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Neuropathy and Integrated Thermal Rehabilitation: a Retrospective Observational Pilot Study on Pain and Functional Outcomes

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Abstract: Neuropathic pain is a highly disabling condition and current management remains chal-lenging; rehabilitation-based strategies, including thermal medicine and balneology, may support symptom control and functional recovery in peripheral neuropathy. This retrospective observational pilot study evaluated changes in pain intensity and functional independence in 20 patients with peripheral neuropathy undergoing a 2-week Integrated Thermal Care (ITC) program (12 sessions) combining crenotherapy and inhalation treat-ments, hydrokinesitherapy, an ozonated vascular walk, mature bentonite-based mud ap-plications, and manual treatment of Key Myofascial Trigger Points; the clinical evolution of the patients was monitored by observing the data of the Numeric Rating Scale (NRS) and the Barthel Index (BI) obtained from their medical records compiled before (T0) and after (T1) the execution of the treatments. At the end of the ITC program it was observed that pain intensity significantly decreased after treatment (mean NRS 7.05 to 3.35; $p < 0.001$) and functional independence significantly improved (mean BI change +12.2 points; $p < 0.001$). These purely preliminary findings suggest that observed neuropathic patients undergoing ITC showed reduced pain and improved ADL performance after completing the protocol; however, prospective controlled studies with larger samples, longer follow-up, and neuropathy-specific outcome measures are necessary to confirm the supposed ef-ficacy of ITC and clarify its mechanisms.

Keywords: peripheral nervous system diseases; pain; thermal medicine; key trigger point; rehabilitation; physical therapy; balneotherapy; mineral waters; manual therapy.

1. Introduction

Neuropathic pain is one of the most disabling pain conditions and represents a major unmet medical need in modern sedentary societies; it is estimated to affect approximately 7–10% of adults in the general population, with many patients receiving inadequate and incomplete treatment [1]. Neuropathic pain is diagnosed when pain of the appropriate character is accompanied by further features such as hypoesthesia/anesthesia, allodynia, or hyperalgesia [2], and it may arise from a wide range of conditions, including painful neuropathies (diabetic or non-diabetic), nerve injuries (often attributable to surgery or trauma), herpes zoster, herniated discs, multiple sclerosis, spinal cord injury, head injury, or stroke [3]. As first-line pharmacological treatment options, tricyclic antidepressants, serotonin–norepinephrine reuptake inhibitors, and gabapentinoids are recommended [4].

In recent years, the number of clinical trials addressing neuropathic pain has increased, alongside improved WHO-endorsed definitions and classifications and

more user-friendly screening and assessment questionnaires. Nevertheless, management remains challenging even with drugs based on novel active ingredients, highlighting the need for innovative therapeutic strategies. In clinical practice, conservative treatment requires realistic goals, such as a pain reduction of at least 30% and improvements in pain-related functions, as suggested by the German Neurological Society [5]. Beyond pharmacological management, rehabilitation-based strategies may contribute to symptom control and functional recovery in patients with neuropathic pain [6].

Within this framework, thermal medicine represents a multimodal intervention exploiting mineral water chemical composition with physical properties (e.g., temperature, osmolarity, and pH), potentially influencing pain modulation and musculoskeletal function through chemical and neurophysiological pathways. Thermal mineral waters are characterized by chemical features (e.g., fixed residue at 180°C, sulfide content) and physical properties (e.g., source temperature, osmolarity, radioactivity, and pH), and their effects have been investigated in clinical and experimental settings [7–9]. In particular, bicarbonate–sulfate–alkaline waters containing bromine and iodine are also used at the study site and have been reported to exhibit spasmolytic properties relevant to gastrointestinal disorders [10], which are consistent also with central and peripheral sedative or relaxant effects directly and indirectly associated to Bicarbonate [11], Bromine [12] and Iodine [13].

Therefore, from a clinical perspective, an Integrated Thermal Care (ITC) program may be of interest also in peripheral neuropathy, since it integrates complementary components, including aquatic rehabilitation, which may facilitate movement through buoyancy and reduced mechanical load and improve exercise tolerance in patients limited by pain and functional impairment [14,15]. Thermal medicine pathways may also include adjunctive procedures (e.g., hydropinic and inhalation treatments and peloid applications), which have been investigated in other painful and inflammatory conditions and may contribute to symptom modulation through anti-inflammatory and/or neuromodulatory effects [16–18]. However, both the magnitude and specificity of these effects remain debated, as improvements may reflect a combination of thermal/physical mechanisms, contextual factors, and heterogeneous protocols, while controlled evaluations are methodologically challenging (e.g., blinding and credible sham interventions) [6,19].

Therefore, to begin addressing this research gap, we conducted a pilot retrospective observational study to assess changes in pain intensity (NRS) and functional independence (Barthel Index) in patients with peripheral neuropathy undergoing an ITC program combining hydropinic and inhalation administration of bicarbonate–sulfate–alkaline-earth mineral water, local application of bentonite clay mud, an ozonated vascular walking path, hydrokinesytherapy sessions, and manual somatic stimulation of Key Myofascial Trigger Points (KMTrPs). The primary aim of the study is to preliminarily verify whether patients undergoing and completing the ITC protocol performed at the data collection institution show improvement in pain and ADL limitations associated with their condition. In particular, this observational evaluation also explored protocol feasibility (tolerability and potential clinical benefit) as a foundation for future experimental research, informed by evidence supporting individual balneotherapy components in other clinical settings [20,21].

2. Materials and Methods

2.1. Study Design

This research is a pilot retrospective observational study carried out at the "Castelnuovo della Daunia Thermal Medicine Center" (Castelnuovo della Daunia, Italy), affiliated with the Italian National Health System and with the rehabilitation

department of the Local Health Authority of Foggia (Italy). The observation was carried-out in cooperation with the staff of the "Center for Physiotherapy, Rehabilitation and Re-Education – (Ce.Fi.R.R.)" (Chieti, Italy). Patients were consecutively enrolled between March 2025 and July 2025. The research project was conducted according to the technical-procedural and ethical standards of the certification of suitability for the implementation of observational studies (certificate no. IT15/0304) issued to the "Ce.Fi.R.R." institution by the Italian National Accreditation Body ACCREDIA, in accordance with the UNI EN ISO 9001:2015 regulation; this certifies the application of good management, clinical and research practices at the institution that collaborated in the collection and processing of data with the main physical location of the study.

All therapeutic procedures complied with national safety regulations. The ITC protocol was offered to patients who did not present specific contraindications at the baseline medical evaluation routinely required for all subjects accessing the study facility. The study was conducted in accordance with the Declaration of Helsinki and Good Clinical Practice guidelines, and written informed consent was obtained in advance at enrolment from participants who were willing and able, including express consent for the potential future use of clinical data for observational research. In line with the evaluation and operational routine applied at the study site, the observed data correspond to those recorded in the medical charts compiled by medical doctors responsible for baseline and follow-up evaluations of patients accessing the center. The national regulatory framework seem to not adequately define competence regarding the ethical approval of retrospective, non-pharmacological observational studies [41]; therefore, given the express competence in the observational field of the territorial ethics committees recognized by national legislation exclusively for the evaluation of clinical investigations on medical devices and observational pharmacological studies, the study design presented was considered exempted from standard ethics committee approval. Furthermore, the privacy of patients, including that of their data previously collected in the medical records, was guaranteed throughout the observation process by anonymizing personal and sensitive data and considering only clinical data relevant to the study, assigning an anonymous numerical identity to each patient during the analysis and writing of the paper.

The thermal medicine center where the study was conducted is characterized by the use of bicarbonate–sulfate–alkaline mineral water containing bromide and iodide, employed both for immersion-based treatments and for direct administration procedures, including inhalation therapy, hydropinic intake (crenotherapy), and the preparation of mud applications (peloids) matured in the same mineral water [10].

2.2. Patients Selection

Patients who presented to the Castelnuovo della Daunia Thermal Medicine Center during the observation reference period with a documented diagnosis of peripheral neuropathy, previously established by non-center physicians, were consecutively considered.

Neuropathy etiologies were heterogeneous (acquired or hereditary) and included:

- diabetes and vitamin deficiencies (particularly vitamins B12, B1, and B6);
- autoimmune diseases (e.g., lupus, rheumatoid arthritis);
- toxic etiologies (alcohol, lead, or drug-related causes, particularly chemotherapy);
- trauma or compression syndromes (e.g., carpal tunnel syndrome).

Patients with contraindications to thermal treatments identified at baseline clinical evaluation were not eligible for the ITC protocol in routine practice and were therefore not included in the present analysis.

In particular, exclusion criteria, as expressed in the informed consent submitted to all patients at the study site, included heart or kidney failure, severe hypertension,

severe thrombophlebitis, acute phases of rheumatic diseases, immunodeficiency, open wounds, psychiatric disorders, severely limited ability to walk, and active infections.

2.3. Assessment Methods

Patients were clinically assessed before the beginning of the ITC treatment cycle (T0) and at the end of the cycle (T1). Clinical data were extracted from medical records routinely compiled by the center's medical doctors, including specialists in Physical and Rehabilitation Medicine and Rheumatology, who performed baseline and follow-up evaluations. The recorded data were routine elements of the clinical evaluation procedure performed at the study site and were retrospectively extracted from medical records for analysis.

Outcome measures included:

- Numeric Rating Scale (NRS): an 11-point scale (0–10) used to assess pain intensity at the time of evaluation, where 0 represents no pain and 10 represents the worst pain imaginable. In the present study, patients were asked to indicate the intensity of their neuropathic pain on the 0–10 scale during the clinical assessment at T0 and T1. It is a widely recommended tool in the general assessment of pain, including neuropathic pain [42].
- Barthel Index (BI): a measure of functional independence in activities of daily living (ADL) based on 10 weighted items, yielding a total score from 0 (total dependence) to 100 (total independence), with supervision classified as a form of dependence. BI was recorded at T0 and T1 as part of routine functional evaluation. This tool is often used to assess the functional independence of patients suffering from neuropathic pain [43].

2.4. Treatment Protocol

The ITC protocol applied at the study site consists of a standardized integrated thermal medicine pathway prescribed after specialist medical evaluation and indication. The protocol includes the approaches described following, which were administered consecutively in the same order as below.

2.4.1 Functional Assessment of KMTrPs

The functional assessment to identify key trigger points applied the so-called Bio-Physico-Metric approach [44]; the identification of KMTrPs was based on a standardized palpation sequence aimed at detecting palpable muscular nodules, together with the assessment of postural asymmetries and alterations in the physiological joint range of motion. This evaluation was performed on the following muscular districts: pectoralis major, rectus abdominis, rectus femoris, adductor magnus, tibialis anterior, adductor hallucis, quadratus plantae, and abductor digiti minimi. The assessment was also extended to the splenius cervicis, upper and lower trapezius, paraspinal longissimus dorsi, quadratus lumborum, gluteus maximus, gastrocnemius, soleus, and hamstrings. On average, approximately three KMTrPs were identified at each session, which were then targeted during the manual treatment component of each subsequently performed therapeutic approach. This brief assessment phase, requiring no more then 5 minutes, preceded the application of the following actual treatments in each session and for each patient.

2.4.2 Manual Treatment of KMTrPs

The manual treatment of key trigger points was delivered concurrently with the inhalation sessions, mud applications, and hydrokinesitherapy (daily, 12 sessions). Based on the baseline KMTrPs assessment, the therapist focused on the muscles identified as clinically relevant for each patient. The manual component consisted of sustained digital pressure (approximately 30 seconds per KMTrP), combined with soft-tissue massage and joint mobilization techniques, and was repeated across sessions according to the individualized trigger point pattern.

2.4.3 Hydropinic Treatment

The application of crenotherapy, locally defined as hudropinic treatment, consisted of the oral intake of locally sourced mineral water from underground springs who irrigate the balneological center where patients have been treated. Each participant was prescribed an individualized daily volume of thermal mineral water ranging from 0.5 to 1.2 liters, based on the routine initial medical evaluation at the study site. The water was consumed by patients freely during the subsquently described phases of each treatment day, under staff supervision, and patients were instructed to maintain adequate hydration and to report any eventual gastrointestinal discomfort or intolerance symptoms during the program.

2.4.4 Thermal Water Inhalation Protocol

Thermal water inhalation consists of the administration of a humidified steam jet via a nozzle situated 50 cm from the patient. The thermal water was aerosolized at a constant pressure of 1.5 atmospheres and maintained at a temperature range of 37°C–38°C for a 20-minute duration. For the initial 10 minutes, a therapist—positioned behind the seated participant—conducted manual stimulation of pre-identified KMTrPs and accessory respiratory muscles, including the diaphragm, pectoralis minor, levator scapulae, and the region corresponding to the stellate ganglion.

2.4.5 Clay Mud Applications

Mature bentonite-based clay mud applications were delivered daily over 12 sessions during the 2-week ITC program. The mud, matured in thermal mineral water, was applied locally on the spine, on all major joints (ankles, knees, hips, wrists, elbows, and shoulders), and on the KMTrPs identified during the baseline assessment of each session, with the patient positioned comfortably on a treatment bed. Each mud application lasted approximately 15 minutes. At the end of the exposure period, the mud was removed by showering with thermal water in a bathtub for around 15 minutes, followed by a short post-treatment rest, defined as "reaction phase", lasting approximately 20 minutes in a thermoneutral environment, according to routine thermal medicine practice and patient tolerance.

2.4.6 Ozonated Vascular Circuit

The ozonated vascular circuit consists of supervised ambulation between two thermal pools maintained at contrasting temperatures (24°C and 38°C) to facilitate venous and lymphatic stimulation in the lower extremities. During each 15-minute session, performed daily during the 12 sessions of the 2-week ITC program, patients alternated between pools at one-minute intervals. Both reservoirs utilized ozonated water jets (4–6 atm) to provide a continuous proprioceptive stimulus. Concurrently, patients were instructed to perform upper limb flexion exercises, reaching their maximum pain-free range of motion in coordination with their gait, to ensure systemic stimulation of both upper and lower limbs. The circuit is based on standard contrast therapy [45] associated to an institution-exclusive administration of ozonated water jets with hydromassage and proprioceptive stimulation purposes.

2.4.7 Hydrokinesitherapy

Water-based treatment sessions were conducted daily for 12 60-minutes sessions in a warm thermal water pool (32.5°C) and followed a standardized progressive program. Each session started with water adaptation and relaxation, followed by global passive static stretching, mainly targeting tonic muscle groups (e.g., pectoral, iliopsoas, spinal extensors, rectus femoris, adductors, triceps surae). The motor component included buoyancy-assisted exercises and controlled floating tasks with respiratory coordination, postural position changes (e.g., seated-to-supine and supine-to-seated transitions), and gait re-education in shallow water (e.g., step pattern and heel-

to-toe walking), taking advantage of reduced weight-bearing and hydrostatic support. The protocol further incorporated fully-active and active-assisted joint mobilization, proprioceptive exercises with underwater tilting boards and global active stretching, with therapist guidance as needed.

2.5. Data Analysis

Statistical analysis was performed through the Statistics Kingdom online calculator (www.statskingdom.com). Since violations of the normality assumption of the datasets have been detected, according to the Shapiro-Wilk test, for both the T1 NRS and T1 Barthel Index, the data were analyzed considering them as not normally distributed. Therefore, the statistical analysis of the pre-post variations of the observed values was carried out for each group through the Wilcoxon signed-rank test for dependent samples. Given the non-parametric analysis adopted, overall data of the study cohort at T0 and T1 were reported both in terms of mean ± standard deviation (S.D.) and in terms of median and interquartile range (IQR). A $p < 0.05$ was used to denote statistical significance. The effect size (r), Z score (Z), and average percentage variation (Δ%) were also calculated. Moreover, to further investigate the available data, a secondary quantitative analysis of the values of the individual Barthel Index items reported at T0 and T1 was conducted. It is important to specify that, given the pilot and exploratory nature of the study, the analysis was conducted for the sole purpose of observing the strength of the variations found in the observed subjects, without direct generalization in the absence of a sufficiently large sample.

3. Results

The cohort consisted of 20 patients with peripheral neuropathy assessed at two time points, including an equal number of women (n = 10; 50%) and men (n = 10; 50%). The following table shows the demographic distribution of the patients considered for the observations of this study (Table 1).

Table 1. Demographic distribution of the cohort.

Variable	Categories	Frequencies	%
Gender	Men	10	50.0
	Women	10	50.0
Age (years)	31-45	1	5.0
	46-60	3	15.0
	61+	16	80.0
T0 NRS Score	0	0	0
	1-3	0	0
	4-6	5	25.0
	7-10	15	75.0
T0 Barthel Index Score	0-20	0	0.0
	21-60	0	0.0
	61-90	16	80.0
	91-99	4	20.0
	100	0	0

Musculoskeletal and neurological comorbidities were observed in the cohort (n = 20). Specifically, polyarthrosis was reported in 12 patients (60%), low back problems requiring "lumbar stabilization" in 7 (35%), shoulder disorders in 4 (20%), knee disorders in 3 (15%), and neurological conditions in 3 (15%). Comorbidities were not mutually exclusive.

At the end of the treatment protocol (T1), a significant reduction in the NRS score was observed, with patients' pain intensity decreasing from T0 to T1, corresponding to an overall reduction of 52.5%. The Barthel Index increased from T0 to T1, corresponding to an overall increase of 14.7% (Table 2). The extremely low significance values detected for both variables ($p < 0.001$), remain substantially below the conservative significance threshold of 0.025 determined by the Bonferroni correction for two variables, minimizing the probability of a Type 1 error, as well as that of Type 2 error (Table 2). Furthermore, robust effect sizes were detected for both outcomes ($r > 0.8$), indicating a substantial and clinically relevant improvement in patients' pain (NRS) and functional autonomy (Barthel Index) within the observed cohort (Table 2). However, given the limited volume of available data, caution is warranted when evaluating the statistical robustness of the observed correlations, which serve a strictly exploratory purpose.

Table 2. Changes in pain intensity and functional independence (T0 vs T1).

Outcome	Time	(mean± SD)	Median	IQR	*p*	r	Z	Δ%
NRS (0-10)	T0	7.05±2.2	7.0	1.7	< 0.001	-0.89	-3.96	-52.5%
	T1	3.35±1.2	3.0	2.0				
Barthel Index (0-100)	T0	82.9±7.7	83.0	14.0	< 0.001	0.87	3.91	14.7%
	T1	95.1±4.4	96.0	8.0				

Quantitative granular analysis of BI items highlighted that improvements were mainly observed in mobility- and transfer-related domains (e.g., stair climbing, walking, and bed–chair transfers), whereas several basic ADL items showed little or no variation between T0 and T1. In particular, feeding and continence items presented baseline values already close to the maximum score, resulting in limited room for further improvement and suggesting a ceiling effect (Table 3).

Table 3. Barthel Index item-level changes

Barthel item	T0 (mean± SD)	T1 (mean± SD)	Δ (T1–T0)	Improved n/N%
Stair climbing	5.80 ± 2.19	8.90 ± 1.02	+3.10	17/20 (85%)
Transfers (bed–chair)	11.45 ± 2.31	14.25 ± 1.33	+2.80	16/20 (80%)
Dressing	7.50 ± 1.85	9.15 ± 1.35	+1.65	12/20 (60%)
Feeding	4.95 ± 0.22	5.00 ± 0.00	+0.05	1/20 (5%)
Bowel continence	4.90 ± 0.31	4.95 ± 0.22	+0.05	1/20 (5%)
Urinary continence	4.95 ± 0.22	4.95 ± 0.22	0.0	0/20 (0%)

No drop-outs were recorded during the study and all patients considered for observation completed the treatment protocol with the expected timing and modality, without reporting any adverse effects during the sessions or in the period immediately following them.

4. Discussion

In this retrospective observational pilot study, it was observed that the observed cohort of neuropathic patients undergoing the application of an Integrated Thermal Care (ITC) protocol in an aquatic thermal environment showed clinically meaningful improvements in two core outcomes relevant to peripheral neuropathy, namely pain intensity and functional independence. Specifically, a marked reduction in NRS scores and a concomitant increase in Barthel Index values were observed from baseline to post-treatment: consequently, it cannot be excluded that the ITC protocol may

have played a role in supporting both symptom control and ADLs performance in the observed patients; however, due to the retrospective nature of the study and the relatively limited amount of data, also in the presence of multiple confounding factors, it is not possible to establish direct causal links between exposure to the treatments and the clinical improvements obtained in the observed cohort, although the relationship appears plausible based on the current evidence in the field and might deserve more in-depth studies in the future.

A more specific interpretation of functional change emerges from the item-level Barthel analysis. Improvements were predominantly observed in domains related to mobility and transfers, which represent key determinants of autonomy in patients with peripheral neuropathy and are commonly compromised by pain, weakness, and impaired sensorimotor control [22,23]. Conversely, several basic ADL items (e.g., feeding and continence) exhibited minimal to no variation, plausibly due to a ceiling effect, with baseline scores already close to the maximum. This pattern is consistent with a reduced sensitivity of the scale to detect further gains when baseline function is preserved, and it supports the interpretation that the greatest measurable benefits of ITC in this cohort were concentrated in mobility-related tasks [24,25]. Since this is a retrospective study with consecutive recruitment, it is possible that the intrinsic characteristics of the patients considered may have determined the misalignment of the Barthel items, in which a regression to the mean cannot be excluded and which should be further investigated through future, possibly randomized and controlled, studies. Furthermore, the regular repetition of the treatment may have induced a practice effect of generalized improvement in motor skills which, however, does not automatically translate into a transfer to ADLs, which according to the literature appear to be more sensitive to home-based treatments than to exercise protocols or other forms of indirect treatments [26]. Therefore, even the results obtained in the single-item analysis of the Barthel Index should be interpreted with extreme caution and considered only as an insight for possible future studies on the proposed approach in the field of neuropathies.

From a pathophysiological standpoint, peripheral neuropathy is frequently characterized by a multifactorial interplay of mechanical, metabolic, and inflammatory contributors that can converge into persistent pain and functional limitation. In this context, an integrated approach such as ITC may be theoretically advantageous because it combines interventions that target different dimensions of disability. Thermal medicine can be conceptualized as a multimodal treatment that merges the physical effects of water-based rehabilitation with potential biological effects derived from mineral-water exposure and adjunctive mud therapy. Prior literature has described beneficial effects of balneotherapy/crenotherapy and related thermal interventions across various painful and inflammatory disorders, including reductions in symptom burden and functional limitation, although indications and protocols remain heterogeneous [9,18,27]. Proposed mechanisms—still not fully elucidated—include modulation of inflammatory mediators (e.g., cytokine- and TNF-related pathways), antioxidant activity, and local effects potentially mediated by skin contact and inhalation/ingestion routes [16]. While direct mechanicistic evidence in neuropathic populations is limited, these pathways provide a biologically plausible framework to interpret the observed reduction in pain intensity in the present cohort.

Thermal medicine may act as a multimodal intervention, combining the physical properties of water-based therapy with the potential biological effects of mineral water composition and adjunctive mud therapy. Previous literature has reported anti-inflammatory and symptom-modulating effects of balneotherapy, crenotherapy, and related thermal treatments across different conditions, including inflammatory and painful disorders [28]. In the present study, the observed improvement in pain and ADL performance may reflect the combined effect of thermal-water-based rehabilitation (including hydrokinesitherapy), adjunctive mud applications, and manual approaches targeting KMTrPs [20,29].

Within the ITC pathway, the potential contribution of peloid therapy warrants consideration. Bentonite-based thermal muds have been described as possessing adsorptive and mineral-releasing properties, with hypothesized local effects when applied to painful areas; however, such mechanisms remain largely inferential and require further clinical validation specifically in neuropathic conditions [17,18,30]. In parallel, the inclusion of manual somatic approaches targeting KMTrPs may complement thermal rehabilitation by addressing secondary musculoskeletal contributors to pain and movement limitation. Considering that patients with peripheral neuropathy may develop maladaptive movement patterns, deconditioning, and segmental overload, a combined program integrating graded exercise, manual therapy, and thermal exposure could support functional recovery through improved movement tolerance and symptom modulation. A further interpretative rationale is the bidirectional interaction between somatic and visceral/autonomic pathways and their role in pain processing and functional limitation, which may offer a theoretical framework for multimodal interventions that concurrently act on somatic and autonomic components of symptom expression [31]. Nonetheless, it is important to emphasize that mechanistic inferences cannot be confirmed by the present study design, therefore, the therapeutic mechanisms described so far can only be reported as plausible but not as directly causative of the observed results, which require more in-depth analyses and more pathway-based investigations in future studies on the subject.

4.1. Study Limitations

Several limitations should be acknowledged. First, the retrospective observational nature of the study, the single-center setting, and the relatively small cohort size limit external validity and preclude strong causal inference. Second, the absence of a control group prevents disentangling treatment effects from nonspecific factors (e.g., regression to the mean, contextual effects, and changes in concomitant care). In particular, since the study venue deals exclusively with balneological treatments, it was not possible to collect data from untreated patients, patients undergoing sham treatment, or patients undergoing therapy other than balneological therapy, for ethical reasons related to the inappropriateness of denying patients access to the requested balneological treatments, in the absence of health conditions expressly falling within the routinely established exclusion criteria. Third, the outcome set was intentionally concise (NRS and Barthel Index) and limited to rapid and non-invasive assessment tools already present in the medical records routinely used for patient monitoring at the practice site, therefore, no disease-specific neuropathic pain questionnaires, quantitative sensory testing, or performance-based mobility measures were collected; consequently, the clinical interpretation should be restricted to pain intensity and ADL function, without extending conclusions to domains not directly assessed (e.g., balance, gait quality, or quality of life) [6]. Finally, although the item-level quantitative analysis suggested a ceiling effect in some Barthel domains, additional instruments with greater responsiveness in mildly impaired patients may be preferable in future studies [22,23,25].

4.2. Implications for Physical and Rehabilitation Medicine

Currently, physical rehabilitation for peripheral neuropathies stands at a critical juncture, bridging the promising frontiers of neuroplasticity and personalized medicine, yet severely constrained by operational gaps, especially in terms of standardized and effective clinical protocols, limiting the translation of evidence-based interventions into widespread clinical practice [32]. In particular, the rehabilitation of peripheral neuropathies might require a synergistic and multimodal approach: while pharmacological therapy and physical means act initially on the neuromodulation of pain and on muscle trophism, therapeutic exercise and orthoses consolidate their effects over time, promoting sensorimotor recovery, functional adaptation and the re-

duction of disability [32]. An intricate clinical overlap and diagnostic mimicry between movement disorders and peripheral neuropathies has been highlighted, emphasizing that a meticulous, integrated management of motor impairment is paramount to prevent diagnostic errors and optimize functional recovery in patients presenting with concurrent central and peripheral nervous system pathology [33]. In this sense, balneotherapy, thanks to its vascularizing, hormone balancing, and physical stimulation properties, could be an interesting therapeutic approach in the rehabilitation field for peripheral neuropathies [34], although increasingly robust and numerous studies are needed to verify whether current protocols, such as the one proposed in this paper, are effective on a large scale and, if so, for which subclasses of neuropathy [34].

4.3. Future Prospects

Despite the limitations, the present pilot observation preliminarly supports the feasibility and, at least, a potential clinical role of an integrated thermal rehabilitation pathway in peripheral neuropathy. However, given the thoughtful limitations, it is important that future studies, which are necessary to confirm these purely preliminary results, prioritize prospective controlled designs with larger, better-characterized cohorts, longer follow-up, and broader outcome batteries, including validated neuropathic pain instruments and performance-based functional tests. Furthermore, mechanistic endpoints (e.g., inflammatory biomarkers and objective measures of neuromuscular function) may help clarify which components of the ITC program drive clinical change and whether benefits persist beyond the treatment window [19,20,35]. In fact, although the study results are encouraging, they do not allow for a thorough investigation of the speculatively hypothesized therapeutic mechanisms, limiting the generalizability and causal inference of the observed clinical evolution of monitored patients. However, the study also demonstrated a certain degree of safety and good short-term compliance, given the absence of reports of adverse reactions to treatment or drop-outs, laying the foundation for new and more in-depth studies on the topic. These studies should not only consider a prospective, randomized, controlled setting, but also more specific and thorough assessment tools, such as the Douleur Neuropathique 4 or Leeds Assessment of Neuropathic Symptoms and Signs scales, as well as the application of electrodiagnostic testing that considers both nerve conduction studies and needle EMG recordings of electrical activity within muscles. In fact, the evaluation of peripheral neuropathies should always ideally include an instrumental electrophysiological evaluation combined with a clinical evaluation based on the use of validated scales [36]. Moreover, the same specific scales could be used in combination, since tools such as the Douleur Neuropathique 4, the Leeds Assessment of Neuropathic Symptoms and Signs scale, and the Neuropathic Pain Symptom Inventory seem to offer different levels of sensitivity and specificity depending on the sub-classes of neuropathies and populations to which they are administered [37-39], possibly making a multimodal test more reliable. These pathology-specific methods could also be considered to be paired with more symptom-specific and sensor-based assessments, in particular with regard to gait and balance motor outcomes that are often relevant in the rehabilitation of peripheral neuropathies [40], on a par with assessments of autonomy of daily activities such as the Barthel Index included in the present study.

5. Conclusions

According to the results of this retrospective observational pilot study, conceived as a preliminary evaluation of the feasibility and potential benefits of the proposed protocol, the application of Integrated Thermal Care (ITC) treatments in patients with peripheral neuropathy seems to be associated with a significant reduction in pain intensity (NRS) and an improvement in functional independence (Barthel Index). Given the non-invasive nature of the intervention, its practical deliverability

within a thermal medicine setting, and its potential to be implemented on relatively large patient populations within a short treatment window, further studies are warranted to confirm and better quantify its therapeutic value and generalizability in peripheral neuropathy.

However, the present findings should be interpreted in light of the many study limitations, including the small cohort size, the retrospective observational design, and the lack of randomization and a control group, which preclude causal inference and markedly reduce the generalizability of the observed results. Future prospective controlled trials with larger samples, longer follow-up, and additional disease-specific and performance-based outcomes are needed to validate these preliminary results and to clarify the clinical role of integrated thermal rehabilitation in the management of peripheral neuropathy.

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Institutional Review Board Statement: ethical board review and approval were waived for this retrospective observational study, since the therapeutic methods observed fall among the non-pharmacological approaches and the analysis was based on routinely collected clinical data recorded as part of standard care and anonymized prior to analysis, and no additional procedures were performed for research purposes. In particular, the exemption from the ethical review board approval was considered due to the express competence in the observational field of the territorial ethics committees recognized by national legislation exclusively for the evaluation of clinical investigations on medical devices and observational pharmacological studies. The study was conducted in accordance with the Declaration of Helsinki and Good Clinical Practice standards.

Informed Consent Statement: Informed consent was obtained in advance from all subjects involved in the study, collecting explicit authorization for any use of their clinical data and any graphic-visual material, provided that it was made anonymous and respectful of their privacy. The research project falls within the scope of certification for the implementation of good practices in the management of clinical procedures and observational studies (certificate no. IT15/0304) issued to the "Ce.Fi.R.R." institution by the Italian National Accreditation Body ACCREDIA, in accordance with UNI EN ISO 9001:2015.

Data Availability Statement: The data presented in this study are available from the corresponding author upon reasonable request due to privacy restrictions.

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