.8)	291.2 (15.2)	292.8 (17.7)	245.6 (13.4)	285.1 (22.0)	300.5 (31.2)	316.3 (20.0)	F = 0.710; P = 0.6638
	Midfoot	124.5 (32.5)	119.1 (42.4)	149.4 (21.0)	141.0 (30.0)	128.9 (10.9)	130.4 (53.2)	115.0 (25.9)	174.8 (58.5)	F = 1.11; P = 0.3589
	Forefoot	347.6 (28.0)	300.7 (18.9) a,b	365.1 (15.8)	351.5 (18.8)	310.7 (7.5)	324.5 (22.7)	390.2 (22.1) b	393.9 (16.9) a	F = 3.836; P = 0.0008 $RO_B < R3_B$ $RO_B < R3_A$
	Toes	185.9 (42.1)	157.8 (48.5)	218.3 (57.9)	145.9 (48.6)	89.9 (68.3)	139.4 (48.1)	146.8 (32.5)	134.4 (50.7)	F = 1.386; P = 0.2168
CA (%insole)	Total	87.3 (8.2) a	82.6 (10.5)	83.8 (13.4)	80.9 (7.2)	87.3 (1.5)	78.0 (10.8) <sup>a</sup>	81.9 (10.1)	77.1 (7.5)	F = 2.836; $P = 0.0009RO_A > R2_B$
	Heel	39.65 (12.6)	38.7 (12.4)	42.5 (12.0)	39.7 (17.6)	43.1 (10.4) a,b	37.4 (15.5) <sup>a</sup>	44.0 (11.6)	41.7 (13.4) b	F = 2.347; P = 0.0275 $R2_B < R2_A$ $R2_A > R3_B$
	Midfoot	24.94 (23.7)	23.0 (27.4)	30.0 (15.7) <sup>a</sup>	25.1 (19.5)	27.8 (22.7)	20.9 (27.2) <sup>a</sup>	25.4 (17.7)	25.1 (31.1)	F = 2.347; $P = 0.0275R1_A < R2_B$
	Forefoot	45.52 (7.2)	43.0 (7.7)	44.3 (8.8)	42.3 (9.0)	44.9 (6.9)	43.0 (8.4)	44.1 (8.2)	43.9 (9.1)	F = 1.867; P = 0.0803
	Toes	13.26 (23.4)	12.6 (30.2)	13.4 (21.7)	12.1 (29.7)	10.3 (49.7)	11.1 (22.5)	13.2 (28.8)	13.8 (13.0)	F = 1.238; P = 0.271
MF (%N)	Total	96.7 (11.6)	97.9 (11.0)	89.1 (9.5)	94.9 (8.9)	85.8 (10.7)	95.7 (8.7)	90.9 (12.5)	94.9 (12.4)	F = 1.535; P = 0.1614
	Heel	63.0 (17.9)	69.6 (14.2) <sup>a</sup>	57.9 (16.1) <sup>a</sup>	65.8 (14.6)	58.8 (16.0)	64.8 (12.6)	62.2 (17.2)	65.0 (15.7)	F = 2.146; $P = 0.0434RO_B > R1_A$
	Midfoot	17.1 (39.7)	17.1 (45.0)	20.0 (32.0)	18.7 (38.6)	19.9 (13.6)	15.4 (40.2)	13.5 (34.0)	21.5 (73.1)	F = 1.064; P = 0.3906
	Forefoot	76.6 (12.3)	76.0 (13.6)	69.2 (11.9)	74.7 (11.6)	72.1 (14.0)	76.1 (13.7)	73.9 (18.9)	72.1 (8.9)	F = 0.522; P = 0.8163
	Toes	11.6 (45.8)	11.8 (55.0)	10.4 (50.1)	8.7 (40.0)	4.9 (83.5)	8.9 (40.4)	8.7 (45.0)	8.5 (42.4)	F = 1.723; P = 0.1092
PTI (kPa*s)	Total	150.2 (19.8)	145.3 (32.7)	161.2 (21.3)	147.0 (18.6)	141.6 (14.1)	147.7 (19.2)	168.6 (16.8)	168.2 (17.6)	F = 0.785; P = 0.6013
	Heel	75.2 (20.9)	82.6 (43.5)	81.7 (15.2)	78.5 (25.4)	79.2 (7.4)	75.1 (22.6)	91.7 (39.4)	79.0 (19.4)	F = 0.555; P = 0.7911
	Midfoot	43.8 (37.0)	41.5 (54.0)	50.9 (16.3)	43.6 (33.5)	48.0 (22.1)	42.5 (52.7)	41.2 (30.1)	54.8 (52.8)	F = 0.438; P = 0.8769

(Continues)

**Table S3** (Continued)

Variable	Foot area	RO <sub>A</sub>	RO <sub>B</sub>	R1 <sub>A</sub>	R1 <sub>B</sub>	R2 <sub>A</sub>	R2 <sub>B</sub>	R3 <sub>A</sub>	R3 <sub>B</sub>	
	Forefoot	104.1 (26.1)	94.2 (38.4)	104.4 (17.1)	99.1 (20.4)	95.7 (17.7)	102.9 (23.2)	118.2 (22.6)	119.6 (26.8)	F = 1.328; P = 0.2423
	Toes	40.9 (52.8)	34.7 (78.9)	50.4 (95.8)	29.9 (47.8)	20.5 (90.7)	31.02 (49.3)	33.3 (44.1)	29.8 (39.6)	F = 0.773; P = 0.6113
FTI (%N*s)	Total	46.4 (8.6)	49.0 (40.8)	43.2 (9.7)	44.8 (10.5)	47.0 (11.5)	46.3 (8.4)	45.5 (8.4)	45.0 (12.7)	F = 0.447; P = 0.8706
	Heel	15.6 (16.0)	18.2 (44.0)	15.0 (14.0)	16.6 (21.0)	18.1 (11.6)	16.6 (19.9)	17.1 (19.9)	15.9 (17.6)	F = 0.7610; P = 0.6209
	Midfoot	5.5 (49.4)	5.4 (60.7)	6.5 (27.9)	5.6 (46.7)	6.3 (27.1)	4.6 (49.8)	4.6 (51.7)	6.3 (73.4)	F = 0.595; P = 0.7587
	Forefoot	22.9 (17.0)	23.0 (40.9)	19.7 (15.2)	20.9 (13.4)	21.4 (15.9)	23.2 (16.0)	22.1 (13.6)	21.1 (24.2)	F = 0.5077; P = 0.8274
	Toes	2.4 (54.9)	2.4 (83.0)	2.1 (57.1)	1.7 (46.5)	1.2 (101.7)	1.9 (48.4)	1.7 (47.9)	1.7 (40.5)	F = 0.873; P = 0.5293
CT (ms)	Total	659.4 (12.5)	709.3 (52.9)	669.4 (7.2)	661.3 (9.0)	697.3 (7.3)	655.8 (7.5)	676.4 (6.1)	670.3 (10.3)	F = 0.2014; P = 0.09846
CT (%stance)	Heel	82.4 (14.4)	83.6 (14.5)	90.6 (9.3)	91.0 (10.6)	91.9 (8.1)	85.5 (11.3)	89.3 (7.3)	90.3 (8.0)	F = 1.785; P = 0.0958
	Midfoot	83.1 (9.0)	83.1 (16.0)	90.6 (6.4)	85.2 (11.5)	90.2 (10.1)	83.0 (13.3)	84.6 (8.0)	87.5 (13.1)	F = 0.577; P = 0.7735
	Forefoot	96.4 (3.1)	95.6 (3.9)	96.9 (2.9)	96.9 (2.2)	97.1 (2.8)	96.6 (2.6)	95.1 (6.9)	97.6 (2.7)	F = 0.67; P = 0.6936
	Toes	67.4 (27.3)	67.3 (30.3)	73.5 (24.9)	72.1 (24.3)	63.1 (41.4)	70.8 (20.8)	72.0 (23.8)	81.2 (14.8)	F = 0.932; P = 0.4841

n: number of patients. Groups:  $RO_A$  = non-neuropathic patients above BMI threshold;  $RO_B$  = non-neuropathic patients below BMI threshold;  $RO_B$  = neuropathic patients without deformities and above BMI threshold;  $RO_B$  = neuropathic patients with deformities and above BMI threshold;  $RO_B$  = neuropathic patients with deformities and above BMI threshold;  $RO_B$  = neuropathic patients with deformities and below BMI threshold;  $RO_B$  = neuropathic patients with previous ulceration and above BMI threshold;  $RO_B$  = neuropathic patients with previous ulceration and below BMI threshold;  $RO_B$  = neuropathic patients with previous ulceration and above BMI threshold;  $RO_B$  = neuropathic patients with previous ulceration and below BMI threshold;  $RO_B$  = neuropathic patients with previous ulceration and above BMI threshold;  $RO_B$  = neuropathic patients with previous ulceration and above BMI threshold;  $RO_B$  = neuropathic patients with previous ulceration and above BMI threshold;  $RO_B$  = neuropathic patients with previous ulceration and above BMI threshold;  $RO_B$  = neuropathic patients with previous ulceration and above BMI threshold;  $RO_B$  = neuropathic patients with previous ulceration and above BMI threshold;  $RO_B$  = neuropathic patients with previous ulceration and above BMI threshold;  $RO_B$  = neuropathic patients with previous ulceration and above BMI threshold;  $RO_B$  = neuropathic patients with previous ulceration and above BMI threshold;  $RO_B$  = neuropathic patients with previous ulceration and above BMI threshold;  $RO_B$  = neuropathic patients with previous ulceration and above BMI threshold;  $RO_B$  = neuropathic patients with previous ulceration and above BMI threshold;  $RO_B$  = neuropathic patients with previous ulceration and above BMI threshold;  $RO_B$  = neuropathic patients with previous ulceration and above BMI threshold;  $RO_B$  = neuropathic patients with previous ulceration and above BMI threshold;  $RO_B$  = neuropathic patients with previous ulceration and above BMI threshold;  $RO_B$  =

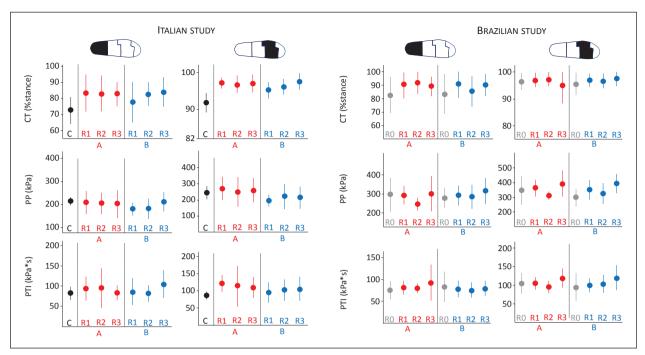


Figure S1 Main results of the BMI-based investigation within both the Italian study (left side) and the Brazilian study (right side): mean values  $\pm$  SD of CT, PP, and PTI under the heel (first and third columns) and the forefoot (second and fourth columns) for controls (C, Italian study, black markers and lines) or non-neuropathic group (R0, Brazilian study, grey markers and lines) and all neuropathic groups, both above (A, red markers and lines) and below (B, blue markers and lines) the BMI threshold.

**Table S4**Results of the 2-way-ANOVA (p < 0.05) conducted on PPD parameters of the two studies (Italian and Brazilian) associated with groups R1, R2, and R3

Variable			p value		
		Factor A	Factor B	Interaction	Interpretation of study values
PP (kPa)	Total	< 0.001	0.086	0.037	Italian < Brazilian. Interaction
	Heel	< 0.001	0.170	0.789	Italian < Brazilian
	Midfoot	< 0.001	0.636	0.622	Italian < Brazilian
	Forefoot	< 0.001	0.059	0.036	Italian < Brazilian. Interaction
	Toes	0.457	0.891	0.267	comparable
CA (%insole)	Total	< 0.001	0.276	0.850	Italian > Brazilian
	Heel	< 0.001	0.719	0.439	Italian < Brazilian
	Midfoot	0.133	0.154	0.413	comparable
	Forefoot	0.006	0.022	0.284	Italian < Brazilian
	Toes	0.495	0.136	0.110	comparable
MF (%N)	Total	0.009	0.991	0.585	Italian > Brazilian
	Heel	< 0.001	0.979	0.939	Italian < Brazilian
	Midfoot	0.022	0.371	0.610	Italian > Brazilian
	Forefoot	< 0.001	0.248	0.303	Italian < Brazilian
	Toes	< 0.001	0.853	0.741	Italian > Brazilian
PTI (kPa*s)	Total	0.816	0.268	0.381	comparable
	Heel	0.024	0.400	0.923	Italian > Brazilian
	Midfoot	0.051	0.995	0.634	comparable
	Forefoot	0.835	0.480	0.244	comparable
	Toes	0.008	0.952	0.661	Italian > Brazilian
FTI (%N*s)	Total	< 0.001	0.778	0.517	Italian > Brazilian
	Heel	< 0.001	0.969	0.938	Italian > Brazilian
	Midfoot	< 0.001	0.792	0.810	Italian > Brazilian
	Forefoot	< 0.001	0.367	0.069	Italian > Brazilian
	Toes	< 0.001	0.918	0.943	Italian > Brazilian
CT (ms)	Total	< 0.001	0.826	0.662	Italian > Brazilian
CT (%stance)	Heel	< 0.001	0.390	0.124	Italian < Brazilian
	Midfoot	0.009	0.512	0.741	Italian < Brazilian
	Forefoot	0.796	0.875	0.421	comparable
	Toes	0.032	0.609	0.624	Italian < Brazilian

Groups: R1 = neuropathic patients without deformities; R2 = neuropathic patients with deformities or vasculopathy; R3 = neuropathic patients with previous ulceration (IWGDF international consensus, Bus et al., 2016). Parameters: PP = peak pressure; CA = contact area; MF = maximum force; PTI = pressure-time integral; FTI = force-time integral; CT = contact time. Statistical analysis: two-way ANOVA (p < 0.05) with multiple comparisons (Holm-Bonferroni correction). ANOVA Factor A: study (two levels: Italian, Brazilian); ANOVA Factor B: groups (three levels: R1, R2, R3). Statistically significant p are written in red.

**Table S5**Results of the 2-way-ANOVA (p<0.05) conducted on PPD parameters of both the Italian and the Brazilian study associated with only neuropathic groups of each study i.e.  $R1_A$ ,  $R1_B$ ,  $R2_A$ ,  $R2_B$ ,  $R3_A$ ,  $R3_B$  (ANOVA Factor A: study, Italian, Brazilian; ANOVA Factor B: groups,  $R1_A$ ,  $R1_B$ ,  $R2_A$ ,  $R2_B$ ,  $R2_A$ ,  $R2_B$ ,  $R3_A$ ,  $R3_B$ )

Variable		Factor A	Factor B	Interaction	Interpretation
PP (kPa)	Total	F=6.887; P=0.010	F=0.117; P=0.989	F=0.521; P=0.760	Italian < Brazilian
	Heel	F=9.467; P=0.003	F=0.210; P=0.958	F=-0.018; P<0.001	Italian < Brazilian. Interaction. All Italian Rn < Brazilian Rn <sub>B</sub> (also, Italian Rn <sub>B</sub> < Brazilian R1 <sub>A</sub> and R3 <sub>A</sub> )
	Midfoot	F=6.691; P=0.011	F=0.105; P=0.991	F=0.831; P=0.530	Italian < Brazilian
	Forefoot	F=9.162; P=0.003	F=0.210; P=0.958	F=0.496; P=0.779	Italian < Brazilian
	Toes	F=0.176; P=0.675	F=0.308; P=0.908	F=1.430; P=0.217	Italian and Brazilian comparable
CA (%insole)	Total	F=1.672; P=0.198	F=0.079; P=0.995	F=0.134; P=0.984	Italian and Brazilian comparable
	Heel	F=0.686; P=0.409	F=0.052; P=0.998	F=0.135; P=0.984	Italian and Brazilian comparable
	Midfoot	F=0.199; P=0.656	F=0.558; P=0.732	F=0.009; P=1.000	Italian and Brazilian comparable
	Forefoot	F=0.329; P=0.567	F=0.066; P=0.997	F=0.033; P=0.999	Italian and Brazilian comparable
	Toes	F=0.043; P=0.836	F=0.129; P=0.986	F=0.265; P=0.931	Italian and Brazilian comparable
MF (%N)	Total	F=0.097; P=0.756	F=0.006; P=1.000	F=0.075; P=0.996	Italian and Brazilian comparable
	Heel	F=1.078; P=0.301	F=0.187; P=0.967	F=-0.155; P<0.001	Italian and Brazilian comparable. Interaction.
	Midfoot	F=1.304; P=0.255	F=0.350; P=0.882	F=0.425; P=0.831	Italian and Brazilian comparable
	Forefoot	F=1.824; P=0.179	F=0.168; P=0.974	F=-0.147; P<0.001	Italian and Brazilian comparable. Interaction.
	Toes	F=6.094; P=0.015	F=0.059; P=0.998	F=1.622; P=0.158	Italian > Brazilian
PTI (kPa*s)	Total	F=0.002; P=0.962	F=0.122; P=0.987	F=0.105; P=0.991	Italian and Brazilian comparable
	Heel	F=1.243; P=0.267	F=0.310; P=0.906	F=-0.068; P<0.001	Italian and Brazilian comparable. Interaction.
	Midfoot	F=1.790; P=0.183	F=0.646; P=0.665	F=-0.196; P<0.001	Italian and Brazilian comparable. Interaction.
	Forefoot	F=0.053; P=0.818	F=0.170; P=0.973	F=0.179; P=0.970	Italian and Brazilian comparable
	Toes	F=3.772; P=0.054	F=0.284; P=0.921	F=1.147; P=0.338	Italian and Brazilian comparable
FTI (%N*s)	Total	F=9.642; P=0.002	F=0.253; P=0.938	F=-0.113; P<0.001	Italian > Brazilian. Interaction
	Heel	F=10.725; P=0.001	F=0.382; P=0.861	F=0.016; P=1.000	Italian > Brazilian
	Midfoot	F=17.855; P<0.001	F=1.467; P=0.204	F=-1.354; P<0.001	Italian > Brazilian. Interaction
	Forefoot	F=4.639; P=0.033	F=0.184; P=0.968	F=0.252; P=0.938	Italian > Brazilian
	Toes	F=19.789; P<0.001	F=0.302; P=0.911	F=1.179; P=0.323	Italian > Brazilian
CT (ms)	Total	F=7.317; P=0.008	F=0.243; P=0.943	F=-0.214; P<0.001	Italian > Brazilian. Interaction.
CT (%stance)	Heel	F=0.378; P=0.540	F=0.010; P=1.000	F=0.059; P=0.998	Italian and Brazilian comparable
	Midfoot	F=0.145; P=0.704	F=0.035; P=0.999	F=0.062; P=0.997	Italian and Brazilian comparable
	Forefoot	F=0.000; P=0.995	F=0.001; P=1.000	F=0.002; P=1.000	Italian and Brazilian comparable
	Toes	F=0.480; P=0.489	F=0.035; P=0.999	F=0.167; P=0.974	Italian and Brazilian comparable

Groups:  $R1_A$  = neuropathic patients without deformities and above BMI threshold;  $R2_A$  = neuropathic patients with deformities and above BMI threshold;  $R2_A$  = neuropathic patients with deformities and above BMI threshold;  $R2_A$  = neuropathic patients with previous ulceration and above BMI threshold;  $R3_A$  = neuropathic patients with previous ulceration and above BMI threshold;  $R3_A$  = neuropathic patients with previous ulceration and above BMI threshold;  $R3_A$  = neuropathic patients with previous ulceration and above BMI threshold;  $R3_A$  = neuropathic patients with previous ulceration and above BMI threshold;  $R3_A$  = neuropathic patients with previous ulceration and above BMI threshold;  $R3_A$  = neuropathic patients with previous ulceration and above BMI threshold;  $R3_A$  = neuropathic patients with previous ulceration and above BMI threshold;  $R3_A$  = neuropathic patients with previous ulceration and above BMI threshold;  $R3_A$  = neuropathic patients with previous ulceration and above BMI threshold;  $R3_A$  = neuropathic patients with previous ulceration and above BMI threshold;  $R3_A$  = neuropathic patients with previous ulceration and above BMI threshold;  $R3_A$  = neuropathic patients with previous ulceration and above BMI threshold;  $R3_A$  = neuropathic patients with previous ulceration and above BMI threshold;  $R3_A$  = neuropathic patients with previous ulceration and above BMI threshold;  $R3_A$  = neuropathic patients with previous ulceration and above BMI threshold;  $R3_A$  = neuropathic patients with previous ulceration and above BMI threshold;  $R3_A$  = neuropathic patients with previous ulceration and above BMI threshold;  $R3_A$  = neuropathic patients with previous ulceration and above BMI threshold;  $R3_A$  = neuropathic patients with previous ulceration and above BMI threshold;  $R3_A$  = neuropathic patients with previous ulceration and above BMI threshold;  $R3_A$  = neuropathic patients with previous ulceration and above BMI threshold;  $R3_A$  = neuropathic patients with previous ulceration and