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# **Real-world treatment patterns and diagnosis of charcot foot in franco-belgian diabetic foot expert centers (The EPiChar Study)**

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**Keywords:**

Belgium; Charcot foot; Diabetic foot; France; Magnetic resonance imaging; Offloading.

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# Abstract

## **Aim:**

To evaluate the real-life diagnosis and therapeutic means of Charcot Neuroosteoarthropathy (CN) in French-Belgian diabetic foot expert centers.

## **Methods:**

We collected clinical characteristics, results of exams and therapeutic pathways of consecutive adult patients with diabetic osteoarthropathy seen in consultation or hospitalization from January 1 to December 31, 2019 in 31 diabetic foot expert centers. The primary outcome was to describe the diagnostic and management methods for CN according to patient clinical characteristics, the clinical-radiological characteristics of acute and chronic CN and discharge means.

## **Results:**

467 patients were included: 364 with chronic CN and 103 in the acute phase. 101 patients had bilateral chronic CN. Most patients were male (73.4%), treated with insulin (73.3%), and with multicomplcated diabetes. In the acute phase, edema and increased foot temperature were present in 75% and 58.3% of cases, respectively. Diagnosis confirmation was usually by MRI and the mode of discharge was variable. In the chronic phase, orthopedic shoes were prescribed in 81.5% of cases.

## **Conclusions:**

This observational study highlights the diagnostic and therapeutic practices in 31 diabetic foot centers. Our results highlight that the use of MRI and the modalities of offloading, an essential treatment in the acute phase, need to be better standardized. Centers were highly encouraging about creating a patient registry.

## Introduction

Charcot Neuroosteoarthropathy (CN) is a severe complication mainly in diabetic patients that arises secondary to severe peripheral neuropathy, with major inflammation leading to progressive bone destruction of the foot or ankle [1]. The origin of this process is not well understood.

CN has an acute and a chronic phase. The acute phase is characterized by the sudden onset of an erythematous, unilateral, slightly painful edema of the foot or ankle with an increase in skin temperature greater than  $2^{\circ}\text{C}$  compared to the contralateral foot. The edema may regress rapidly after discontinuation of weight-bearing and recur when weight-bearing is resumed [2–5]. In some cases, the acute phase is triggered by foot minor trauma, foot surgery, an infection, or a foot ulceration. Without optimal treatment, osteoarticular lysis can develop, leading to multiple fractures or spontaneous dislocation. Initially, the loss of sensitivity may hint at a peripheral neuropathy and a discrete inflammatory syndrome without a clear increase in leukocytosis or CRP found in blood samples. To confirm the diagnosis, Magnetic Resonance Imaging (MRI) of the foot and ankle is the reference examination because it is the most sensitive (between 77 and 100%). It can generally show bone marrow edema and non-displaced fractures, while foot radiographies may appear normal at a very early stage [6].

The primary treatment for acute Charcot foot is early immobilization and offloading of the affected foot with a non-removable Total Contact Cast until abatement of inflammation (difference of temperature less than  $2^{\circ}\text{C}$  between the feet). This should be started as soon as possible to reduce the risk of subsequent fractures and deformities. Inappropriate management leads to a gradual destruction of the foot architecture, abnormality of the morphostatics of the foot and an increased risk of foot ulceration. There is no consensus on whether to allow weight-bearing or the duration of immobilization. The foot can recover with optimal treatment, but delayed diagnosis and treatment is frequent, leading to aggravated chronic phase.

However, although CN is a major complication of diabetes, data about diagnosis and treatment are sparse and frequently retrospective, without consensus. [16, 7–10]. The prevalence of CN varies between 0.1 and 0.4% in the general diabetic population to 12% in diabetes mellitus with long duration, rising to 18% after simultaneous kidney-pancreas transplantation [11–13]. The annual incidence of CN is less than 1% per year in the diabetic population [14]. Recently, in the Danish National Patient Register, a prevalence of 0.56% for hospitalized patients with diabetes was reported from 1995 to 2018 and an incidence rate of 7.4 per 10,000 person-years [15]. As CN is rare, clinician knowledge of this complication is limited, leading to non- or delayed diagnosis and treatment in about 25% of cases [16]. The midfoot is preferentially affected, leading to the “rocker bottom foot” with collapse of the midfoot [17–20]. The incidence of foot ulcer varies between 10 to 17% annually, and is 3.5–fourfold greater in diabetic patients with CN compared with those without CN [17–20]. Foot

ulcer increases the risk of foot amputation [21], causes deterioration in the quality of life [22] and decreases life expectancy [23].

The aim of this study was to evaluate the diagnostic means and management modalities of chronic and acute CN in diabetic foot centers in France and Belgium and explore the feasibility of a future registry for patients with CN.

## **Materials and methods**

This prospective multicenter observational pilot study was conducted from 1 January 2019 to 31 December 2019. Thirty French and one Belgium hospital, reference center for diabetic foot management participated in the study. Our work was performed according to the guidelines of good clinical practice and the Declaration of Helsinki. Written informed consent was obtained from all patients before participation. The study was approved by the ethical committee (CPP Est-III, #2018-A01721-54) and registered on clinical-trials.gov (#NCT03744039).

The study population consisted of all patients with diabetes mellitus aged  $\geq 18$  years, with a previous diagnosis of CN admitted to hospitalization or consultation for acute or chronic CN.

No follow-up was performed.

The primary objective was to describe and analyze the diagnostic and management methods for CN in diabetic foot centers according to the clinical characteristics of patients, the clinical-radiological characteristics of acute and chronic and the discharge means used. Secondary objectives were to determine the prevalence of diabetic patients with acute and chronic CN over a 12-month period treated by each center, and to identify the diabetic foot centers offering surgical management of CN, to specify the type of procedure offered and the indications. Finally, the feasibility of creating a CN patient register was explored by asking centers whether they would be willing to participate in such a registry.

The information collected included sociodemographic data, medical history, and clinical data. Clinical and imaging methods used to investigate the CN and management of the neuropathic osteoarthropathy were recorded. Diabetes was classified into three categories: i) type 1 diabetes mellitus, ii) type 2 diabetes mellitus, iii) other, comprising secondary and glucocortico-induced diabetes. CN was classified as acute or chronic using Eichenholtz stage [24] and the Chantelau classification based on MRI when available [6, 25], a CN was considered as chronic if it presented more than 6 months of progression with no inflammatory sign of the foot. Neuropathy was verified by the presence or absence of suggestive symptoms/signs (paresthesia or cramps, dry skin or hyperkeratosis on the foot, foot deformities) and using the 10-g Semmes–Weinstein monofilament test, as recommended by the International Work Group of Diabetic Foot (IWGDF) [26]. Nephropathy corresponded to a glomerular filtration rate  $< 60 \text{ mL/min/1.73 m}^2$  (modification of diet in renal disease formula). Peripheral artery disease was clinically assessed by the presence or absence of suggestive symptoms/signs (intermittent claudication and leg pain at rest, cold legs or feet, pale or bluish-looking skin), examination of foot pulses [27]. This diagnosis could be

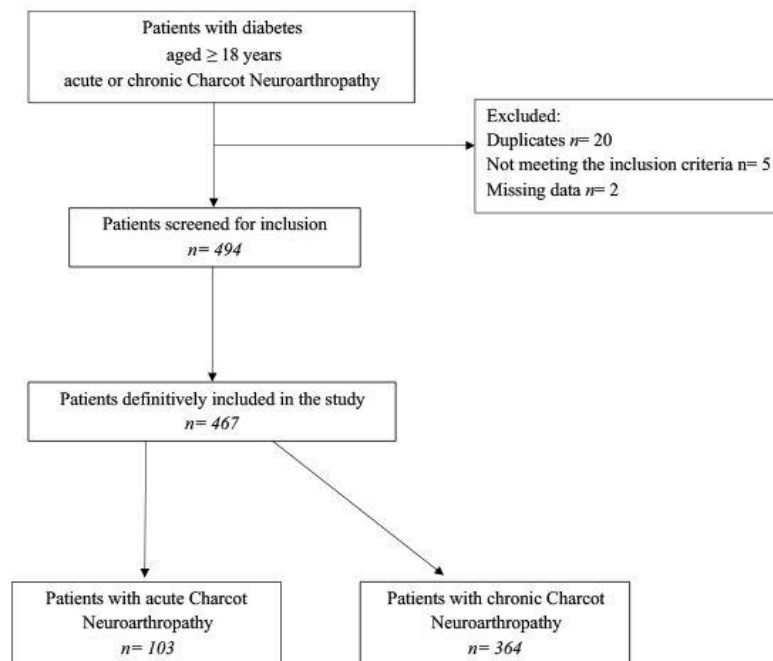
completed by Doppler ultrasound, ankle-brachial pressure index (ABPI), transcutaneous oxygen pressure (TcPO<sub>2</sub>) or great-toe systolic pressure examinations.

## Statistical analysis

Anonymized data were collected in RedCap. Statistical analyses were carried out using SAS software (Statistical Analysis System, version 9.4, SAS Institute, Cary, NC, USA). Population characteristics were expressed as means  $\pm$  standard deviation (SD) or medians, using the first and third quartiles for the quantitative variables, and percentages for qualitative variables. For qualitative variables, comparisons between groups were carried out using the Chi-square test, or Fisher test when appropriate. For quantitative variables, the Student's t-test was used when distribution was Gaussian, and with the Mann–Whitney test otherwise.

A p-value  $< 0.05$  was considered to be statistically significant.

Fig. 1 Patient flowchart



## Results

Overall, 494 patients were screened during the inclusion period. We excluded patients who were previously included and those not meeting the inclusion criteria, leaving a total of 467 participants for analysis (Fig. 1). Of the 467 patients included, 103 had acute CN and 364 had chronic CN. As 101 patients had bilateral CN (21.6%), 568 CN feet were analyzed.

### Baseline characteristics of the study population

The demographic and clinical characteristics of the study population are reported in Table 1. Most patients were male (73.4%) with an average age of  $62.0 \pm 11.5$  years, and had type 2 diabetes mellitus (79.8%) for at least ten years (87.9%).

**Table 1** Demographic and clinical characteristics of the study population (n = 467)

	Total	Acute CN	Chronic CN	P
	<i>n</i> = 467	<i>n</i> = 103	<i>n</i> = 364	<i>Acute vs chronic</i>
Age, mean years ± SD	62.0 ± 11.5	60.2 ± 12.2	62.5 ± 11.2	0.0777
Men, <i>n</i> (%)	343 (73.4)	74 (71.8)	269 (73.9)	0.6765
Body mass index (kg/m <sup>2</sup> ), median (IQR)	30.82 (26.87; 35.06)	30.11 (25.74; 33.14)	31.07 (27.15; 35.25)	0.0247
Missing data, <i>n</i>	8	4	4	
<b>Type of diabetes mellitus</b>				
Type 1, <i>n</i> (%)	80 (17.2)	22 (21.6)	58 (15.9)	0.3752
Type 2, <i>n</i> (%)	372 (79.8)	77 (75.5)	295 (81)	
Other, <i>n</i> (%)	14 (3)	3 (2.9)	11 (3)	
<b>Diabetes duration, <i>n</i> (%)</b>				
> 20 years	237 (51.2)	41 (40.2)	196 (54.3)	0.0262
10–20 years	170 (36.7)	43 (42.2)	127 (35.2)	0.0505
5–10 years	24 (5.2)	10 (9.8)	14 (3.9)	0.0061
< 5 years	32 (6.9)	8 (7.8)	24 (6.6)	0.2928
Insulin use, <i>n</i> (%)	340 (73.3)	69 (67.6)	271 (74.9)	0.1458
<b>HbA1c</b>				
%, median (IQR)	7.4 (6.5; 8.4)	7.5 (6.5; 8.5)	7.3 (6.5; 8.3)	0.9771
mmol/mol, median (IQR)	57 (48; 68)	58 (48; 69)	56 (48; 67)	0.9771
Missing data, <i>n</i>	125	25	100	
Microangiopathy, <i>n</i> (%)	451 (96.8)	96 (94.1)	355 (97.5)	0.1594
Dialysis, <i>n</i> (%)	22 (10)	4 (10.3)	18 (10)	1.0000
GFR (mL/min/1.73m <sup>2</sup> ) median (IQR)	51 (37; 71)	64 (46.5; 90)	49 (35; 69)	0.0078
Missing data <i>n</i>	292	71	221	
Macroangiopathy, <i>n</i> (%)	191 (42.7)	30 (31.3)	161 (45.9)	0.0103
DFU history (grade 3 IWGDF) <i>n</i> (%)	390 (83.9)	63 (61.8)	327 (90.1)	<.0001

IQR, Interquartile Range; GFR, glomerular filtration rate; DFU, Diabetic foot ulcer; IWGDF, International Working Group on Diabetic Foot; SD: Standard Deviation

Most patients were treated by insulin (73.3%, *n* = 340) with a high prevalence of microangiopathy complications (96.8%, *n* = 451) and a history of diabetic foot ulcer and/or amputation of lower limb (83.9%, *n* = 390).

Approximately 39.0% of patients recruited were already followed in a specialized center for C, while 24.5% were newly referred by an endocrinologist following a diagnosis of CN. 11.8% were newly referred by their general practitioner following a diagnosis of CN and 11.6% were self-referred following a diagnosis of CN. Finally, 9% were newly diagnosed CN cases discovered in the recruiting specialized centers.

MRI data were incomplete for certain scores; 21 patients did not have Sanders classification, 20 patients had missing data for Eichenholtz classification, and 302 for Chantelau. According to the Eichenholtz classification [24], 77% were at stage 3 (chronic phase), 10.8% at stage 2 and 11.5% at stage 1 (Table 2).

Using the Chantelau MRI classification [25], 81.6% of the feet presented grade IV or V abnormalities (fracture or bone callus). Using the Sanders classification [28], the CN was mainly localized on the midfoot: the Lisfranc joint line (Sanders II) was affected in 53.7% of cases and the Chopart joint line (Sanders III) in 54.0% of cases. The forefoot (Sanders I) was affected in 14.9% of the cases, the ankle (Sanders IV) in 11.8% and the calcaneus (Sanders V) in 3.1%. At least two areas were affected simultaneously in 34.8% of cases and patients could therefore be classed into more than one Sanders group.



## Acute phase of the disease

In the study population, 108 acute or subacute CN (stages 0/1 and 2 with Eichenholtz classification) were included from 103 patients (22%), with a mean age of  $60.2 \pm 12.2$  years, and a median BMI of 30 kg/m<sup>2</sup>. Twenty-two (21.6%) of patients in the acute group had type 1 diabetes and they had fewer complications than patients with chronic CN in terms of renal function, and macroangiopathy ( $p < 0.05$ ). The absence of foot ulcer history was also significantly different between patients in acute vs chronic phase (61.8% vs 90.1%, respectively;  $p < 0.001$ ) (Table 1).

**Table 2** Progressive stage of Charcot neuroarthropathy (CN) according to Eichenholtz, Chantelau and Sanders classifications ( $n = 568$  Charcot feet)

Classification	Patients, <i>n</i> (%)
<b>Eichenholtz classification [24]</b> <sup>a</sup> (a patient is classified in only one category)	
Stage 0: in situ CN	5 (0.9)
Stage 1: Acute CN	63 (11.5)
Stage 2: Sub-acute CN	58 (10.6)
Stage 3: Chronic CN	422 (77.0)
<b>Chantelau classification [25]</b> <sup>b</sup> (a patient is classified in only one category)	
Grade I (Medullary edema at MRI <sup>c</sup> / Normal X-ray)	10 (3.8)
Grade II (Periosteal and medullary edema at MRI / Normal X-ray)	19 (7.1)
Grade III (Muscular, periosteal and medullary oedema at MRI / Normal X-ray)	19 (7.1)
Grade IV (Fracture at MRI / X-ray abnormalities)	65 (24.4)
Grade V (Bony cortical callus at MRI / X-ray abnormalities)	153 (57.6)
<b>Damaged area, according to Sanders classification [28]</b> (a patient can present damages in multiple categories)	
Sanders I	85 (14.9)
Sanders II	305 (53.7)
Sanders III	307 (54)
Sanders IV	67 (11.8)
Sanders V	18 (3.1)
Sanders unknown	21 (3.7)

20 missing data; b, 302 missing data; c, MRI: Magnetic resonance imaging

Most cases had local inflammatory signs ( $n = 88$ , 81.5%), of which edema was the main symptom ( $n = 81$ , 75.0%), followed by an increase of local warmth ( $n = 63$ , 58.3%), pain ( $n = 55$ , 50.9%) and redness (37, 34.3%) (Table 3).

A triggering factor was observed in 45 cases (41.8% of acute CN) mainly due to foot trauma ( $n = 28$ , 25.9%). Vascular surgery was never recorded as a triggering factor and only 4 cases of orthopedic surgery (Table 3). Acute CN onset occurred in younger patients with type 1 than type 2 diabetes ( $52.5$  years  $\pm 12.3$  vs  $62.1 \pm 10.4$ , respectively;  $p = 0.0043$ ).

Imaging was performed in 92 acute cases (87.2%) to confirm the diagnosis, including MRI ( $n = 70$ , 64.8%), X-ray ( $n = 53$ , 49.1%), Computed Tomography (CT) scan ( $n = 16$ , 14.8%), bone scan ( $n = 8$ , 7.4%), and Positron Emission Tomography (PET)-scan ( $n = 5$ , 4.63%). Other investigations (biology, vascular evaluation) were performed in 51 cases (47.22%) to rule out a differential diagnosis (Table 3).

Offloading was proposed in 88.9% of cases. Standard removable cast walker was most commonly prescribed (n = 39, 36.1%), followed by irremovable boot (n = 22, 20.4%), wheelchair (n = 23, 21.3%), removable custom boot (n = 7, 6.5%), temporary or permanent orthopedic shoes (n = 10, 9.3%), and canes, crutches or walker (n = 8, 7.4%).

**Table 3** Clinical description and management of acute Charcot neuroarthropathy (CN) (n= 103 patients, 108 acute Charcot feet)

	n (%)
<b>Triggering factor</b> <sup>a, e</sup>	45 (41.67)
Trauma	28 (25.93)
Orthopedic surgery	4 (3.70)
Vascular surgery of lower limb	0 (0)
Contralateral discharge	7 (6.48)
Foot Ulcer	6 (5.56)
<b>Local inflammatory signs</b> <sup>b, e</sup>	88 (81.48)
Edema	81 (75.00)
Local warmth	63 (58.33)
Pain	55 (50.93)
Redness	37 (34.26)
<b>Complementary exams</b> <sup>c, e</sup>	92 (87.19)
Standard radiography	53 (49.07)
MRI	70 (64.81)
Computed tomography	16 (14.81)
Bone scan	8 (7.41)
Leukoscan	1 (0.93)
Colloid scintigraphy	5 (4.63)
<b>Other exams</b> <sup>d, e</sup>	51 (47.22)
Whole blood count	47 (43.52)
C-reactive protein (CRP)	49 (45.37)
Uricemia	19 (17.59)
Lower limb venous ultrasound	16 (14.81)
Lower limb arterial ultrasound	4 (3.70)
Aero-anaerobic blood cultures	3 (2.78)
Phosphorus-calcium level, vitamin D	4 (3.70)

<sup>a</sup>, 51 missing data; <sup>b</sup> 3 missing data; <sup>c</sup>, 6 missing data; <sup>d</sup>, 5 missing data; <sup>e</sup>, one or more

### Chronic phase of the disease

460 chronic CN were studied in 364 patients, with a mean age of  $62.5 \pm 11.2$  years, and median BMI of  $31 \text{ kg/m}^2$ . The majority had type 2 diabetes (81%) for longer than 10 years. Insulin treatment was established in 74.9% of patients. Patients with chronic CN had at least two microangiopathic complications in 75% of cases, and dialysis in 10% of cases. Diabetic foot ulcer history was present in 90.1% of patients (Table 1). Specific footwear was noted in

81.5% of cases (370 patients) with custom orthopedic footwear (66.7%), medical series footwear (6.5%) or standard series footwear (5.9%).

Comparison between patients with unilateral (n = 366) and bilateral (n = 101) CN showed a significant difference in the diabetic foot ulcer history: 86% (87 patients) of bilateral CNs had a history of a trophic disorder versus 74% of unilateral CNs (271 patients),  $p = 0.011$ ). No other statistical difference in the demographic and clinical characteristics was observed between the two groups (Table 4).

### **Presence of a diabetic foot ulcer**

All stages combined, 228 patients had a diabetic foot ulcer (48.8%) during examination. A soft tissue infection was suspected and/or documented in 37.7% of cases (86 patients, 13 acute CN, 73 chronic CN), whereas a bone infection was suspected and/or documented in 33.3% of cases (76 patients, 18 acute CN, 58 chronic CN).

### **Surgical approach**

Surgery was proposed for 123 CN (21.6%) overall, and performed in 73 patients (59.3%, 73/123) including 64 (87.7%) chronic CN and 9 (12.3%) acute CN. The main indications were for infection, with positive bacteriological samples (n = 26, 35.6%) and surgical correction of foot deformities (i.e. correction of static disorders of the forefoot (n = 21, 28.8%). Minor and/or major amputations represented 11 indications of surgery (15%). Eleven of the 31 centers offered surgery, all indications combined.

In total, 30 (98%) of centers were willing to supply information to a diabetic foot registry.

## **Discussion**

This multicenter study recruited a large panel of patients with CN, treated in 31 expert centers belonging to the “diabetic foot” group of the Francophone Society of Diabetes. This is one of the largest observational studies carried out on this pathology.

The profile of our patients was comparable to that described in the literature. The male predominance was more pronounced in our study than in previous studies [23, 29, 30, 31], which had not found an increased risk of developing CN by sex [16, 32, 33]. The average age of our population was  $62.0 \pm 11.5$  years. However, CN was also seen in younger patients with type 1 diabetes: 22 of our patients were under 40 years old (4.7% of the population), the youngest being 26 years old. Our results indicated that onset of acute CN was earlier in subjects with type 1 versus type 2 diabetes mellitus (with a significant difference of about 10 years), in accordance with a British study from 2004 [34].

Patients with CN generally had long-standing diabetes (for more than 10 years), most often type 2, insulin dependent and multi-complicated. Microangiopathies were by far the most frequent complications observed (96.8%). However, autonomic neuropathy was only reported in 11.1% of patients. This number was probably underestimated due to an insufficient diagnosis. Most patients had a podiatric history (n = 390, 83.9%). In addition, 9% of CN

were incidentally discovered, confirming the lack of knowledge of this pathology by clinicians.

According to our results, 19% of patients presented an acute CN, of which less than 1% were at the in situ stage (Stage 0, e.g., without deformation or fracture). The presence of local inflammatory signs in the acute phase and, in particular the edema of the foot, is a strong indicator for diagnosis. In accordance with the literature, we found that foot pain was present in over half of the patients (50.9%) [2, 4, 35]. Due to the very good prognosis of the in situ stage, diagnosis of acute CN must be made as early as possible, i.e. as soon as local inflammatory signs appear in a patient with diabetes with peripheral neuropathy. A triggering factor was also noted in 41.7% of our patients, most often corresponding to a foot trauma. Other studies [36] have reported cases following surgery, whereas only four cases were noted in our work

**Table 4** Comparison between unilateral and bilateral Charcot neuroarthropathy (CN)

	Total	Bilateral	Unilateral	P
	<i>n</i> = 467	<i>n</i> = 101	<i>n</i> = 366	
Age (years), mean $\pm$ SD	61.97 $\pm$ 11.45	63.85 $\pm$ 11.65	61.45 $\pm$ 11.35	0.0620
Men, <i>n</i> (%)	343 (73.4)	68 (67.3)	275 (75.1)	0.1156
Body mass index (kg/m <sup>2</sup> ), median (IQR)	30.82 (26.87; 5.06)	31.02 (27.14; 35.19)	30.73 (26.79; 34.94)	0.4210
Missing data, <i>n</i>	8	2	6	
<b>Types of diabetes</b>				
Type 1, <i>n</i> (%)	80 (17.2)	11 (10.9)	69 (18.9)	0.1646
Type 2, <i>n</i> (%)	372 (79.8)	87 (86.1)	285 (78.1)	
Other, <i>n</i> (%)	14 (3)	3 (3)	11 (3)	
<b>Diabetes duration, <i>n</i> (%)</b>				0.6247
> 20 years	237 (51.2)	57 (56.4)	180 (49.7)	
10–20 years	170 (36.7)	34 (33.7)	136 (37.6)	
5–10 years	24 (5.2)	5 (5)	19 (5.2)	
< 5 years	32 (6.9)	5 (5)	27 (7.5)	
<b>Insulin use, <i>n</i> (%)</b>	340 (73.3)	74 (74)	266 (73.1)	0.8534
<b>HbA1c</b>				0.6395
% median (IQR)	7.4 (6.5; 8.4)	7.2 (6.5; 8.3)	7.4 (6.6; 8.4)	
mmol/mol, median (IQR)	57 (48; 68)	55 (48; 67)	57 (49; 68)	
Missing data, <i>n</i>	125	18	107	
<b>Microangiopathy, <i>n</i> (%)</b>	451 (96.8)	95 (95)	356 (97.3)	0.3326
<b>Dialysis, <i>n</i> (%)</b>	22 (10)	7 (12.7)	15 (9.1)	0.4446
<b>GFR (mL/min/1.73m<sup>2</sup>) median (IQR)</b>	51 (37; 71)	42 (30; 63)	53.5 (40; 72)	0.0680
Missing data, <i>n</i>	292	60	232	
<b>Macroangiopathy, <i>n</i> (%)</b>	191 (42.7)	47 (48.5)	144 (41.1)	0.1978
<b>DFU history (grade 3 IWGDF), <i>n</i> (%)</b>	390 (83.9)	94 (94)	296 (81.1)	0.0019
<b>Acute CN</b>	103 (22.06)	17 (16.83)	86 (23.50)	0.1526

To confirm the diagnosis of acute CN, MRI of foot was performed in two-thirds of cases. However, the classification proposed by Chantelau in 2014 to describe the osteoarticular involvement was largely unknown and difficult to interpret. Many patients had missing data (*n* = 302) in the description of the lesions [6, 25]. Radiography, less sensitive than MRI, was only performed in half of patients in the acute phase, yet standard foot X-rays and MRI are essential elements of the initial assessment. X-rays are used to rule out a fracture, and radiographs will be normal in the very early phase of CN. MRI is used to confirm the early diagnosis by showing intra- osseous edema. At this stage, unloading is essential to avoid fractures and changes in the foot architecture. In addition, in the context of diabetes, complications should be assessed regularly (ophthalmological, nephrological, cardiological,

vascular assessment) to detect asymptomatic anomalies, but this can prove challenging in some cases.

The modalities of foot offloading in acute CN varied between the centers. The removable boot (standard or custom-made, going up to the knee or ankle, or a bivalved cast) was most frequently prescribed. The frequency of prescription of an irremovable device (20.4%), which is the reference, was similar to that of other European countries (between 20 and 35%) [29, 36, 37] but lower than American practices (about 50%) [38]. This could be explained by the need for expert opinion, with close monitoring. It could also arise from the removal of the boot due to wounds, or readjustment of the boot in accordance with edema levels, or preventive anticoagulant treatment. Of note, almost 10% of patients in the acute phase were not given a solution to immobilize their foot. This highlights the need for rigorous information and communication to guide appropriate offloading of acute CN.

In the chronic phase, adaptation of footwear was prescribed in 81.5% of cases, with a clear predominance of custom-made orthopedic footwear, performed by a podiatrist. Orthopedic shoeing is standard in the chronic phase of CN, to limit the occurrence of ulceration in case of deformities and to protect the contralateral foot. However, the modalities of this shoeing are not clearly established and should be further studied.

Our study also confirmed that CN is at high risk of foot ulceration, since 84% of our patients had a history of foot wounds and 42% had a wound at inclusion, including a third with a suspicion of soft tissue or bony infection. 21% of our patients had bilateral CN, which is consistent with data from the literature [39]. These patients with bilateral CN showed a higher prevalence of podiatric history (ulceration or amputation) than in patients with unilateral involvement (94.0% vs 81.1%;  $p = 0.0019$ ). No significant difference was observed in other clinical characteristics between the two groups. Bilateral involvement rarely occurred immediately, but the high number of bilateral forms in our study must encourage a close care of patients with CN to avoid bilateral progression.

Finally, CN surgery was often discussed, but rarely practiced, requiring very specialized surgical teams. It should be noted that nine patients (8.7% of acute CN) were operated in the acute phase. While not recommended, this surgery was performed during the acute phase to treat infections (osteitis, osteomyelitis or osteoarthritis) in two-thirds of cases. The remaining surgeries were used to correct severe morphostatic disorders, with often complex interventions, which is normally reserved, and increasingly considered, in the chronic phase. The aim is to improve footwear and limit the risk of ulceration to improve the quality of life of patients. There is no consensus on the indications or type of surgery, which can be internal and/or external osteosynthesis. Similarly, the long-term efficacy on the reduction or prevention of these wounds remains to be evaluated. Several studies seek to clarify its value on functional prognosis and quality of life [40].

This study had several limitations. We used a questionnaire without follow-up, and some information regarding diabetes complications such as the presence of nephropathy were only available as declarative information. In addition, some data were missing due to the different management between centers. Imaging data were often incomplete, highlighting the frequent

ignorance of radiological classifications, and an absence of clear description and interpretation of MRIs. Furthermore, it demonstrates the lack of consensus regarding the imaging technique to be used in the diagnosis of Charcot foot, which may have contributed to the heterogeneity observed in the study. Standard radiography is the first-line examination because it is accessible and inexpensive, but it does not allow for an early diagnosis. MRI is currently the most sensitive examination to confirm the diagnosis of acute Charcot foot, but its interpretation remains delicate and requires a radiologist experienced in this pathology. Finally, no follow-up was carried out, making it impossible to establish the future of patients. However, the main aim of this work was to describe the population of CN followed in France and Belgium and to describe the disparities in management in order to propose future recommendations. The diabetic foot working group has two on-going projects focusing either on acute or chronic CN (CharQUAM study), and 30 (98%) of centers were willing to supply information to a diabetic foot registry.

## Conclusion

This study confirms the frequent diagnostic delay, the lack of consensus on the imaging necessary for the diagnosis, the often removable offloading modes and the transition to the chronic form secondary to non-adapted management. In the acute phase, foot offloading associated with a good observance is essential until inflammation reduces. This management must be followed by provision of suitable footwear in the chronic phase. This study carried out by the diabetic foot working group of the Francophone Society of Diabetes provides an initial inventory of this rare but serious complication of diabetes mellitus. A medium- and long-term evaluation of practices, particularly in terms of benefits on morbidity and mortality, and clear international guidelines is necessary to improve the prognosis of CN, and this should soon be addressed by the upcoming international working group on diabetic foot recommendations.

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patients. S.S. is the guarantor of this works 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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## **Data availability**

The datasets generated and analysed during the current study are available from the corresponding author on reasonable request.

## **Declarations**

### **Conflict of interest**

The authors declare that they have no conflict of interest. Ethical approval Our work was performed according to the guidelines of good clinical practice and the Declaration of Helsinki. The study was approved by the ethical committee (CPP Est-III, #2018-A01721-54) and registered on clinicaltrials.gov (#NCT03744039). Consent to participate Written informed consent was obtained from all patients before participation.

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