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Use, tolerability, benefits and side effects of orthotic devices in Charcot-Marie-Tooth disease

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ABSTRACT

Background Shoe inserts, orthopaedic shoes, ankle-foot orthoses (AFOs) are important devices in Charcot-Marie-Tooth disease (CMT) management, but data about use, benefits and tolerance are scanty.

Methods We administered to Italian CMT Registry patients an online ad hoc questionnaire investigating use, complications and perceived benefit/tolerability/emotional distress of shoe inserts, orthopaedic shoes, AFOs and other orthoses/aids. Patients were also asked to fill in the Quebec User Evaluation of Satisfaction with assistive Technology questionnaire, rating satisfaction with currently used AFO and related services.

Results We analysed answers from 266 CMT patients. Seventy per cent of subjects were prescribed lower limb orthoses, but 19% did not used them. Overall, 39% of subjects wore shoe inserts, 18% orthopaedic shoes and 23% AFOs. Frequency of abandonment was high: 24% for shoe inserts, 28% for orthopaedic shoes and 31% for AFOs. Complications were reported by 59% of patients and were more frequently related to AFOs (69%). AFO users experienced greater emotional distress and reduced tolerability as compared with shoe inserts ($p<0.001$) and orthopaedic shoes ($p=0.003$ and $p=0.045$, respectively). Disease severity, degree of foot weakness, customisation and timing for customisation were determinant factors in AFOs' tolerability. Quality of professional and follow-up services were perceived issues.

Conclusions The majority of CMT patients is prescribed shoe inserts, orthopaedic shoes and/or AFOs. Although perceived benefits and tolerability are rather good, there is a high rate of complications, potentially inappropriate prescriptions and considerable emotional distress, which reduce the use of AFOs. A rational, patient-oriented and multidisciplinary approach to orthoses prescription must be encouraged.

WHAT IS ALREADY KNOWN ON THIS TOPIC

⇒ Foot orthoses are important assistive devices in Charcot-Marie-Tooth disease (CMT) management, but data about use, benefits and tolerance are scanty.

WHAT THIS STUDY ADDS

⇒ Although 70% of patients were prescribed foot orthoses, 19% of them did not use the devices, 31% of users later abandoned them and 59% experienced complications.

⇒ Disease severity, degree and distribution of foot weakness, and both performance and timing of customisation impacted on ankle-foot orthoses (AFOs)' benefit and tolerability.

⇒ At least 19% and possibly up to 58% of AFO prescription might be inappropriate or inadequate.

HOW THIS STUDY MIGHT AFFECT RESEARCH, PRACTICE OR POLICY

⇒ A personalised and rational approach in prescribing AFOs is needed and is likely to improve compliance and tolerability, avoiding waste of resources.

BACKGROUND

Distal motor weakness and foot deformities are the most disabling symptoms in Charcot-Marie-Tooth disease (CMT), the most prevalent group of inherited peripheral neuropathies; variable distal sensory loss, sometimes with sensory ataxia and decreased-to-absent deep tendon reflexes are other characteristic findings.[1]

Orthotic devices such as shoe inserts, orthopaedic shoes and ankle-foot orthoses (AFOs) are important assistive devices in the management of CMT patients, by alleviating symptoms, improving gait, reducing energy costs and ameliorating quality of life. Their reported use ranges between 25% and 55% for shoe inserts and 19% and 49% for AFOs, across different large cohorts of CMT patients.[2–5]

However, data regarding the employment of the different types of orthotics in real life and the related patients' issues and compliance are still scanty. Indeed, clinical experience indicates that patients often find the prescribed orthotic device

uncomfortable or unsuitable, which is consequently used less than prescribed and advisable, or not at all.

AFOs encompass a heterogeneous group of devices. According to their different mechanical characteristics, namely the support provided rather than their material, AFOs can be divided into plastic AFOs (P-AFO) (eg, Codivilla spring, Toe-off and Peromed), which support plantar and dorsal flexion ankle movements, and elastic band AFOs (E-AFO) (eg, Foot-up and Dyna-ankle), which only assist foot dorsiflexion.[6] Among P-AFOs, Peromed guarantees a partial foot sole coverage. A further subdivision splits AFOs into low (L-AFOs) (eg, Peromed, Foot-up) and high (H-AFOs) (eg, Codivilla spring, Toe-off, Dyna-ankle) orthoses.[4]

Lusardi and Nielsen[7] summarised the five main features of an ideal orthosis as being cosmesis, comfort, cost, function and fabrication. Phillips and colleagues[8] explored the benefits, characteristics, barriers to use of AFOs, as perceived by a small cohort of patients with CMT; they highlighted the reported disadvantages and the problems with device supply and repair. Despite users understood the potential benefits of AFOs and identified drawbacks, which might be remedied, they were frustrated by the difficulties of translating this into practice.[8] Indeed, as AFOs are not strictly necessary for gait, the physical and psychological discomfort associated with their use as well as supply issues may have an important role in patients' decision whether to use them or not. Accordingly, it was pointed out that CMT patients, especially women, had a poor compliance with AFOs and orthopaedic shoes, which was attributed to their poor aesthetics.[9] Indeed, Vinci and colleagues found low compliance with AFOs in CMT, with only 20% of patients using the prescribed AFO outside their house.[10] In 2021, Zuccarino *et al*[11] reported a higher rate of satisfaction in a large series of CMT patients recruited through the Inherited Neuropathy Consortium Contact Registry, but one-third of them found the device uncomfortable and reported pain and skin irritation. A very recent report by Bluoin and coauthors, assessing prescription and use of foot orthotics in France, found that out of 795 CMT patients who were prescribed to wear orthotic devices only 391 were users.[5]

Taken all these considerations together, we aimed at exploring the patients' direct experience with regard to benefit, tolerance and disadvantages of the prescribed devices.

METHODS

We administered a series of online questionnaires to patients registered in the National CMT Registry[2] (www.registronmd.it) as previously reported.[12–14] Recruitment was conducted before the COVID-19 pandemic and lasted 3 years (2015–2017). Patients were asked to fill online: (a) an ad hoc questionnaire which collected information about the prescription and use of shoe inserts, orthopaedic shoes, AFOs and upper limb orthoses (with images of the different devices for facilitating identification by the patient, online supplemental figure 1); about side and total period of use; indication of who prescribed them; use at home and/or outside and for how much of the time for both situations; 10-point Visual Analogue Scales (VAS, 0 lowest, 10 highest) for their tolerability, perceived benefit and the emotional distress they caused; past or present complications (ulcers, sores, pressures, pain, others); reasons for choice of use or for non-tolerability/withdrawal; questions about use of knee orthotics, need of cane or crutch (unilateral or bilateral), scooter, wheelchair, electric wheelchair were also included; (b) the validated Italian version of the Quebec User Evaluation of Satisfaction with assistive Technology (QUEST), a self-assessed questionnaire composed of 12 statements, exploring the patient's degree of satisfaction with their currently used AFO and the related

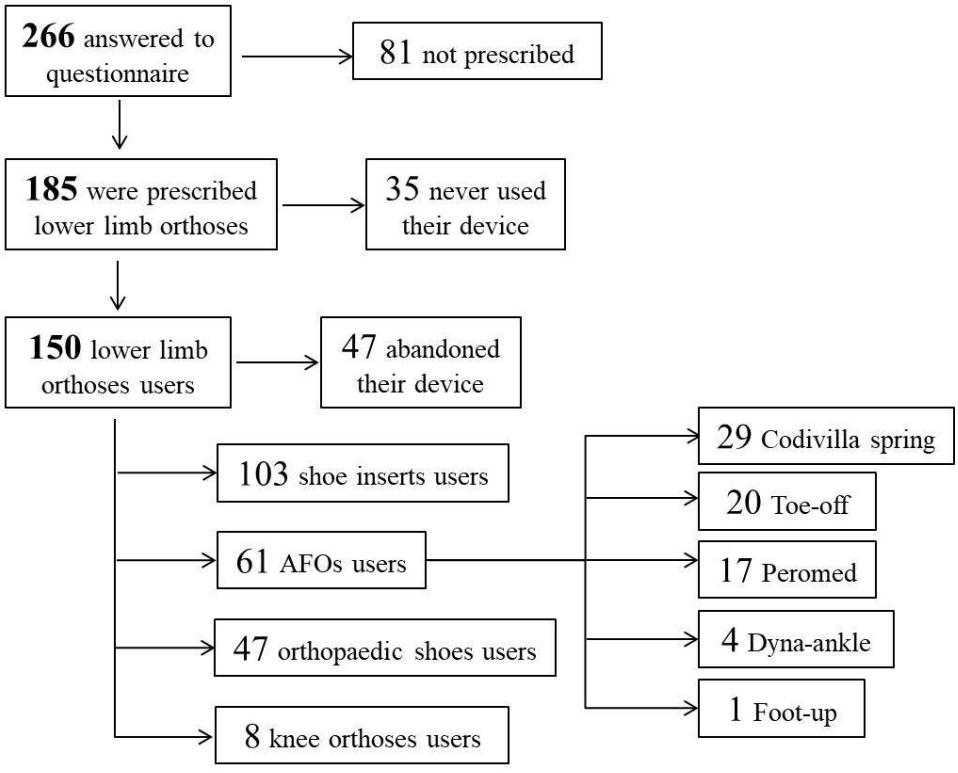

Figure 1 Prescription, use and type of orthoses among the investigated CMT population (n=266). AFO, ankle-foot orthosis; CMT, Charcot-Marie-Tooth.

services experienced. Each statement of QUEST is rated by a 5-point system (1 not satisfied at all, 5 very satisfied).[15]

Patients were at the same time asked to fill in also other questionnaires, including the Hospital Anxiety and Depression Scale (HADS, Italian version)[16] concerning the presence of anxiety, depression and general distress, and the Modified Fatigue Impact Scale (MFIS, Italian version)[17] investigating the perception of fatigue; we could, thus, explore the correlation of orthotic devices prescription/use with neuropsychiatric status—HADS-T, total score and its HADS-Anxiety (HADS-A)/Depression (HADS-D) subscores[12]—and fatigue—MFIS-T total score (general fatigue) and its MFIS-Physical (MFIS-P)/Cognitive (MFIS-C) subscores.[13] HADS-A and HADS-D scores ≥11 define the presence of anxiety/depression and HADS total score (HADS-T) ≥22 of general distress according to Singer and colleagues[18] while a total MFIS score >38 indicates abnormal fatigue, according to Flachenecker and colleagues.[19]

The national CMT Registry contains a series of information about CMT type, including disease severity (CMT examination score-CMTES), duration, muscle strength and body mass index.[2]

Statistical analysis

A description of participant characteristics at baseline was provided in terms of absolute numbers and percentages for categorical data and means with SDs for continuous data. We then used the Mann-Whitney U test, Fisher's exact test and Spearman's rank-order correlation to analyse associations between data on orthoses (prescription, use, side effects, tolerability, perceived benefit, emotional distress) and data from the registry including gender, age, disease duration, disease severity (CMTES), foot strength walking ability and/or use of orthotics, hand disability, sensory symptoms; and data from other questionnaires (HADS, MFIS). Throughout the statistical analysis, the significance level was set at 0.05 (significant: <0.05).

RESULTS

We analysed answers from 266 CMT patients (136 women; mean age 47.5±12.9 years, range 20–77). One hundred and eighty-five (70%) subjects were prescribed lower limb orthoses but 35/185 (19%) never used them. Among the 150 (56%) users, 103 (69%) reported a current use while 47 (31%) abandoned their device. Overall (n=150), 103 (39%) subjects wore shoe inserts, 61 (23%) carried AFOs, 47 (18%) orthopaedic shoes and 8 (3%) knee orthoses (figure 1, table 1). Forty-one (16%) patients wore both AFOs and orthopaedic shoes.

Forty-five patients (17%) used walking aids, which included 21 devices for unilateral support, 24 for bilateral support and 14 wheelchairs (total aids=59). Eventually, 10 upper limb orthoses (two for fingers extension, six for thumb opposition, two for wrist extension) were carried by nine (3%) patients (table 1).

Among AFOs, Codivilla spring (41%), Toe-off (28%) and Peromed (24%) were the most frequently used, followed by Dyna-ankle (6%) and Foot-up (1%), for a total of 71 employed AFOs (table 1). Physiatrists were the main prescribers (62% of cases) followed by neurologists (39%) and orthopaedic surgeons (27%). Prescribed but unused orthoses were 25% of shoe inserts, 20% of orthopaedic shoes and 21% of AFOs. Frequency of abandonment was high among orthotic devices users, namely 24% for shoe inserts, 28% for orthopaedic shoes and 31% for AFOs, after a mean time of use of 4.9±5.5, 4.9±4.5 and 6.3±9.1 years, respectively (online supplemental table 1, figure 2). Abandonment was more frequent for men than women (33% vs 20%, p=0.026).

Table 1 Prescription and use of the different orthotics and aids in the investigated CMT population (n=266)

	Prescription*		Use*	
	Prescribed patients	Prescribed devices†	Users	Used devices†
A) Lower limb orthoses	185/266 (70%)	302	150/266 (56%)	235/302 (78%)
Age	48.0±13.4 (20–77)	/	48.5±13.5 (20–77)	/
CMTES	9.8±5.1 (0–27)	/	9.9±5.5 (0–27)	/
Shoe inserts	145/266 (55%)	137/302 (49%)	103/266 (39%)	103/302 (34%)
Orthopaedic shoes	66/266 (25%)	66/302 (22%)	47/266 (18%)	53/302 (18%)
AFOs	79/266 (27%)	90/302 (30%)	61/266 (23%)	71/302 (24%)
Codivilla spring	40/79 (51%)	38/90 (42%)	29/61 (48%)	29/71 (41%)
Toe-off	24/79 (30%)	21/90 (23%)	20/61 (33%)	20/71 (28%)
Peromed	23/79 (29%)	20/90 (22%)	17/61 (28%)	17/71 (24%)
Dyna-ankle	10/79 (13%)	8/90 (9%)	4/61 (7%)	4/71 (6%)
Foot-up	4/79 (5%)	3/90 (3%)	1/61 (2%)	1/71 (1%)
Knee orthosis	9/266 (3%)	9/302 (3%)	8/266 (3%)	8/302 (3%)
B) Walking aids	45/266 (17%)	59	45/266 (17%)	59/59 (100%)
Age	52.4±12.4 (20–74)	/	52.4±12.4 (20–74)	/
CMTES	15.0±5.2 (4–27)	/	15.0±5.2 (4–27)	/
Unilateral	21/45 (47%)	21/59 (36%)	21/45 (47%)	21/59 (36%)
Bilateral	9/45 (20%)	10/59 (17%)	9/45 (20%)	10/59 (17%)
Walker	14/45 (31%)	14/59 (24%)	14/45 (31%)	14/59 (24%)
Wheelchair	14/45 (31%)	14/59 (24%)	14/45 (31%)	14/59 (24%)
C) Upper limb orthosis	9/266 (3%)	10	9/266 (3%)	10/10 (100%)
Age	47.6±11.1 (28–63)	/	47.6±11.1 (28–63)	/
CMTES	14.2±6.8 (3–25)	/	14.2±6.8 (3–25)	/

*Mean±standard deviation (range), or n (%).
†Some patients did not give complete information about their device.
AFOs, ankle-foot orthoses; CMTES, CMT Examination Score.

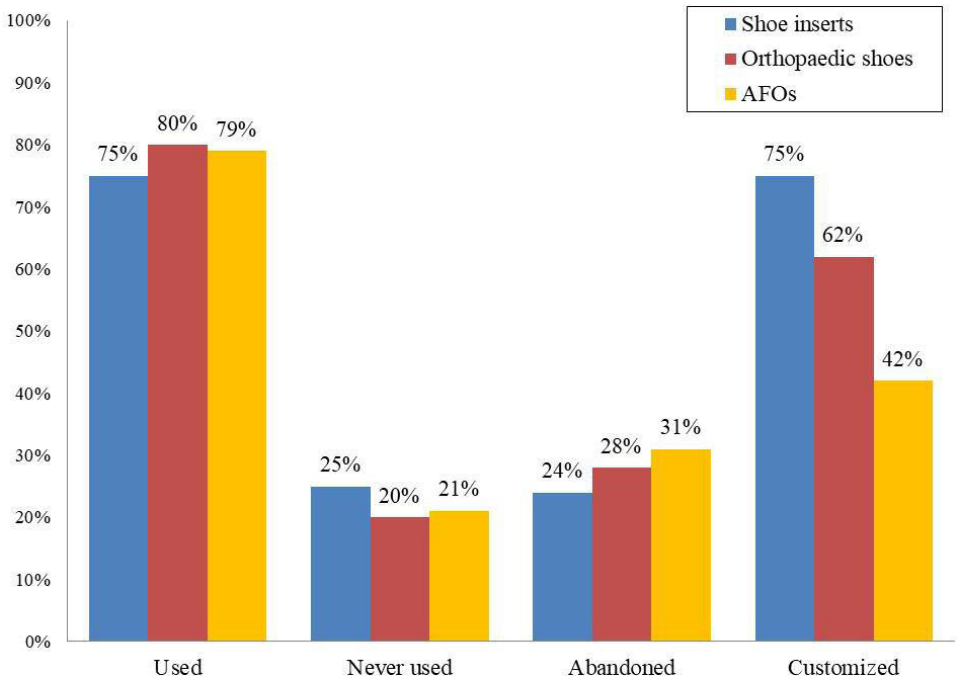

Figure 2 Frequency of use and non-use of orthotic aids after prescription and frequency of their abandonment and customisation. AFOs, ankle-foot orthoses.

Frequency of orthotic use varied across the most frequent CMT types: 49% (59/120) in CMT1A, 62% (13/21) in CMTX1, 38% (5/13) in CMT2I/J, 50% (9/18) in CMT1B and 43% (3/7) in CMT2A.

Patients who were prescribed AFOs, as compared with those who were not prescribed any orthoses, were older, had longer disease duration, higher overall disease severity and foot weakness; they also reported more frequently depression, physical and general fatigue (see online supplemental table 2).

Complications were reported by 59% of patients and were more frequently related to AFOs (69%) as compared with shoe inserts (47%) and orthopaedic shoes (59%). AFO users complained mostly of skin reddening (52%) and moderate-to-severe pain (41%), while calluses were a more frequent issue for both shoe inserts (36%) and orthopaedic shoe (36%) users. Seventeen per cent of orthopaedic shoe users, 13% of AFO carriers and 9% of those wearing shoe inserts reported foot ulcerations (figure 3). Notably, frequency of complications differed among AFOs and was higher in H-AFOs as compared with L-AFOs (73% vs 57%). More specifically, Codivilla spring users were those more liable to develop calluses (41%), while skin reddening, and moderate-to-severe pain were less frequently related to Dyna-ankle (25% for both complaints). Remarkably, Peromed users quite frequently reported foot ulcerations (25%). Overall, complications accounted for 37%–42% of orthosis abandonment. In detail, foot ulcerations were responsible for 16% of abandonments, skin reddening for 32%, foot calluses for 21%, and moderate-to-severe pain for 37%.

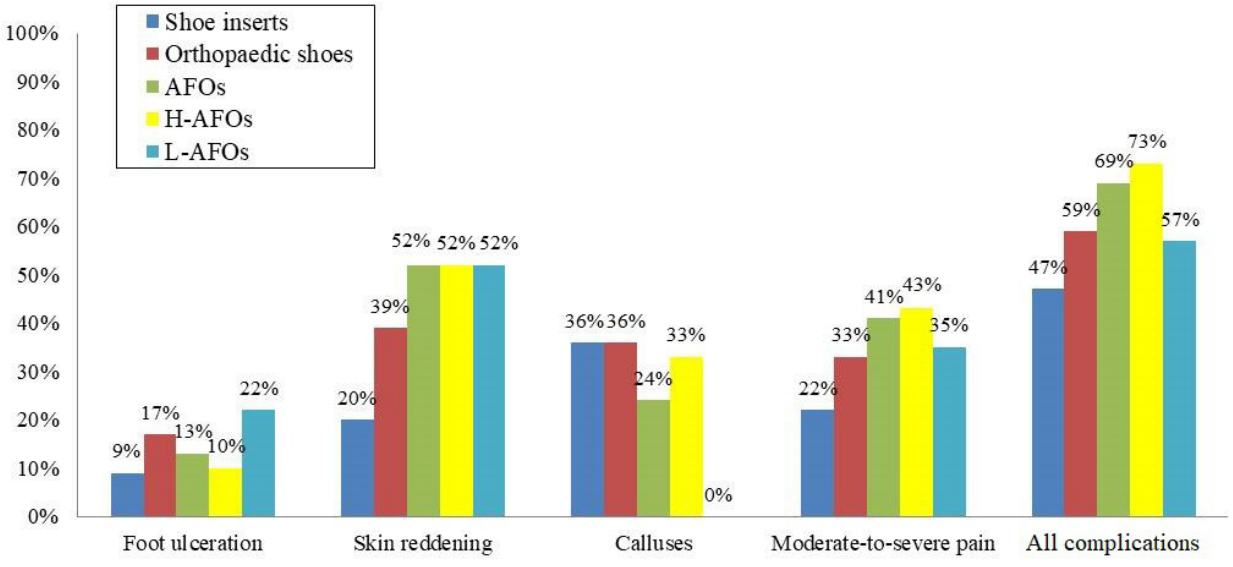

Figure 3 Complications of orthotic devices. AFOs, ankle-foot orthoses; H, high; L, low.

Table 2 Emotional distress, tolerability and perceived benefit of orthoses and walking aids and correlations with disease severity, foot strength, neuropsychiatric status and fatigue

	Emotional distress*	Tolerability*	Perceived benefit*
Overall	3.7±3.6 (0–10)	6.6±3.2 (0–10)	6.6±3.3 (0–10)
Shoe inserts	**2.5±3.2 (0–10)**†	**7.1±3.1 (0–10)**‡	6.6±3.2 (0–10)
Orthopaedic shoes	**3.7±3.5 (0–10)**§	**6.8±3.1 (0–10)**¶	6.7±3.4 (0–10)
AFOs	**5.5±3.5 (0–10)**† §	**5.9±3.2 (0–10)**‡ ¶	6.3±3.3 (0–10)
A) CMTES≤8	5.4±3–6 (0–10)	**4.5±3.2 (0–10)****	**5.1±3.3 (0–10)**††
A) CMTES>8	5.6±3.4 (0–10)	**6.6±2.9 (0–10)****	**6.9±3.2 (0–10)**††
B) MRC df≥4-	5.1±3.7 (0–10)	**5.0±3.2 (0–10)**‡‡	**5.0±3.4 (0–10)**§§
B) MRC df≤3	5.7±3.4 (0–10)	**6.3±3.1 (0–10)**‡‡	**6.9±3.1 (0–10)**§§
C) P-AFOs and MRC pf≥4-	5.9±2.9 (0–10)	**5.6±2.9 (0–10)**¶¶	**5.9±3.2 (0–10)*****
C) P-AFOs and MRC pf≤3	5.0±3.7 (0–10)	**7.3±3.2 (0–10)**¶¶	**7.5±2.9 (0–10)*****
D) HADS-Anxiety<11	4.7±3.7 (0–10)	6.1±3.4 (0–10)	6.7±3.4 (0–10)
D) HADS-Anxiety≥11	6.2±3.5 (0–10)	7.1±2.4 (0–10)	7.6±2.5 (0–10)
B) HADS-Depression<11	4.9±3.7 (0–10)	5.0±3.7 (0–10)	6.8±3.3 (0–10)
B) HADS-Depression≥11	8.0±1.4 (7-10)	6.6±1.7 (5-9)	7.2±2.8 (4-10)
C) HADS-Total score<22	5.0±3.7 (0–10)	6.2±3.3 (0–10)	6.7±3.3 (0–10)
C) HADS-Total score≥22	5.8±3.6 (0–10)	7.2±1.8 (5-10)	8.0±2.2 (4-10)
D) MFIS-Total score≤38	4.3±3.5 (0–10)	6.1±3.4 (0–10)	6.7±3.2 (0–10)
D) MFIS-Total score>38	5.8±3.7 (0–10)	6.6±2.9 (0–10)	7.1±3.3 (0–10)
Walking aids	4.3±3.5 (0–10)	/	/

Significant p values are in bold. P values were calculated using the Mann-Whitney U Test.
*Mean ± standard deviation (range).
†p<0.001.
‡p=0.003.
§p<0.001.
¶p=0.045.
**p=0.002.
††p=0.005.
‡‡p=0.038.
§§p=0.007.
¶¶p=0.004.
***p=0.026.
AFOs, ankle-foot orthoses; CMTES, CMT examination score; df, foot dorsiflexion; E-AFOs, elastic AFOs; HADS, Hospital Anxiety and Depression Scale; MRC, Medical Research Council Scale for Muscle Strength; P-AFOs, plastic AFOs; pf, foot plantar flexion.

Patients' compliance was relatively low, with 35% and 70% of orthotics being used less than half of the time outdoors and indoors, respectively. Remarkably, only 47% of patients used their AFO more than half of the time outdoors.

Regarding the VAS scores (table 2), overall orthotic users rated the emotional distress 3.7±3.6, tolerability 6.6±3.2 and perceived benefit 6.6±3.3. Women showed greater emotional distress as compared with men (4.4±3.7 vs 2.9±3.3, p<0.001), while no gender differences were found for either tolerability or perceived benefit. AFO users showed greater emotional distress and reduced tolerability as compared with both shoe inserts (p<0.001) and orthopaedic shoe (p=0.003 and p=0.045, respectively) users. However, perceived benefit did not differ across the three groups. Among AFOs, Toe-off had not only the best tolerability (6.4±2.3) and benefit (6.9±2.8) but also the greatest perceived emotional distress (6.1±3.3), while Peromed was the most balanced one (5.9±3.4; 6.3±3.3; 4.7±3.3, respectively). Emotional distress was a reason for 17% of abandonment of orthoses.

Concerning AFOs, as compared with patients with mild disease (CMTES ≤8), those with moderate-to-severe CMT (CMTES>8) had a higher tolerability (6.6±2.9 vs 4.5±3.2, p=0.002), perceived benefit (6.9±3.2 vs 5.1±3.3, p=0.005) and higher compliance (62% vs 17%, p<0.001, for use ≥half of time outdoors) to the adopted device. Interestingly, distal weakness influenced AFO acceptance, as users with moderate-to-severe (MRC ≤3) weakness on foot dorsiflexion reported overall higher tolerability and perceived benefit (6.3±3.1 vs 5.0±3.2, p=0.038; 6.9±3.1 vs 5.0±3.4, p=0.007) than those with mild or no weakness (MRC ≥4-). Notably, moderate-to-severe weakness of foot plantarflexion (MRC ≤3 vs MRC ≥4-) was related to higher tolerability (7.3±3.2 vs 5.6±2.9, p=0.004), perceived benefit (7.5±2.9 vs 5.9±3.2, p=0.026) and compliance (68% vs 38%, p=0.012, for use ≥half of time outdoors) in those using P-AFOs, but not E-AFOs (table 2).

We found no correlation of BMI, abnormal HADS-A ≥11, HADS-D ≥11, general distress (HADS-T ≥22 and general fatigue (MFIS >38) (table 2) with perceived benefit, tolerability, and emotional distress.

Overall, there was a significant direct correlation between the degree of tolerability (rs=0.37, p=0.003) and perceived benefit (rs=0.27, p=0.035) and the duration of AFO employment.

Customisation was required for 60% of the prescribed orthotics, ranging from 42% for AFOs to 75% for shoe inserts, and was prompt in 85% of cases and delayed in 15%. Importantly, customisation was related to higher compliance, since those who personalised their orthotics were more prone to use it outdoors as compared with those who did not (75% vs 52%, p=0.001). Moreover, delayed customisation was associated to lower tolerability (5.7±2.2 vs 7.3±2.0, p=0.006) and perceived benefit (6.2±1.9 vs 7.2±2.1, p=0.031), and to higher

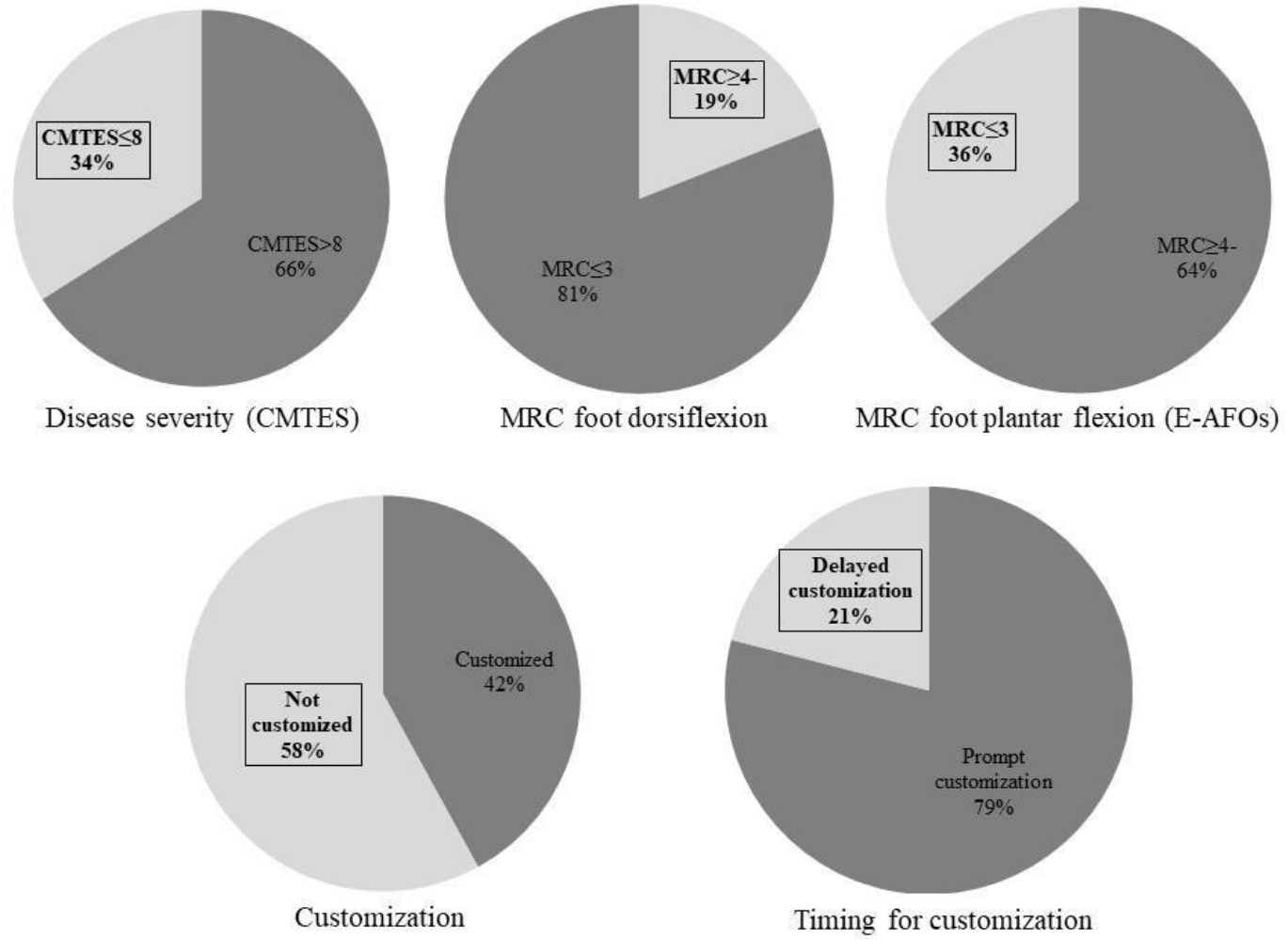

Figure 4 Data on potentially inappropriate or inadequate AFO prescriptions in our cohort with respect to the determinant factors in AFOs' tolerability. E-AFOs, Elastic AFOs. AFOs, ankle-foot orthoses; CMTES, CMT examination score; MRC, Medical Research Council Scale for Muscle Strength.

emotional distress (5.5±2.1 vs 3.2±1.7, p=0.004) with respect to quick personalisation.

Patients were asked a good reason to use and not to use AFOs: improvement in gait (32 pts.), in stability/balance (22 pts.) and reduction in falls (11 pts.) and in steppage (seven pts.) were the most appreciated aspects, while discomfort/pain (15 pts.), emotional distress (eight pts.) and size (three pts.) the most criticised. Interestingly, two patients complained about difficulty in using AFO because of moderate hand weakness.

We then explored the degree of satisfaction with the currently used assistive AFO and the related services experienced in 46 CMT patients through the QUEST questionnaire (scores between 0, worst score and 5, best score). There was a relatively high satisfaction with device safety (3.6±1.1), longevity (3.5±1.0) and weight (3.8±1.2). Safety, easiness and effectiveness were deemed as the three most important features by patients (60%, 50% and 43%, respectively). Conversely, the quality of the professional services (information, attention, answering questions or concerns) (2.8±1.3) and follow-up services (3.0±1.3) were the items with the lowest degree of satisfaction.

DISCUSSION

In this study, we extensively explored the use of orthoses, and, in particular, of AFOs, in a large cohort of well-characterised CMT patients, focusing on patients' direct experience concerning benefit, tolerance, disadvantages and complications of the prescribed device. Furthermore, our study allowed investigating correlations with disease severity, clinical characteristics, general distress, fatigue and body weight, to assess factors affecting the use and tolerability of orthoses.

We found that 56% of CMT subjects used the prescribed lower limb orthoses, with 39% of patients wearing shoe inserts and 23% carrying AFOs, which is in keeping with what reported by Pisciotta *et al* from the Italian registry.[2] In contrast, both Prada and colleagues[4] and Blouin and coauthors[5] found more frequent use for both shoe inserts (55% and 47%, respectively) and AFOs (30% and 46%, respectively). In our series, patients answered on a voluntary basis to several questionnaires, so they were not biased towards the use of orthotics, as may happen for a population specifically investigated for orthotic devices as in the case of the study by Blouin *et al*[5] or where patients lacking information about use of insoles or orthoses were excluded as for the series by Prada *et al*.[4] We were not able to retrieve any data from the literature to compare with the rate of almost 20% of orthopaedic shoe users among our patients.

Patients' compliance was relatively low as 22% of the prescribed devices were never used, 35% were carried for less than half of time outdoors and 27% were abandoned. Although abandonment was more frequent among men, emotional distress was higher in women; the latter finding is in keeping with the

observation by Vinci and colleagues[9] that women showed scanty compliance with orthoses due to poor aesthetics. We found that complications were a main issue, as they were reported for 47%–69% of orthotic devices and were responsible for 37%–42% of orthosis abandonment overall. H-AFOs were associated with a higher frequency of complications, especially foot calluses (33% vs 0%), as compared with L-AFOs. Indeed, almost all H-AFOs are P-AFOs (Codivilla spring, Toe-off) as well, thus providing plantar support, which may be responsible for plantar microtraumatisms whenever the foot does not fit properly to the AFO. Conversely, foot ulcerations were more frequent in L-AFOs, which might reflect the complete (Foot-up) or partial (Peromed) lack of plantar protection with these orthoses.

The occurrence of more frequent complications may partially account for AFO users to report higher emotional distress and lower tolerability, perceived benefit and compliance as compared with both shoe inserts and orthopaedic shoes carriers.

However, some other factors were determinant for AFOs' tolerability in CMT patients.

First, we found that subjects with moderate-to-severe burden of disease (CMTES >8) had a higher tolerability, perceived benefit and compliance for the prescribed AFO as compared with patients with mild CMT (CMTES ≤8). This result supports the findings of Ramdharry and colleagues[20] as severity of presentation seemed to determine patients' compliance to the prescribed AFO. Indeed, as explained by the authors, the more the disease burden increases, the more the balance between perceived benefits and drawback of using AFOs tips towards AFO use.

Second, AFOs overall were better borne by patients with MRC ≤3 on foot dorsiflexion as compared with those with milder or no weakness (MRC ≥4-). Similarly, more severe weakness on plantarflexion (MRC ≤3) predicted a better tolerability of P-AFOs, but not of E-AFOs. Indeed, P-AFOs, despite assisting foot plantarflexion (besides dorsiflexion), bind the foot and, thus, may be poorly tolerated by patients with spared gastrocnemius strength in the last phase of stance of gait.[21] Hence, it follows that (1) AFO prescription is not appropriate in patients without significant distal weakness, (2) P-AFO is recommended in subjects with moderate-to-severe impairment of foot dorsiflexion and plantarflexion while (3) E-AFO is more appropriate in those with preserved or partially spared plantarflexion strength.

Third, we highlight that patients who customised the prescribed AFO were more prone to use it as compared with those who did not. The timing of the customisation was crucial as well, since prompt personalisation was associated to higher tolerability and perceived benefit and to lower emotional distress as compared with a delayed one. Interestingly, Bean and colleagues[22] have previously shown the potential benefit of customisation as a custom-made AFO was effective in reducing perceived exertion, cardiac stress and oxygen consumption in a CMT patient.

We did not find a correlation between abnormal anxiety, depression, general distress and fatigue with emotional distress, tolerability and perceived benefit of AFOs. Hence, these were not determinant factors in AFOs' tolerability in our cohort.

Remarkably, in the present series, we found a high rate of potentially inappropriate or inadequate prescriptions, which leads to waste of resources as well as to reduced compliance and lack of benefit for patients. Indeed, 34% of AFOs were prescribed to patients with mild CMT (CMTES ≤8) and 19% to patients with relatively mild or no weakness at all in foot dorsiflexion (MRC ≥4-); 36% of Elastic-AFOs was prescribed to patients with moderate-to-severe plantarflexion weakness (MRC ≤3); 58% of AFOs was not personalised and 21% of AFOs customisation was not prompt (figure 4). Moreover, patients frequently were rather dissatisfied of the professional services (received information and attention) and of follow-up and monitoring services, as highlighted through the QUEST.

We acknowledge some limitations of our study. First, information about orthoses was self-reported by patients rather than physicians. However, the questionnaire included pictures illustrating the different orthotic devices, thus minimising the risk of inaccuracies (see online supplemental figure 1). Second, we did not encompass paediatric patients in our study as the Italian CMT Registry includes mainly adults.

In conclusion, although improving performance and walking economy, AFOs are associated with frequent complications and considerable physical and psychological discomfort. Therefore, the appropriateness of their prescription in CMT should be justified accordingly on a case-by-case base, to optimise the cost–benefit ratio. We suggest a patient-oriented, multidisciplinary approach focusing on the different aspects of the disease. Biomechanical and kinesiological analysis of gait when possible, proper assessment of degree and pattern of distal weakness and presence of tendon retraction and severe foot deformities, which may modify the tibio-tarsal joint angle, should be evaluated. Patient's needs, attitudes (work, hobbies, habits) and expectations should be always considered. Furthermore, clinicians should advise a prompt customisation of the orthoses, and a periodic reassessment aimed at evaluating whether the device is still appropriate for the current disease stage, or whether disease progression or occurring events (ie, foot surgery) have modified the situation. Indeed, we recommend a step-by-step approach, namely, not to prescribe the patient more than she/he needs (less is more!). Eventually, as revealed by the analysis of QUEST answers, in accordance with previous observations by Zuccarino *et al*,[11] it is crucial that the physician places the patient at the centre of the orthosis prescription pathway, dedicating time to listening and addressing questions or concerns. We believe that rational approaches to orthoses prescription, together with improvement in AFO's material and novel customisation techniques including 3D printing,[23 24] will significantly improve tolerability and benefit and minimise discomfort and emotional distress.

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